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EDITORIAL

COVID-19 Healthcare Management in Sabah

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Recent Development of COVID-19 Cases in Malaysia

The first case of COVID-19 in Malaysia was detected on 24 January 2020.[1] As of 10 September 2020, when this editorial article is written, the total cases have increased to 9,628 cases, with active cases of 333 are being isolated and undergoing treatment, while 9,167 cases achieved recovery.[2] The number of deaths in Malaysia due to COVID-19 is 128 people. Within the past few months, there has been increased in the number of clusters of infection in some states including Sabah. The number of cases in Sabah is currently at 592 cases.

Following the increase in the import of COVID-19 cases into the country, the Ministry of Health of Malaysia has developed a risk assessment matrix on countries in the world to measure the risk of importing COVID-19 infection into Malaysia. This is important in deciding the implementation of the Movement Control Order [Perintah Kawal Pergerakan (PKP)] and international border control. Each country is assessed based on the above criteria and placed within a specific risk category. The results of the assessment on all 23 countries that have been restricted to travel to Malaysia are found to have a high risk of bringing in COVID-19 infection into our country. Criteria for assessing the risk of importing COVID-19 infection are based on the Scoring Board: Merit System developed by MOH using data sources from the European Centre for Disease

Prevention and Control (ECDC) and Our World in Data. The six criteria used are the number of COVID-19 cases in the last 14 days, the incident rate per 1 million population in the last 14 days, recent death rates in the last 14 days per 1 million population, cumulative case mortality rate, recovery index and COVID-19 cumulative cases exceed 150,000 cases. However, this risk assessment is one of the mechanisms to assess a country's COVID-19 risks.

The Recovery Movement Control Order (Recovery MCO), which was originally scheduled to end on 31 August, has been extended to 31 December 2020. This was a necessary move to continue to curb the spread of the COVID-19 by reducing the risk of infection through social awareness and individual responsibilities.

Management of COVID-19 by Sabah State Healthcare Providers

The state of Sabah healthcare providers including doctors and nurses as frontliners handling COVID-19 cases can be tricky. It is a new disease that none of the physicians has seen. The challenge for physicians is to recognise the presentations, diagnostic tests as managing the disease and its complications. The symptoms are broad and range from one spectrum to the other. The patients could be asymptomatic but still can spread the disease. In January, when it first alerted an outbreak in Wuhan, China, it was thought that the main presentation involved respiratory systems such as cough, runny nose and shortness of breath. However, as the disease is more widespread to other parts of the world, we learnt that this presentation might be different especially among children and the elder population. It was later by a UK physician that anosmia is also a symptom of the disease. Whereas studies in Spain and Italy have shown children presented with a purpuric-like rash that was not seen or documented at an earlier stage of the disease when it was reported. In terms of complications, in the course of the pandemic in later March and early April 2020, that the disease is associated with pulmonary embolism and in rare cases can be presented with stroke. A coordinated and comprehensive response in a pandemic requires a public health system.

Management of Personal Protective Equipment (PPE) Shortages and Management of Test Kits

As the disease comes to a pandemic stage where it hits the whole part of the world, personal protective equipment (PPE) supply becomes an issue when each country was seeking for this item that makes it hard-to-get. However, from the joint effort of NGOs, corporations together with Sabah State administration and other key players, the Sabah State Health Department managed to find their connections in many possible ways to connect with people with PPE factories inside and outside the country to supply PPE materials. The Sabah State Health Department also connected with prisons officers to help to sew the PPE.

Likewise, reagents and lab materials were at short in global supply. Thus, again the Sabah State Health Department reached the NGOs and corporations, with all help, managed to secure some of the supplies. The constant help from all parties in securing the PPE and lab materials was real-life evidence that nothing is impossible to achieve if we work together. To safely deliver these PPE and lab materials, the Sabah State Health Department was helped by the Royal Malaysian Air Force to transport these materials twice weekly by aircraft. To send those materials to Sabah requires tremendous and tedious coordination that was carried well by the logistic teams. In terms of logistics, the Sabah Health team has done very tremendously albeit the restriction order limited the people movement. This affects the movement of our COVID-19 samples that need to reach Kota Kinabalu, the state capital from the East Coast of Sabah. Thus, Sabah State

Health Department managed to ensemble the transportation team that will drive 8 hours daily to Lahad Datu with few pit stops along the way to send PPE to the Sabah East Coast districts as well fetch the COVID-19 samples from those districts to bring and run in Kota Kinabalu Public Health Laboratory.

COVID-19 Crisis Preparedness and Response Centre (CPRC)

Since 12th of March where the first case of COVID-19 in Sabah was detected, Sabah State Health Department CPRC COVID-19 team have worked tirelessly days and nights. Mainly become the technical advisor, liaison officers, risk communicator, Protocol and Standard Operation Procedure (SOP) development as well as coordinating the needs of the districts in terms of human resources and others. Daily CPRC led by the State Health Director, Datuk Christina Rundi would host reporting and sharing of confirmed and suspected cases from the districts, the meeting might last from 2 – 6 hours of discussions. Through this meeting, any issues that need urgent attention are discussed as well as coordinating resources to its maximum capacity. The daily meeting is important as districts shared their experience with others as well as be informed of any issues. CPRC also will report the cases to the Ministry of Health daily. During this meeting too, any new instructions, SOPs or protocols will be shared and discussed. This is to ensure that all instruction will be conveyed to the ground level.

COVID-19 Personal Preventive Measures

Since there is no safe and effective medicine against COVID-19, the WHO has developed a strict guideline to adhere to during the pandemic. Standard precautions are especially important to set out and adhere to curb the spread of SARS-CoV-2 worldwide. Preventive measures such as regular handwashing with soap or sanitizer, avoiding handshaking, wearing masks and gloves, social distancing of 1 – 2 metres apart, coughing into disposable tissues or a flexed elbow, self-isolating if symptomatic, avoidance of gatherings and unnecessary travel to affected areas can suppress the spread of viral infection.

Sabah State Protecting Its Borders

The Sabah State Government has issued restriction on in-bound travellers via air, land, or sea with a history of travelling to mainland China. Through a state document dated 7 February 2020, all foreigners and non-Sabahans with history of travelling to mainland China within 14 days prior entry to Sabah, including transit passengers from mainland China are prohibited from entering Sabah effective from 8 February 2020. Sabahans, permanent residents or residents of Sabah under work pass, student pass, long-term social visit pass or any exemption order, returning from mainland China would be subjected to compulsory 14-day home quarantine. Chinese nationals who were in the state at the time of issuance of order were advised to depart before the expiry of their visa. On 29 February 2020, travel restrictions on arrivals from South Korea were imposed and later 10 March 2020, immigration restriction included Iran and Italy.

Mass Students Movement Incident

On the 26 April 2020, the Minister of Higher Education issued a statement to allow students who were stranded on campus due to the movement control order to be sent home to their respective hometowns. The movement was to commence on the following day, involving travels via air flight and land. For Sabah alone, an estimated 11,000 students were involved in this mass movement inter-states and intra-state. The flights started from 30 April through 4 June 2020. All the students outbound to Peninsular, Sarawak and Labuan were performed PCR. The approval for departure only after a negative result was obtained. Students bound from Peninsular, Sarawak and Labuan are expected

to have their COVID-19 testing done before arrival, otherwise, they will be sampled upon arrival and be quarantined until negative results obtained.

Public information by Sabah State Health Department

The Director of Sabah State Health Department, Datuk Dr Christina Rundi issued a daily press statement on the status of COVID-19 in Sabah with statements include a description of cases, specific advice for people in Sabah on protection against infection, as well as introduced special commemorative dates on health celebrated either nationally or internationally.

Strategic Control by Sabah Disaster Management Committee, State and District Level

Sabah Disaster Management Committee Command Centre started daily meeting since 10 March 2020, with the Malaysian Civil Defence Force as secretariat and technical input from Sabah State Health Department, National Security Council, Malaysian Royal Police Force, Malaysian Royal Army Force, Fire Brigades, Welfare Department, RELA Voluntary Department and Information Department. The committee discusses operational issues on the state level, while individual districts run groundwork with committee mirroring the state set up.

Conclusion

Overall, the work accomplished has been tremendous and praised by many parties both locally and international recognition. The works may be seemingly smooth sailing but there are many challenges faced and continued to be faced daily, as one of the hindrances would be the lack of communication between decision-makers and technical members of the committee before any state regulation are made and released. Unless there is an effort to combine the strength of each team member, the optimum cost benefits or cost-utility will not be attained.

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ORIGINAL ARTICLE

Factors Associated with Brain Multiple Sclerosis Lesions Detected by Magnetic Resonance Imaging

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ABSTRACT

Multiple sclerosis (MS) is a demyelinating disease that mainly impacts the central nervous system (CNS) and spinal cord. Several factors may affect the risk of MS lesions. Hence, this study was carried out to determine factors associated with brain MS lesions detected by Magnetic Resonance Imaging (MRI). A prospective cross-sectional survey was carried out in this study. An unenhanced T1, T2, Fluid Attenuated Inversion Recovery (FLAIR) with axial, sagittal, and coronal sections were performed. The respondents who had exposed to radiotherapy or chemotherapy had previous brain pathology or surgery, and brain congenital anomalies were excluded from this survey. A *P*-value of < 0.05 was considered significant. A total of 71 subjects underwent MRI and included in the statistical analysis. The mean age of the subjects was 31.5 ± 11.5 years, with predominance for females (59.2%) among this study population. Moreover, the findings reported that the family history of MS was highly significantly associated with MS (*P* = 0.001). Besides, there was no significant association found between gender (*P* = 0.682), smoking (*P* = 0.272), alcohol intake (*P* = 0.986), hypertension (*P* = 0.792), diabetes mellitus (DM) (*P* = 0.198), and body mass index (BMI) (*P* = 0.650). From this study, the family history of MS is found to develop the risk of MS.

INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune demyelinating, inflammatory, and neurodegenerative disease of the central nervous system (CNS)[1]. A histopathological study carried out in 1838 by Carswell, in which

the underlying pathological mechanism of MS lesions was described[2]. Then, in 1868, Charcot has named the disease as "la sclerose en plaques" and confirmed an association between the histopathological and clinical aspects of MS lesions[3]. Besides, Charcot has also described the MS disease as "plaques" and focal demyelination lesion, gliosis, inflammation, and various degrees of axonal loss as well as distribution and the histopathological manifestation of these plaques in the CNS. The diagnosis of MS is based on evidence of the dissemination of white matter lesions[4]. In the early stages of the MS, evidence of plaques, demyelination, and inflammation are abundant, while in the later stages, neuronal loss and axonal damage are predominant[3]. This characterization of the MS lesions is still valid as a gold reference nowadays.

In 2010, McDonald criteria for MS indicated that dissemination in space (DIS) could be observed on T2 at least one lesion in 2 out of 4 locations characteristics for MS (juxtacortical, periventricular, infratentorial, and spinal cord). In the same context, dissemination in time can be noted at least on one new T2 and/or contrast-enhancing lesion on follow-up MRI. Furthermore, the simultaneous presence of asymptomatic contrast and non-contrast enhancing lesions could be at any time[5].

There are several environmental and genetic factors associated with MS progression[6]. Evidence is increasing with environmental factors, including vitamin D deficiency, smoking, altered lipid metabolism, and Epstein-Barr virus are related to the development of MS[7 – 15]. MRI usually reveals several lesions in many individuals at the clinical onset of MS[16].

A recent study showed that there are other risk factors, including underlying comorbidities associated with the progression of MS[17]. Patients who have more than one cardiovascular (CV) risk factors such as hyperlipidaemia, hypertension, and heart disease are more likely to increase the risk of MS[18]. A histopathological mechanism of CV disease associated with the progression of MS is resulting in hyperplasia of brain white matter and hypotrophy of grey matter, leading to damaging the myelin sheath[19 – 21]. Moreover, several previous studies reported a positive association between smoking and dyslipidaemia with MS lesions[12, 15, 22, 23].

MS lesions cannot be diagnosed by a single test, including MRI. However, MRI is a more accurate and sensitive tool for diagnosis of MS than other diagnostic modalities such as biochemical tests[4]. This study was designed to determine factors associated with brain MS lesions detected by MRI.

MATERIALS AND METHODS

A prospective cross-sectional survey was carried out over two months from March 2019 to May 2019. All subjects who have clinical symptoms of MS lesions underwent MR imaging and were eligible for this study. A total of 71 subjects were selected based on a systematic random sampling method. Inclusion criteria included age ranging from 16 years and above, Iraqis (no other races/ethnicities), both genders, and subjects who could complete their questionnaire. The study was conducted in four provinces in the middle and south of Iraq, including Baghdad, Diyala, Babil, and Al-Najaf. Firstly, the respondents were informed verbally about the nature and aims of the study. Secondly, all respondents were given an informed consent form before the information was taken. A structured self-administered questionnaire was used as an instrument to collect information from the respondents. The subjects with an age range from 16 years and above, Iraqis, the respondents who had exposed to radiotherapy or chemotherapy, had previous brain pathology or surgery, and brain congenital anomalies were excluded from this survey. Ethical approval was obtained from

the scientific committee in the Radiological Techniques Department, College of Health and Medical Technology, Middle Technical University, Baghdad.

After the weight and height of the respondents have been measured, Body Mass Index (BMI) was calculated. BMI is weight in kilogram (kg) divided by metre square (m^2). It was classified according to World Health Organization guidelines for the Asia-Pacific region[24]. BMI of less than 18.5 kg/m^2 was classified as underweight, 18.5 – 24.9 kg/m^2 were classified as normal, ≥ 25.0 – 29.9 kg/m^2 were classified as overweight, and 30.0 kg/m^2 and above were classified as obese. A respondent was considered having hypertensive if he/ she has been taking antihypertensive medication(s), if he/ she has a self-reported history of hypertension, or if he/ she had systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg[25].

Conventional MRI (SEIMENS and PHILIPS with 3 Tesla) with an 8-channel head and neck coil have been used for diagnosis MS lesions. Sagittal, axial, and coronal sections have been taken for each case. T1-weighted, T2-weighted, Fluid Attenuated Inversion Recovery (FLAIR) sequences have been imaged. A contrast agent has not been given to the patients because it is not available in the imaging screening centres while the study was conducting. MRI diagnosis was blinded to the respondent's physical and neurological pathology.

Data Analysis

Data analysis was performed using Statistical Package for Social Science (SPSS) program version 22.0. First, descriptive analysis was carried out to calculate the percentages of each factor among our study population. A Chi-square test was performed to determine the association between categorical variables. Then, an independent samples *t*-test was used to compare a mean between two groups with normally distributed data. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

The distribution of the study population is shown in Table 1. The mean age of the subject was 31.5 ± 11.5 years. Females were predominant (59.2%) in the study population. A higher percentage was reported for non-hypertensive subjects (56.3%) than hypertensive subjects (43.7%). Likewise, a percentage of non-diabetic subjects was higher (64.8%) than diabetic subjects (35.2%). Moreover, the normal BMI subjects had the highest percentage (40.8%), whereas underweight subjects had the lowest (9.9%). Besides, 35.2% of the subjects tend to be overweight, whereas only 14.1% of the subjects were obese. Out of 71 subjects, there were 24 subjects (33.8%) were reported to have MS lesions.

Table 1 Characteristics of the study population (*n* = 71)

Variables	*n* (%)	Mean ±SD
Age	–	31.5 ± 11.5
Gender		
Male	29 (40.8)	
Female	42 (59.2)	
Smoking		
Yes	27 (38.0)	
No	44 (62.0)	
Alcohol consumed		
Yes	3 (4.2)	
No	68 (95.8)	
Hypertension		
Yes	31 (43.7)	
No	40 (56.3)	
DM		
Yes	25 (35.2)	
No	46 (64.8)	
BMI categories		
Underweight	7 (9.9)	
Normal	29 (40.8)	
Overweight	25 (35.2)	
Obese	10 (14.1)	
Family history of MS		
Yes	15 (21.1)	
No	56 (78.9)	
MS		
Yes	24 (33.8)	
No	47 (66.2)	

n = Sample size

According to an independent samples *t*-test, our results revealed that differences of mean age between subjects with and without MS were not found to be significant ($P = 0.877$) (Table 2). Furthermore, A Chi-square test showed that the prevalence of MS between males and females was close to each other (31.0 % and 35.7%, respectively). This indicates that gender was not significantly associated with MS ($P = 0.682$). Regarding smoking and alcohol intake, this study showed an association between smoking and alcohol intake with MS was not found to be significant ($P = 0.272$ and $P = 0.986$, respectively). According to the medical history of the disease, the study findings confirmed that hypertension and diabetes mellitus (DM) were also not significantly associated with MS ($P = 0.792$ and $P = 0.198$, respectively). Nevertheless, the prevalence of MS was significantly higher among subjects who had a family history of MS than those without ($P = 0.001$). In terms of BMI, although half of the MS patients were obese, an association between MS and BMI was not noted to be significant ($P = 0.650$).

Table 2 Factors associated with MS lesions

Variables	MS findings		*p*-value
	Yes	No	
Age	31.8 ± 11.9	31.4 ±11.4	0.877
Gender			0.682
Male	9 (31.0)	20 (69.0)	
Female	15 (35.7)	27 (46.3)	
Smoking			0.272
Yes	7 (25.9)	17 (38.6)	
No	20 (74.1)	27 (61.4)	
Alcohol consumed			0.986
Yes	1 (33.3)	2 (66.7)	
No	23 (33.8)	45 (66.2)	
Hypertension			0.792
Yes	11 (35.5)	20 (64.5)	
No	13 (32.5)	27 (67.5)	
DM			0.198
Yes	6 (24.0)	19 (76.0)	
No	18 (39.1)	28 (60.9)	
Family history of MS			0.001*
Yes	13 (86.7)	2 (13.3)	
No	11 (19.6)	45 (80.4)	
BMI categories			0.650
Underweight	2 (28.6)	5 (71.4)	
Normal	10 (34.5)	19 (65.5)	
Overweight	7 (28.0)	18 (72.0)	
Obese	5 (50.0)	5 (50.0)	

* Significant as $p < 0.05$

DISCUSSION

MS is a complex idiopathic inflammatory disease that mainly affects the myelin sheath of the CNS or spinal cord. It is essential to know that no specific markers to diagnose MS lesions, where it primarily depends on neurological investigation and medical history. Thus, MS lesions attack should be defined precisely and correctly. The neurologists define MS lesions attack as a neurological defect that persists more than one day and can be correlated with an anatomical localization with no evidence of any infection or fever. The neurological defect always evolves from 2 – 4 weeks, and it entirely or partially recovers between 6 and 8 weeks, either spontaneously or with corticosteroid medication[26, 27]. However, patients with presenting an attack, MRI is the most accurate and vital diagnostic modality to confirm the diagnosis, especially with intravenous contrast agent given. This can serve to monitor the characteristics of lesion (demyelinating and inflammatory) as well as distribution and localization of the lesions within CNS[28]. Moreover, on the MR imaging, one anatomical region is presented by monofocal attack or more than one anatomical CNS region concurrently, such seen by multifocal attacks[26, 27].

In terms of sociodemographic factors such as age and gender, the previous studies stated that female gender and individuals

over 11 years old are more likely to have MS[29]. Besides, 2–10% of all patients with MS lesions have clinical onset before 18 years of age[30]. Simpson et al. demonstrated that females were predominant in the most prevalent studies[31]. Otherwise and surprisingly, we did not find an association between age and gender with MS lesions. The lifestyle and environmental factors, including exposure to smoking, high BMI, and vitamin D deficiency, increase the risk of MS disease, whereas alcohol consumption has potentially reduced the risk of MS[16, 32].

In contrast, Kappus et al. revealed that the prevalence of overweight/obesity among MS subjects did not differ from that in healthy controls[33]. This indicates that the association of overweight/ obesity was not significantly associated with MS lesions. Similarly, the researchers also have identified that smokers or hypertensive subjects are more likely to have MS lesions as compared to their counterparts who are non-smokers or having normal blood pressure. Nevertheless, our study showed that smoking was not significantly associated with MS. Based on BMI status, our findings showed that an association between BMI and MS was not noted to be significant although there is a higher prevalence of MS (50%) was found among obese patients compared to those who were underweight, normal or overweight. Regarding the family history of MS, a study by Montgomery et al. suggested increased the risk of MS in offspring was probably associated with the older father's age[34]. This finding was consistent with findings from our study, where the latter demonstrated that the prevalence of MS lesions in subjects with a family history of the disease itself was significantly higher than in those without a family history of the disease.

Description of MS by MRI is based on the presence of focal lesions in the white matter of CNS. These focal lesions are considered as typical criteria for this disease in terms of distribution, morphology, evolution, and signal changes on MRI sequences (T2-weighted image, T2- FLAIR, pre- and post-contrast T1- weight images)[35]. However, evidence of hypointense lesions on non-enhancing T1-weighted image it is not likely to consider a criterion for detecting MS lesions[36].

The limitation of this study is a small sample size due to a preliminary study to determine factors associated with MS lesions diagnosed by MRI. Hence, we recommended future studies to carry out a cross-sectional-based population study and increased the sample size to determine the overall prevalence of MS among the whole Iraqi population as well as studying other affecting factors. Importantly, a contrast-enhanced T1-weighted image is also highly recommended for future work as an additional sequence to assess and monitor the number and dissemination of MS lesions.

CONCLUSION

The family history of MS lesions is noted to increase the risk of MS lesions. Otherwise, other factors such as age, gender, smoking, alcohol consumed, hypertension, DM, and BMI were not associated with MS lesions.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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ORIGINAL ARTICLE

Knowledge, Attitude and Practice of Blood Donation: A Single-Centred Experience in Sandakan, Sabah

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ABSTRACT

Many factors contribute to the reluctance towards blood donation, but available studies done in Malaysia involving University students does not reflect the knowledge of the public in general. The objective of this study is to determine knowledge, attitude practice towards blood donation among the Sandakan population. A cross-sectional study was employed using an adapted 29-item structured validated questionnaire available in English and Bahasa, consisting of subject's demography, questions regarding knowledge, attitude, and perception of blood donation. Convenient random sampling was done within the hospital compound, 79 healthy adults consented, and their data were used for the final data analysis, yielding an excellent internal consistency (Cronbach's α coefficient = 0.816). Out of all, 74.7% of the respondents had a high level of knowledge, and independent t-tests showed that those who were not married, had tertiary education, donated blood in the past, had a statistically significant higher level of knowledge and 96.2% of respondents have a positive attitude. Some donors (40.6%) donated blood for moral satisfaction, and only a quarter (25%) experienced adverse events. Fear of pain, needle, fainting was the highest reason for reluctance in blood donation (36.2% of non-donors), followed by self-perception of being medically unfit to donate (31.9% of non-donors). Even though the sampled population in Sandakan showed an adequate level of knowledge as well as a positive attitude towards blood donation, blood product shortage is still present. This study may contribute by serving as an educational platform for awareness and education to improve the number of blood donors.

INTRODUCTION

Blood products are always required by hospitals, whether in a rural or urban setting. From the year 2004 to 2014, the number of blood transfusions increased by 52% from 222,807 to 338,598[1, 2]. Blood products are needed continuously in hospitals, with indications such as major surgical procedures, trauma from accidents, and anaemia from various causes, especially thalassaemia[3]. According to the Malaysian Thalassaemia Registry, from 2016 to 2017, there was a 22% increase in transfusion-dependent thalassaemia patients, from 3,657 to 4,463 cases[4, 5]. Sabah state had the most number of registered patients standing at 1,272 and the prevalence continues to increase[6]. In Sabah, α- and β -thalassaemia were confirmed in 33.6% and 12.8% respectively among Kadazandusuns, which makes up 60% of the population of Sabah[7]. Furthermore, screening done at primary health clinics done in 2017 showed that out of 645 samples, up to 28% of the female sample and 41% of the male sample were tested positive for abnormal haemoglobin subtypes[8].

Based on the crossmatch lab registry in Hospital Duchess of Kent, Sandakan, from January to September 2018, an average of 202 packed cells per month was transfused into thalassaemic patients in the local daycare centre, among which 53% of the products require O-positive donors. Furthermore, the demand for blood products throughout the hospital was 8,945, but only 8,377 were supplied within the nine months, with 3,994 of it are blood group O positive, which makes up to 47.6% transfusions consist of blood products from group O donors. Unfortunately, only 45.7% (n = 3,231) of the blood donors are group O from the overall donors (n = 7,076). Hence, the constant supply of blood products are required, and can only be obtained from blood donors[9].

According to the local registry, 80.2% of the blood donors are regular donors, with the remaining 19.2% are first-time or occasional donors, for the year 2018[10]. More new donors need to be recruited and encouraged to donate blood to increase the number of regular donors to be able to meet the demand for blood products. Many factors may encourage new donors to become repeated donors such as appeals on radio, a reminder to donate during the shortage, and incentives[11]. However, many factors contribute to reluctance for blood donation, such as inadequate information to non-donors, fear of the procedure of donating blood, and lack of courage[12]. Available studies were done in Malaysia with samples taken from university students. However, it does not reflect the knowledge of working people as well as those who did not receive tertiary education[13, 14].

This article focuses on the factors causing the public to be reluctant to donate blood, as well as assess the depth of knowledge and attitude of the public for donating blood. It is essential to know the knowledge and understand the expectations of our local population so that strategies to promote blood donation during campaigns can be revised[15] and the issues causing the public to be reluctant in donating blood can be addressed to achieve the goal of retaining blood donors. The objectives of this study were to estimate the proportion of blood donors that have adequate knowledge as well as having a positive attitude towards blood donation and to review the perception of blood donation of the population of Sandakan.

MATERIALS AND METHODS

The cross-sectional study design was employed in this research at Duchess of Kent Hospital between January and March 2019. A 29-item structured pre-tested validated questionnaire adapted from Suzilawati et al.[13] was made available in English and Bahasa Melayu.

The questionnaire consisted of four parts. Part A consisted of questions regarding the subject's demography. Parts B, C, and D consist of 18-items regarding knowledge, 4-items regarding attitude, and 7-items on perception about blood donation, respectively. This study was registered in the National Medical Research Registry (NMRR) of Malaysia under NMRR-18-2926-44329. Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia.

Based on the study conducted by Suzilawati et al., a pilot test was done, yielding an internal consistency Cronbach's alpha of more than 0.7[13]. Using sample size calculator for Cronbach's alpha estimation by W.N. Arifin[16], with Cronbach's alpha of 0.7, and precision of 0.1, two-tailed significance level (α) of 0.05, number of items (*k*) of 29, the drop-out rate of 10%, the sample size calculated to be 86 subjects.

Stratified random sampling was done among adults who are present around several areas, including the hospital cafeteria, grocery store, waiting area for in-patients' relatives and outpatient clinics. Subjects were randomly approached, asked to read the subject information sheet and sign the consent form if they consent to participate.

Data from returned questionnaire was directly entered into SPSS version 21, data management and analysis was done using similar software. Demographic data are presented as descriptive statistics. Independent *t*-test and one-way ANOVA were used to detect any statistical association between demographic factors and knowledge score as well as attitude score, with a *p*-value of less than 0.05 considered as statistically significant.

RESULTS

Demography

Among the 86 participants consented in this study, seven subjects were removed due to incomplete answered questionnaires. Seventy-nine respondents were used for the final data analysis, and an excellent internal consistency was obtained (Cronbach's α coefficient = 0.816). The significant proportion of the participants were from the Malay ethnic (19%), self-employed (19%), and of blood group O (27.8%) (Table 1).

Table 1 Socio-demographic variables of the respondents

***N* = 79**	**Frequency (*n*)**	**Percentage (%)**
Age		
Less than 20	2	2.5
21 – 30 Years old	36	45.6
31 – 40 Years old	29	36.7
41 – 50 Years old	9	11.4
Above 50 years old	3	3.8
Monthly income (RM)		
Below 1,000	17	21.5
1,000 – 1,999	17	21.5
2,000 – 2,999	12	15.2
3,000 – 3,999	10	12.7
4,000 – 4,999	8	10.1
5,000 and above	3	3.8
Refuse to answer	12	15.2
Gender		
Male	33	41.8
Female	46	58.2
Marital status		
Single	23	29.1
Married	54	68.4
Divorced / Widowed	2	2.5
Education level		
Primary school	4	5.1
Secondary school	36	45.6
College / University	39	49.4
Occupation		
Student	10	12.7
Self-employed	15	19.0
Healthcare	7	8.9
Business	6	7.6
Education / Teaching	9	11.4
Engineering	6	7.6
Police / Army / Defence	5	6.3
Not working	11	13.9
Others[†]	10	12.7
Blood group		
A	10	12.7
B	19	24.1
AB	12	15.2
O	22	27.8
Do not know	16	20.3

[†]: Other occupations include janitor, clerk, labourer, cashier and librarian

Knowledge

Almost three-quarters of the participants have a high level of knowledge (74.68%) (Figure 1). Independent *t*-tests showed that those who donated blood in the past had a statistically significant different level of knowledge (p = 0.049) (Table 2), which suggests that subjects who have donated blood have a higher level of knowledge compared to those who have not.

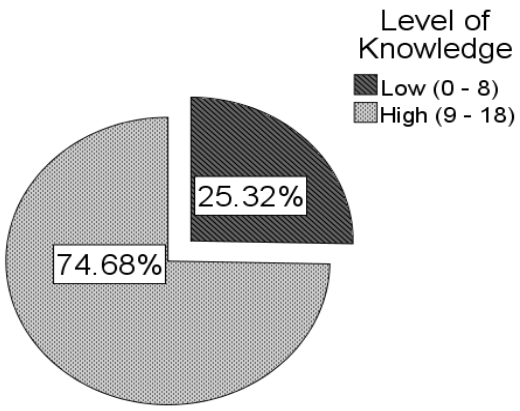

Figure 1 Level of knowledge of participants based on total score

Table 2 Independent *t*-test on demographic factors with knowledge score

Variables	Descriptive			Inferential				
	N	Mean	SD*	Mean difference	95% CI†	*t*	df	*p*-value
Gender								
Male	33	10.55	3.684	−0.281	−2.221, 1.660	−0.288	77	0.774
Female	46	10.83	4.644					
Donation history								
Yes	32	11.84	3.828	1.908	0.006, 3.809	1.997	77	**0.049**
No	47	9.94	4.381					

*: Standard deviation †: Confidence interval

Table 3 One-way ANOVA on knowledge score among participants from different marital status

	N	Mean	SD#	df † (within groups)	*F*	*p*-value	Mean difference (posthoc Tukey HSD)		
							Single	Married	Divorced / Widowed
Single	23	13.00	3.920	76	9.396	< 0.001	–	3.5 **	−4
Married	54	9.50	3.855				−3.5 **	–	−7.5 *
Divorced / Widowed	2	17.00	1.414				4	7.5 *	–
Total	79	10.71	4.246						

#: Standard deviation, †: Degree of freedom | *$p < 0.05$, ** $p < 0.01$

A one-way ANOVA (Analysis of Variance) was conducted to compare marital status to the level of knowledge among those who are single, married, and divorced or widowed. There were statistically significant differences in the level of knowledge among the three groups of participants, F (2, 76) = 9.396, $p < 0.001$ (Table 3).

Post hoc comparisons using the Tukey HSD test indicated that the mean knowledge score among married subjects (M = 9.5, SD = 3.86) were significantly different than those who were single (M = 13.0, SD = 3.92, $p = 0.001$), and those who were divorced or widowed (M = 17.0, SD = 1.41, $p = 0.023$) (Table 3). However, those who were single did not significantly differ from subjects who were divorced or widowed. These results suggest that subjects who are married had a lower level of knowledge about blood donation compared to those who are single or divorced or widowed.

Table 4 One-way ANOVA on knowledge score among participants from different education levels

	N	Mean	SD#	df † (within groups)	*F*	*p*-value	Mean difference (posthoc Tukey HSD)		
							Primary school	Secondary school	College / University
Primary school	4	5.00	3.559	76	18.852	< 0.001	–	-3.83	−8.03 ***
Secondary school	36	8.83	3.558				3.83	–	−4.19 ***
College / University	39	13.03	3.475				8.03 ***	4.19 ***	–
Total	79	10.71	4.246						

#: Standard deviation †: Degree of freedom | *$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

A one-way ANOVA was also conducted to compare education level to the level of knowledge among those who received primary, secondary or tertiary education. There were significant differences in the level of knowledge among the three groups of subjects, F (2, 76) = 18.852, $p < 0.001$. Post hoc comparisons using the Tukey HSD test shows that the mean knowledge score among subjects who received tertiary education (M = 13.0, SD = 3.48) was significantly different than those who only went primary school (M = 5.0, SD = 3.56, $p < 0.001$) or secondary school (M = 8.8, SD = 3.56, $p < 0.001$) (Table 4).

Attitude

Results from 78 respondents showed almost all (94.87%) (Figure 2) of them have a positive attitude towards blood donation. Independent *t*-tests showed no statistical significance between participants' demography and the attitude score (Table 5).

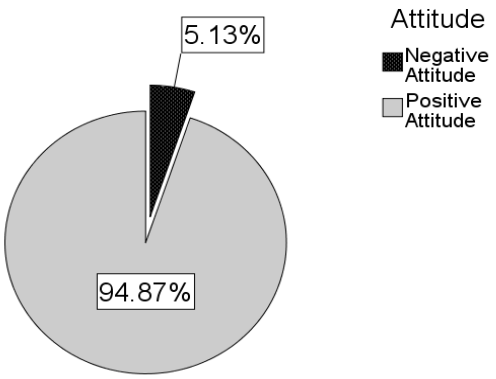

Figure 2 Attitude of participants based on score range

Table 5 Inferential statistics on demographic factors with attitude score

Variables	Descriptive			Independent *t*-test				
	N	**Mean**	**SD***	**Mean difference**	**95% CI†**	***t***	**df**	***p*-value**
Gender								
Male	33	10.88	1.193	0.079	–0.452, 0.609	0.296	76	0.768
Female	45	10.80	1.140					
Donation history								
Yes	32	11.13	1.185	0.495	–0.027, 1.016	1.890	76	0.063
No	46	10.63	1.103					
*: Standard deviation †: Confidence interval								

Most participants agreed that donating blood is voluntary and a noble act. However, only half of them (55.3%) (Table 6) intend to be regular donors.

Table 6 Item and responses on attitude towards blood donation

Items	*n*	Agree (%)	No idea (%)	Disagree (%)
Blood donation is a noble act, one should donate blood	78	92.3	7.7	0
You intend to become a regular blood donor	76	55.3	34.2	10.5
Blood should be collected only from voluntary donors	78	91.0	7.7	1.3
Blood collected during donation is sold to needy people	78	14.1	6.4	79.5

One-way ANOVA was also performed to compare marital status and education level to the attitude score of the subjects but yielded no statistical associations in between variables (Table 7).

Table 7 One-way ANOVA on demographic factors with attitude score

Variables	Descriptive			Inferential					
	N	Mean	SD*		Sum of squares	df †	Mean Square	*F*	*p*-value
Marital Status									
Single	23	10.96	1.261	Between groups	0.660	2	0.330	0.242	0.786
Married	53	10.79	1.133	Within groups	102.174	75	1.362		
Divorced / Widowed	2	10.50	0.707						
Education level									
Primary school	4	11.00	1.414	Between groups	3.459	2	1.729	1.305	0.277
Secondary school	35	10.60	1.117	Within groups	99.374	75	1.325		
College / University	39	11.03	1.158						

*: Standard deviation †: Degree of freedom

Practice

Among 79 participants, there were 32 subjects (40.5%) had history blood donation, with half of them, $n = 17$ (53.12%) were occasional donors, and only 5 (15.6%) of them were regular donors. Most donors, $n = 13$ (40.6%), donated blood for moral satisfaction, and only a quarter, $n = 8$ (25%), experienced adverse events (Table 8). Fear of pain, needle, the sight of blood, fainting was the commonest factor for discouraging blood donation (Table 9).

Table 8 Practice towards blood donation for known donors ($n = 32$)

Question		Frequency	%
How often do you donate?	Regularly at every 3 – 4 months	5	15.6
	1 or 2 times every year	7	21.9
	Occasionally	17	53.1
	Only at times of need	3	9.4
Why do you donate blood?	Moral satisfaction or humanity	13	40.6
	Blood needed for someone you know	3	9.4
	Being in a group of donors	4	12.5
	As an experience	10	31.3
	Others	2	6.3
Have you experienced any adverse effects while donating blood?	No	24	75
	Yes	8	25
If yes, what were the adverse events?	Remarkable pain	2	16.7
	Fainting	2	16.7
	Dizziness	7	58.3
	Marked weakness	1	8.3
	Total responses	12	100.0
How do you regard your experience of adverse effects?	Mild, you will ignore them	24	75
	Moderate	8	25
	Severe, you have hesitation to donate again	0	0
	Serious, you do not want to donate anymore	0	0

Table 9 Factors discouraging non-donors from donating blood (*n* = 47)

	Responses		Percentage of cases
	N	**Percentage**	
Fear of pain, needle, the sight of blood, fainting	17	19.3%	36.2%
Self-perception being medically unfit to donate	15	17.0%	31.9%
Fear of weakness as a result of blood donation	14	15.9%	29.8%
Could not manage time	12	13.6%	25.5%
Fear of other adverse effects	10	11.4%	21.3%
Do not know where, when, and how to donate	9	10.2%	19.1%
Fear of contracting the disease while donating	6	6.8%	12.8%
Nobody has requested me to donate	3	3.4%	6.4%
Parents / guardian do not allow	1	1.1%	2.1%
Others*	1	1.1%	2.1%
Total	88	100.0%	
*Others: Oversupply of subject's specific blood group at the event of donation			

DISCUSSION

Education Level on Blood Donation

The majority of the subjects (74.7%) have an adequate level of knowledge regarding blood donation, lesser than from the previous literature where a similar questionnaire was used. However, the sample population for both studies was different, whereby previous literature were students from a university, including those from nursing programme[13], in which part of their curriculum includes healthcare-related skills and knowledge that may coincide with subjects related to blood donation, as compared to the general population. Multiple studies have shown that those who received tertiary education had a higher level of knowledge on blood donation, due to better literacy level[17, 18, 19]. On the other hand, the education level of a person does not influence the attitude towards blood donation[20] since the will of an individual to donate blood is influenced by the person's behaviour, and the intention to donate depends on the individual's belief[21].

Previous History of Donation

Before blood donations, donors are required to complete a standardized donor questionnaire, to screen the suitability of the donor based on specific selection criteria[22], which may expose donors to specific knowledge and facts regarding blood donation. In Malaysia, the administered questionnaire is obtained from Appendix III of the Transfusion Practice Guidelines for Clinical and Laboratory Personnel by Ministry of Health Malaysia, and it shows that there are some similarities in terms of the content of the questions,[23] which may explain the difference in knowledge score between donors and non-donors. Lownik et al. described that those who have donated in the past were more likely to have a higher knowledge of blood donation than non-donors as donors understood the process of blood donation[24].

In this study, although generally, most subjects have a positive attitude towards blood donation, which is comparable to other developing countries[24], only 37.5% among the donors from this study regularly donate blood every year. Reasons for this occurrence is not being explored, and consequently, it is part of a limitation of this study, as factors causing new or occasional donors to be reluctant in regular donating were not part of the questionnaire. This issue serves as a possible area for future researches to understand the rationale behind donor retention.

Experiencing Adverse Events

In this study, results showed 25% of the participants experienced adverse events, which were comparable to some studies where the range of proportion of adverse events during blood donation can be as low as 0.003% up to 84%[25, 26]. Symptoms of our study subjects experienced were mainly vasovagal. It is essential to take into consideration of donor's experience during the blood donation, as such adverse events and negative experience may cause them to be less willing to donate in the future[27, 28]. Some preventable steps can be taken to prevent such adverse events from taking place to retain donors, such as pre-donation hydration[29].

The unknown time frame between blood donation and participating in the study might result in recall bias. The sample size is also not sufficient. Nevertheless, study results showed those who experienced these adverse events, graded it as moderate, and possibly might donate blood again in the future. This situation implies that non-donors can rest assure that the severity of adverse events is not severe enough to cause a person to hesitate to donate again.

Fear of Blood Donation

The results of the present study showed that fear of needle is the most common factor for non-donors to avoid blood donation, with a proportion of 36.2% of the study subjects, which is comparable to other studies done in Malaysia[30] and other countries[24]. Unusually, the second most prevalent reason for not donating is the self-perception being medically unfit, as well as other reasons such as not knowing where and when to donate, which are modifiable factors that could be prevented through raising awareness, education, and infographics. A study done in China found that self-perception of poor health was a significant barrier to blood donation, and television and the internet were to most effective ways of recruiting donors[31], which may perhaps be a way to clear misconceptions regarding blood donation as well as self-perceived health status to the public.

CONCLUSION

Even though the sampled population in Sandakan showed an adequate level of knowledge as well as a positive attitude towards blood donation, there is still a demand for blood products. This study managed to determine a few modifiable risk factors that can be quickly addressed, and information acquired from this group of participants can serve as an educational platform for awareness campaigns to improve the number of blood donors.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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ORIGINAL ARTICLE

Variation of Diffusion Distance from Foetal to Maternal Circulation at Different Gestational Periods

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ABSTRACT

Diffusion distance varies according to the gestational age of a mother. Moreover, this diffusion distance must be within a physiological range. Thus, the survivability of a growing foetus depends on this distance. For this study, 90 products of conception and placenta were collected and divided into three groups based on the trimester of pregnancy, and each group included 30 samples. Two tissue blocks were collected from each specimen after the sample was fixed with 10% formol saline for 48 hours. Afterwards, with further processing of the tissue, followed by H&E staining, the diffusion distance was measured among the three groups by using crossed sealed ocular micrometre under the light microscope. The ANOVA test was considered for further statistical analysis. In the first trimester, the placenta diffusion distance from foetal to maternal circulation ranged from 53.20 – 68.30 (µm), and the mean ± SD was 60.46 ± 3.58 (µm). In the second-trimester placenta, the diffusion distance of placenta from foetal to maternal ranged from 23.20 – 45.30 (µm), and the mean ± SD was 36.05 ± 6.01 (µm). In the third-trimester placenta, diffusion distance from foetal to maternal ranged from 1.80 – 2.90 (µm) and the mean ± SD was 2.52 ± 0.22 (µm). Diffusion distance significantly reduced with the ageing of the placenta ($p < 0.00$). With the help of this result, we can assume that the exchange of nutrients and gases proportionally increases with the advancement of pregnancy.

INTRODUCTION

The foetal tissue consists of mesodermal projections known as chorionic villous, which are the structural unit of the placenta. Chorionic villous are extra-embryonic and comprises of the syncytiotrophoblast, and the cytotrophoblast. Syncytiotrophoblast and cytotrophoblast are the outer and inner cellular layers, respectively. Syncytiotrophoblast lies within the intervillous space, which is a conjunction for the syncytiotrophoblast to be in close proximity with the maternal blood. For the formation of mature chorionic villi, subsequent histological changes occur during the development, starting from primary villi formation, with there being cytotrophoblast propagation which perforates syncytiotrophoblast near the end of the second week of gestation, followed by the development of secondary villi. During the secondary villi development, the extra-embryonic mesenchyme penetrates the primary villi centre. Finally, the appearance of blood vessels near the mesenchymal centre leads to the formation of tertiary villi during the end of the third week of gestation[1] (Figure 1). However, each villus branch out with the advancement of pregnancy but basic structural architecture remain almost same throughout the pregnancy[2].

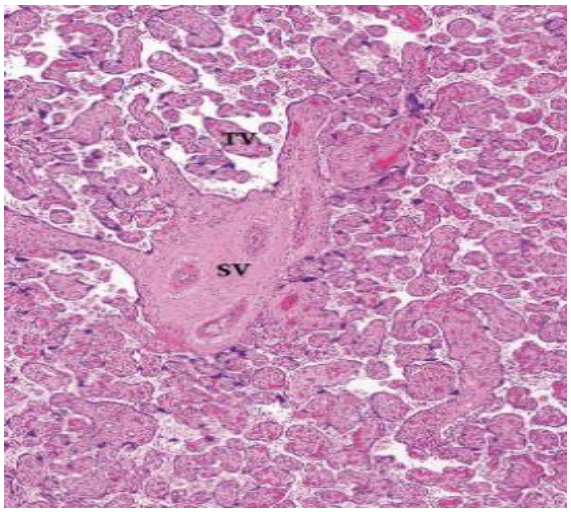

Figure 1 Micrograph of the full-term placenta at low magnification (SV indicates stem villi; TV indicates terminal villi)[3]

Mature chorionic villi consist of a little amount of cytotrophoblast. The maternal blood is isolated from the foetal capillary by a single syncytiotrophoblast layer after a certain period[4]. However, the syncytiotrophoblast and foetal capillary can be considered as an individual unit, in terms of their functionality, known as the vasculo-syncytial membrane that is the only structural barrier between foetal and maternal blood[5] (Figure 2). Three principal morphological characteristic features can describe the vasculo-syncytial membrane. Firstly, the capillary of the foetal blood vessel become widely dilated, up to 40 – 50 µm in diameter[6,7]. Secondly, basal lamina of the foetal capillary intimate with the syncytiotrophoblast with intervening littlest stromal tissue, and thirdly the syncytiotrophoblast is very thin and anuclear. Therefore, there may be an overall reduction in the width of the vasculo-syncytial membrane up to 1 – 2 µm. Consequently, vasculo-syncytial membranes are generally considered the significant sites of diffusional exchange between mother and foetus[8,9].

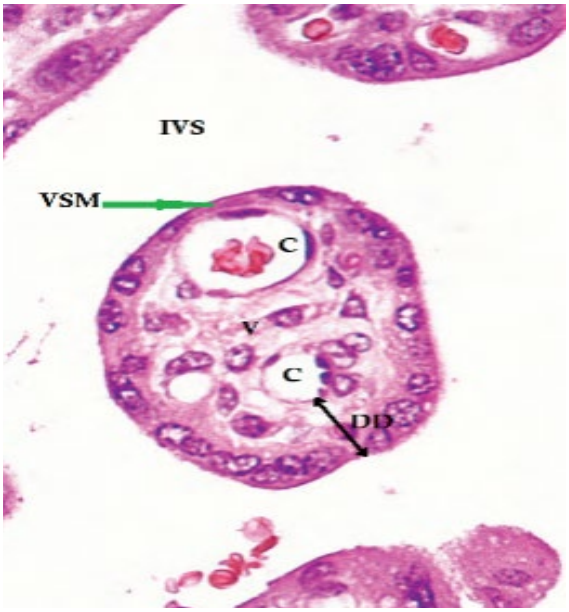

Figure 2 Micrograph of full-term placental terminal villi at high magnification (IVS indicates intervillous space, VSM indicates vasculo-syncytial membrane, C indicates foetal capillary, DD indicates diffusion distance)[10]

The vasculo-syncytial membranes are developed due to protrusion of the foetal capillaries into the trophoblastic layer[11]. Due to high transmural pressure and localised proliferation of endothelium, the foetal capillaries become dilated and make close contact with trophoblast[12]. The most important properties of the vasculo-syncytial membrane are the maintenance of exchange surface area and sufficient diffusion distance of foeto-maternal surfaces[13]. A recent study shows that there is a consistent relationship between the volume of the foetal capillaries and the mean thickness of the vasculo-syncytial membranes[14]. It is essential to know about the chronological changes of diffusion distance from foetal to the maternal circulation of the placenta. The slight alteration may cause intense foetal damage. For example, increasing thickness of vasculo-syncytial membrane results in increased diffusion distance may lead to maternal pre-eclampsia, which may cause maternal and foetal death. Diffusion distance from foetal to maternal circulation vary at different gestational periods. So, it can be a critical anatomical data for correlation with the pathology of the placenta.

MATERIALS AND METHODS

This was a cross-sectional, analytical type of study. This study was conducted in the Department of Anatomy, Dhaka Medical College, Dhaka from January 2016 to December 2016. Ethical permission was approved by the Ethical Review Committee (ERC) of Dhaka Medical College, Dhaka MEU-DMC/ECC/2016/189. Total of 90 samples was collected from adult Bangladeshi women. It calculated by the following equation,

$$n = \frac{(z_\alpha + z_\beta)^2 \times ({\sigma_1}^2 + {\sigma_2}^2)}{(\mu_1 - \mu_2)^2}$$

where,

n (Sample size) = 30

z_α (z - Value of standard normal distribution at 99.99% confidence level) = 3.89

z_β (z - Value of standard normal distribution at 2.33 at power) = 0.99

σ_1 (SD of one group) = 1.4

σ_2 (SD of another group) = 1.5

μ_1 (Mean of one group) = 1.5

μ_2 (Mean of another group) = 1.66

In this study, the mean percentage volume of fibrin was used for the calculation of sample size measurement[15]. The sampling technique was stratified random sampling. The participants provided informed consent without being exploited or forced. Either date of the last menstrual period or ultrasonic measurement of the biparietal diameter was used to calculate gestational age. Depending on the conclusion by enrolled specialists and the medical clinic records, the selection of the study group was made and divided into three examination groups named as Group A (6 to 12 weeks of aborted material), Group B (13 to 27 weeks of the conveyed placenta), and Group C (28 to 40 weeks of the conveyed placenta).

From all products of conception, chorionic tissue was recognised by its gross attributes. Chorionic tissues were thin, fragile, white, and a leaf of a fern-like papillary fronds[16]. The tissue block was prepared out of each of the chorionic samples, after careful removal of blood clots from it. The placental membranes were trimmed off the margins, and 2 cm of the umbilical string was kept with the placenta after cutting rest of it. At that point, faucet water was used to clean the placenta and later on, it was completely dehydrated. For microscopic examination, two full-thick tissue blocks were taken from each specimen; one from the central portion of cotyledon and then another from the peripheral position of the placenta. The region of the placenta seemingly having minimal pathology and standard features were selected for harvesting tissue blocks[17].

Then the tissue blocks were successively subjected to fixation with 10% formol saline for 48 hours, washing in running tap

water, dehydration with ascending grades of alcohol, clearing with xylene, infiltration and embedding in paraffin. After cutting the paraffin blocks at 6µm thickness, paraffin sections are then stuck to glass slides, deparaffinised, and stained with Haematoxylin and Eosin (H&E).

Diffusion distance from foetal to maternal circulation was measured in terminal villi cross-sections by Olympus optical crossed scaled ocular micrometre. Stratified random sampling was used to select three terminal villi from each field. With the aid of Olympus optical crossed scaled ocular micrometre, the diffusion distance from foetal to maternal circulation was measured (in micrometre) at 100×10 times magnification at the light microscope (Figure 4) after calibration with the Olympus Optical Stage micrometre.

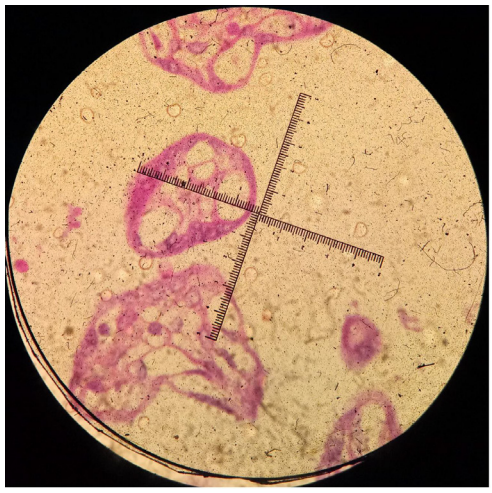

Figure 4 Photomicrograph of H&E stained placenta at 100×10 times magnification (view through an integrating eyepiece marked with a crossed scale used to measure the diffusion distance from foetal to the maternal circulation)[18]

Data Analysis

The data were statistically analysed after collection and checking of all data by a software package, SPSS for Windows (Version 24.0), keeping the objective of the study in view. Statistical test ANOVA was done to achieve the variation of diffusion distance at different trimester placenta. Data were expressed as Mean ± Standard deviation (± SD) as descriptive statistics among the three groups. Statistical significance was acknowledged at the *p*-value equal to or less than 0.05 ($p \leq 0.05$).

RESULTS

In group A (1st-trimester placenta), diffusion distance from foetal to maternal circulation ranged from 53.20 – 68.30 µm. There was a vast distance from foetal endothelium to intervillous space, and foetal capillaries are comparatively narrow and less in amount; chorionic villi contain lots of mesodermal tissue. Stem villi are comparatively more than the terminal villi. Cytotrophoblast and syncytiotrophoblast were visible. In group B (2nd-trimester placentae), diffusion distance from foetal to maternal ranged from 23.20 – 45.30 µm. In group C (3rd-trimester placentae), diffusion distance from foetal to maternal ranged from 1.80 – 2.90 µm (Table 1). Numerous terminal villi with few mesodermal tissues were found. Capillaries were widely dilated; the basement membrane of capillary endothelium fused with syncytiotrophoblast and trophoblastic tissue was not visible. Aggregation of syncytial nuclei (syncytial knot) was found at the syncytiotrophoblast. Mean diffusion distances were statistically significant ($p < 0.00$) among the three groups of placentae.

Table 1 Mean diffusion distance in different groups (n = 90)

Group	Vasculo-syncytial membrane thickness (μm)
	Mean ± SD
Group A (n = 30)	60.46 ± 3.58 (53.20 – 68.30)
Group B (n = 30)	36.05 ± 6.01 (23.20 – 45.30)
Group C (n = 30)	2.52 ± 0.22 (1.80 – 2.90)
Statistical analysis	***p*-value**
Group A vs Group B	0.00*
Group A vs Group C	0.00*
Group B vs Group C	0.00*

*Significant as $p < 0.05$

DISCUSSION

The study aimed to provide data on the growth of the placenta by analysing the different histomorphological structure. The mean diffusion distance in first, second and third-trimester placentae of the present study were 60.46 ± 3.58 μm, 36.05 ± 6.01 μm and 2.52 ± 0.22 μm respectively. A statistically significant difference ($p < 0.00$) was observed between first, second and third trimester placentae in mean diffusion distance.

Kaufmann and Scheffen[19] found mean diffusion distance in first, second and third-trimester placenta 55.9 ± 4.74 μm, 27.7 ± 5.84 μm, and 1.12 ± 0.73 μm respectively. A statistically significant difference ($p < 0.05$) was observed between the first, second and third-trimester placenta in mean diffusion distance. Though the values of the present study were different from the findings of the study mention above, mean diffusion distance was increased as pregnancy advances.

Since no published data was available on the histomorphological study of the placenta at different gestational periods, so, the result of the study could not be compared with such other studies. Few numbers of publications by other researchers with a similar study were available in other countries to compare with the findings of the present study. For the collection of second-trimester placenta foetal weight according to gestational age counted as a principal factor. In the present study, routine Haematoxylin & Eosin (H&E) stain and the light microscope were used.

Chorionic villi and placenta should be studied using Masson's trichrome, toluidine blue or periodic acid-Schiff (PAS) stains for improved visualisation. Further studies using ultrastructural and histochemical techniques are recommended. A similar study on gestational hypertension, gestational diabetes, anaemia, spontaneous abortion, and to compare with the present study is recommended.

CONCLUSION

In the present, study, it has been found that diffusion distance from foetal to maternal circulation found to be reduced with the advancement of pregnancy. So, it assumes that the exchange of gas and nutrition from foetal to maternal circulation increases according to the need of a growing foetus. Result of this study acts as baseline data from which we can compare histological changes of the normal placenta with diabetic, hypertensive, anaemic mother at different gestational periods in our population for future research.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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CASE REPORT

SLE/ Polymyositis Overlap Syndrome

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ABSTRACT

Inflammatory myopathies (IM) is a rare inflammatory muscle disorder, which can be broadly divided into 5 subgroups. The accurate diagnosis of subtype of IM can be challenging due to a diverse presentation of the disease. On the other hand, skeletal muscle complication is common in patients with systemic lupus erythematosus (SLE) in the form of myalgia or myopathy. Inflammatory myopathy is a rare association of SLE and the diagnosis and treatment can be quite challenging. A 43-year-old lady with underlying systemic lupus erythematosus (SLE), presented with subacute onset progressively worsening muscle weakness involving upper limbs and lower limbs. Neurological examination showed findings consistent with proximal myopathy, with proximal power of 3/5 and distal power of 4/5. She has elevated creatinine kinase, ALT and AST level. Her myositis-specific autoantibodies were positive for anti-Ku antibodies. Her electromyography showed evidence of active myopathy of the upper and lower limb. Here, we would like to report a case of polymyositis in a patient with SLE.

INTRODUCTION

Inflammatory myopathies (IM) is a heterogeneous systemic muscle disorder that can affect multiple organs apart from muscle and often enough, it leads to significant morbidity to the patients[1]. Traditionally, IM was classified into 2 entities, namely dermatomyositis (DM) and polymyositis (PM)[2].

With the improvement in understanding of muscle pathology and introduction of myositis-specific antibodies (MSA), the understanding of IM has largely evolved[3]. At present, IM can be classified into 5 subgroups, namely, (1) polymyositis, (2) dermatomyositis, (3) immune-mediated necrotizing myopathy, (4) sporadic inclusion-body myositis and (5) overlap myositis (including antisynthetase syndrome)[4]. On the other hand, overlap syndrome is defined by the presence of two or more connective tissue diseases, primarily systemic lupus erythematosus (SLE), systemic sclerosis and IM[5].

CASE PRESENTATION

A 43-year-old lady with underlying systemic lupus erythematosus (SLE), presented with subacute onset progressively worsening muscle weakness involving upper limbs and lower limbs for 2 months duration. She also noticed difficulties in climbing stairs and stand from sitting position. Otherwise, she did not have dysphagia, dysphonia, difficulty in breathing or Raynaud's phenomenon. There was no numbness, headache or back pain. She also did not complain of urinary or bladder incontinence. There were no skin rashes, no symptoms of hyperthyroid or hypothyroidism. She does not consume alcohol or other supplements.

On examination, her blood pressure was 113/69 mmHg, pulse rate was 107 bpm, and the temperature was 37°C. There were no rashes, no oral ulcers and her nails were normal. She had marked alopecia with multiple areas of scarring. Neurological examination showed findings consistent with proximal myopathy, with proximal power of 3/5 and distal power of 4/5. Her reflexes and sensory examinations were normal. There was no fatigability and her cranial nerve were normal. Respiratory and cardiovascular examinations were normal.

She was then admitted for further investigation. Her full blood count showed normochromic normocytic anaemia with haemoglobin of 10.9 g/dl. Her renal function test was normal. She has elevated creatinine kinase level of 5976 U/L, ALT of 127 U/L, AST of 268 U/L (Table 1).

Table 1 Investigations of patient

	Day 1 of treatment	Day 5 of treatment	Day 19 of treatment	Day 30 of treatment	Day 48 of treatment	Day 86 of treatment	Day 99 of treatment	Normal value	Unit
Hb	10.9	11.4	12.4	11.6	13.4		13.3	13 – 18	g/dl
TWBC	5.4	7.9	11.7	9.83	11.8		13.1	4.0 – 10.0	10^9/L
Platelet	280	390	252	368	367		313	150 – 400	10^9/L
ESR	81		80						
Sodium	138		138	142	139	141	138	135 – 148	mmol/L
Potassium	4		4.3	3.7	4.6	4.4	3.9	3.5 – 5.1	mmol/L
Urea	3.5		3	2.5	4.7	1.9	3.3	2.8 – 7.8	µmol/L
Creatinine	41		21	23	29	25	29	61 – 110	mmol/L
Tbili	8.1	4.7	12.61	9.8	11.24	12.6	13.2	0 – 17	µmol/L
ALT	127	129	125	110	93	40	34	0 – 31	U/L
ALP	60	55	50	44	70	50	48	35 – 104	U/L
Alb	35	35	39	37	42	41	41	34 – 48	g/L
Globulin	52	49	34	35	38	31	32	20 – 35	g/L
AST	268	93	160	149	95	61	43	10 – 40	U/L
CK	5,976	1,146	2,740	3,345	1,559	1,185	717	22 – 198	U/L
LDH			712	646	536	359	327	140 – 280	U/L
SLE workup				Extractable nuclear antigen (ENA)			Myositis Specific antibodies (MSA)		
ANA	Positive 1:320			U1RNP	Negative		Mi-2	Negative	
C3	45	90 – 180 mg/dL		Anti Sm	Negative		PM-Scl100	Negative	
C4	9	10 – 40 mg/dL		SS-A	Negative		PM-Scl75	Negative	
Anti-DsDNA	Positive 1:40	<1:10		SS-B	Negative		SRP	Negative	
				Scl-70	Negative		PL-7	Negative	
T4	15.3	12.2 – 22.4		Jo-1	Negative		PL-12	Negative	
TSH	1.59	0.35 – 4.55					EJ	Negative	
							OJ	Negative	
Tumour markers:		Normal range					Ro52	Negative	
Alpha Feto protein	1.8	<10 ng/ml					Ku	Positive	
CEA	0.8	<2.5 ng/ml							
CA125	9.1	0 – 35 units/ml							
CA15-3	26.6	<30 U/ml							
CA19-9	13.6	0 – 37 U/ml							

Her extractable nuclear antigen (ENA) was negative, myositis-specific autoantibodies were positive for anti-Ku antibodies. Her electromyography showed evidence of active myopathy of the upper and lower limb (Table 2).

Table 2 Electromyography of the patient

Side	Muscle	Nerve	Root	Ins Act	Fibs	PSW	Fasc	Myotonia	Myokimia	CDR	Amp	Dur	Poly	Recrt	Int Pat	Interpretation
Right	Biceps	Musculo-cutaneous	C5-6	Incr	2+	2+	Nml	Nml	Nml	Nml	Decr	Decr	2+	Reduce	Nml	Proximal Myopathy
Right	Ext Dig Brevis	Dp Dr Fibular	L5,S1	Incr	2+	2+	Nml	Nml	Nml	Nml	Decr	Decr	2+	Reduce	Nml	Proximal Myopathy
Right	Deltoid	Axillary	C5-6	Incr	3+	2+	Nml	Nml	Nml	Nml	Decr	Decr	2+	Rapid	Nml	Proximal Myopathy
Right	Vastus Lateralis	Femoral	L2-4	Incr	3+	3+	Nml	Nml	Nml	Nml	Decr	Decr	2+	Reduce	Nml	Proximal Myopathy
Right	1st Dorsal Interosseous	Ulcer	C8-T1	Incr	Nml	Nml	Nml	Nml	Nml	Nml	Nml	Nml	0	Reduce	Nml	Myopathy

Abbreviation:
CRD: Complex Rep Disch
Amp: Amplitude
Dur: Duration
Fasc: Fasciculation potentials
Fib: Fibrillation potentials
Ins Act: Insertion activity
Recrt: Recruitment
PSW: Positive sharp waves

She was then diagnosed to have SLE/polymyositis overlap syndrome and treated with intravenous methylprednisolone 500 mg once daily for 3 days followed by oral prednisolone 1 mg/kg. She was discharged after a week in the hospital. One month after corticosteroids, her muscle power markedly improved. She was able to ambulate without help. Azathioprine was added as steroid-sparing agent and prednisolone was subsequently tapered down. She was keeping well since then. Her malignancy screening was also negative with negative whole-body computed tomography scan. Gynaecological and otorhinolaryngology evaluation also excluded malignancy.

DISCUSSION

SLE is an autoimmune disease that affects virtually any organs in the body. It affects females more commonly than males. Skeletal muscle complication is common in SLE patients, which is seen in the form of myalgia, muscle weakness and atrophy[6]. Myalgia is the most skeletal muscle manifestation, affecting 40 – 80% of patients[7]. On the other hand, muscle weakness can be caused by myopathy, neuropathy or central nervous system complications. Myopathy in SLE can be caused by a range of pathologies, such as endocrine, inflammatory, paraneoplastic or infectious etiologies[8]. Other differential diagnoses that we need to consider in SLE patient with muscle weakness include myasthenia gravis, lupus myositis or drug-induced neuromyotoxicity[9]. Hydroxychloroquine and corticosteroids are established treatment of SLE and muscle weakness are a well known side effect of the drugs. It is important to diagnose the underlying cause of muscle weakness as the treatment is different.

Inflammatory myopathies (IM) is a group of acquired myopathy characterized by muscle inflammation and motor weakness of varying severity[2]. Its incidence is estimated to be around 4.27 – 7.89 cases/100,000 population per year[10]. IM is broadly classified

into 5, namely polymyositis, dermatomyositis, immune-mediated necrotising myopathy, sporadic inclusion body myositis and overlap myositis[4]. Clinically, a patient can present with acute or subacute onset muscle weakness of different pattern, often accompanied by raised creatinine kinase (CK)[1]. In severe cases, respiratory and oesophageal muscles can be affected[11]. The diagnosis of IM requires careful clinical evaluation paired with serological markers, neurophysiological testing and muscle biopsy. In history taking, we need to take a relevant family history, myopathic drugs, alcohol and features of endocrinopathy[12]. Magnetic resonance imaging (MRI) of muscle can help in certain cases.

In this patient, she has underlying SLE, currently presented with subacute onset of proximal muscle weakness. There were no extraskeletal manifestations. Clinical examination was consistent with proximal muscle weakness. At this point of time, the possible differential diagnosis to consider for her weakness includes myopathy, pure motor peripheral neuropathy or transverse myelitis. Absence of sensory involvement excluded transverse myelitis. Elevation of creatinine kinase confirms the weakness is likely due to myopathy. Possible causes of myopathy include polymyositis, dermatomyositis, overlap myositis, myasthenia gravis or drug-induced neuromyotoxicity. We think that she most likely has polymyositis as she does not have any extraskeletal findings to suggest dermatomyositis. There was no fatiguability to suggest myasthenia gravis. There were also no features to suggest possible antisynthetase syndrome. Her anti-Ku antibodies positive, which can be seen in SLE with polymyositis. Electromyography was also consistent with the myopathic pattern. Muscle biopsy was not done as service was not available.

Inflammatory myopathy is rare in SLE patient with only 4 – 16% patients affected[13]. Both dermatomyositis (DM) and polymyositis (PM) can be associated with SLE with DM more commonly seen in SLE. PM commonly affects those age from infancy to late adulthood, with 40 – 60 years old more common[14]. Patients usually present with subacute onset proximal muscle weakness of both upper and lower limbs[13]. In the later stage of the disease, trunk muscles, pharyngeal muscles and respiratory muscle can be involved. Extramuscular features such as Gottron papules, Raynauds phenomenon are usually absent[1]. A laboratory test will show raised CK, aspartate aminotransferase and alanine transaminase. Antibodies such as extractable nuclear antigen (ENA), myositis specific autoantibodies (MSA) are helpful serological markers[12]. Characteristics electromyography include spontaneous fibrillation at rest or with needle insertion, spontaneous high-frequency discharges and positive sharp waves[15]. Importantly, we also need to screen the patient for malignancy[16].

The optimal treatment of IM remains a challenge due to its low prevalence and wide clinical heterogeneity. In general, immunosuppressive therapy with a corticosteroid and steroid-sparing agents remains the mainstay of treatment. Majority of patients respond well to immunosuppressive therapy. Induction of steroid with 1 mg/kg or pulse parenteral steroid can provide rapid response[17]. The steroid should be continued for 4 – 12 weeks and reduction should be considered based on the improvement of power strength and CK level[1]. Steroid sparing agent such as azathioprine or methotrexate should be started based on patient clinical profile[10]. Intravenous immunoglobulin can be given in those with the severe disease while rituximab and cyclophosphamide are options for refractory disease[1].

CONCLUSION

In conclusion, inflammatory myopathy is a rare inflammatory disorder with diverse and heterogeneous clinical presentation.

Diagnosis of IM requires thorough clinical evaluation, coupled with a laboratory test, electromyography and muscle biopsy. In approaching SLE patients with muscle weakness, IM needs to be excluded. Immunosuppressant therapy remains the mainstay of treatment for IM.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

CONSENTS

Written informed consent was obtained from the patient to publish this case. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Gliosarcoma of a Brain: A Challenging Diagnosis

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ABSTRACT

Gliosarcoma is a rare primary malignant tumour of the central nervous system. A 28-year-old radiographer without a history of neurological disorder, malignancy or trauma presented with unprovoked seizures. He was symptom-free for 3 years but developed relapsed. Computed tomography of the brain was consistent with anaplastic convexity meningioma which was identical via intraoperative findings. However, the final histology revealed gliosarcoma of the brain. He recovered well postoperatively without any neurological deficit and had completed adjuvant chemo-radiotherapy. He was asymptomatic during follow up with no tumour recurrence. Gliosarcoma with predominant sarcomatous component mimicking a meningioma has prolonged survival as compared to a case with predominant glioblastoma component. Hence, the discordance between clinical, radiological, intraoperative and histopathological findings is a challenge in establishing a diagnosis of gliosarcoma.

INTRODUCTION

Gliosarcoma is a rare primary malignant tumour of the central nervous system with reported cases of 0.59 – 0.76% of all adult brain tumours. It is a variant of glioblastoma describing a biphasic tissue component displaying glial and mesenchymal differentiation. Gliosarcoma constitutes approximately 2% to 8% of all glioblastoma[1]. The age distribution is equivalent to glioblastoma which occurs between the ages of 40 to 60. Rare cases may

occur in children, even in the very young. Males are more frequently affected. Gliosarcoma is usually located in the cerebral hemispheres, involving the temporal, frontal, parietal and occipital lobes, in decreasing order of frequency. It has abrupt symptoms reflecting tumour location and raised intracranial pressure[2].

The histopathological evaluation shows a GFAP-negative malignant mesenchymal component, which is important to distinguish gliosarcoma from glioblastoma with a florid fibroblastic proliferation (desmoplasia) in the presence of meningeal invasion. Reticulin stain reveals a biphasic tissue pattern consisting of reticulin-rich sarcomatous and reticulin-free gliomatous elements[2]. Gliosarcoma has a poor prognosis with an average of 4 months of survival in untreated patients. It may show prolonged survival after surgical excision combined with radiotherapy and chemotherapy[3]. Gliosarcoma that mimics meningioma histologically has been reported to have a more favourable prognosis[4]. We present here a case of gliosarcoma in a young adult with the clinical impression of anaplastic convexity meningioma that has a prolonged survival after treatment.

CASE PRESENTATION

A 28-year-old radiographer presented with two episodes of unprovoked seizure. He had no past medical history especially neurological disorder or family history of malignancy. He denied a history of trauma, fall, motor vehicle accident and fever. He had plain computed tomography (CT) brain done which showed normal findings. He was started on Tablet Sodium Valproate 400 mg twice daily. There was no further test done to investigate the seizure. He had defaulted his follow-up and medication subsequently.

He remained symptom-free for 3 years until the unprovoked seizure recurred. This episode of seizure was followed by an attack of severe headache 2 weeks after. He sought medical attention after 2 days of the headache. He experienced the headache on the parietal and periorbital region of both sides. It was throbbing in nature and worsened in the morning. There was nausea but no vomiting. There was no blurring of vision or other symptoms of neurological impairment. Upon presentation, he was conscious with no neurological deficit on peripheral and cranial nerves examination.

Contrast-enhanced CT brain revealed an intracranial right parietal mass with surrounding mass effect. Magnetic resonance imaging (MRI) of the brain showed a heterogeneous solid lesion on right parieto-occipital region measuring 4.5×2.9×5.4 cm which was gadolinium-enhanced. There was multi-age haemorrhage within the solid lesion with an adjacent rim enhancing, well-defined homogeneous cystic lesion measuring 3.3×2.3×3.2 cm, surrounded by the oedematous white matter. There was a midline shift to the right and mass effect with no dilation of ventricles. Right parieto-occipital craniotomy and excision of the tumour was performed by the neurosurgical team. The clinical impression was anaplastic convexity meningioma. There was no residual tumour seen on post-operative imaging.

Histopathological report of the tumour revealed an irregular piece of tissue measuring 50×45×20 mm with multiple areas of haemorrhage on gross examination. Microscopic examination showed a biphasic cellular tumour composed of glial and sarcomatous components (Figure 1A). The glial component exhibited pleomorphic astrocytic cells with palisading necrosis (Figure 2A) and endothelial hyperplasia or microvascular proliferation with glomeruloid in appearance (Figure 3A). The tumour cells were moderately pleomorphic, having round to oval nuclei, fine chromatin, some showed visible nucleoli and cytoplasm of indistinct cell border with numerous mitoses (Figure 4A).

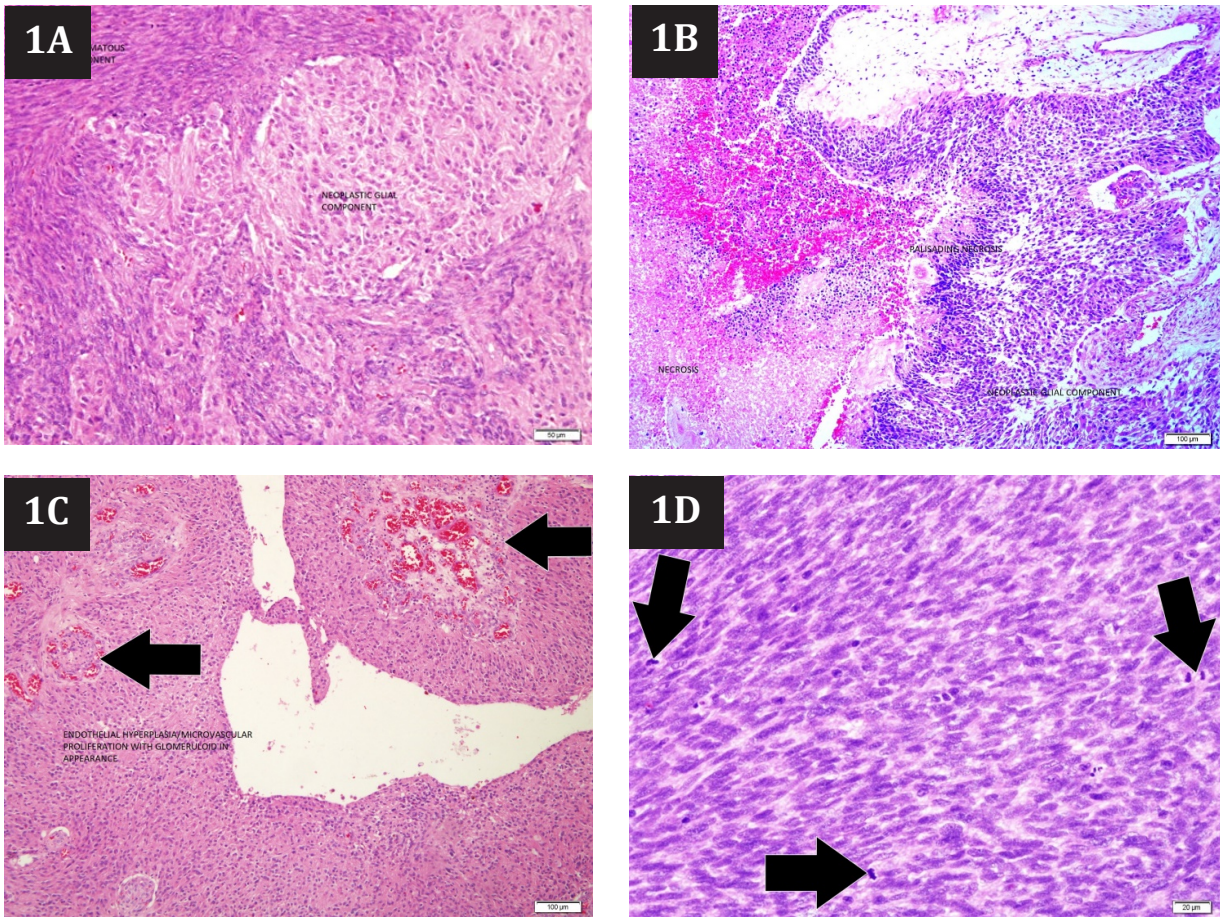

Figure 1 Photomicrograph: (1A) Biphasic cellular tumour composed of glial and sarcomatous components (H&E, ×20), (1B) Glial components with pleomorphic astrocytic cells and palisading necrosis (H&E, ×20), (1C) Endothelial hyperplasia or microvascular proliferation with glomeruloid in appearance (arrow) (H&E, ×10), (1D) Pleomorphic spindle cells with numerous mitosis (arrow) (H&E, ×40)

The tumour cells expressed Glial Fibrillary Acid Protein (GFAP) (Figure 2A), S-100 (Figure 2B) and Vimentin (Figure 2C) but did not express Epithelial Membrane Antigen (EMA), Progesterone Receptor (PR), E-cadherin, Pan Cytokeratin AE1/AE3, Cytokeratin 7, Cytokeratin 5/6 and Smooth Muscle Actin (SMA). Thus, a diagnosis of meningioma was excluded. Proliferative index Ki-67 was high (Figure 2D). Hence, the findings were in favour of Gliosarcoma, WHO grade IV.

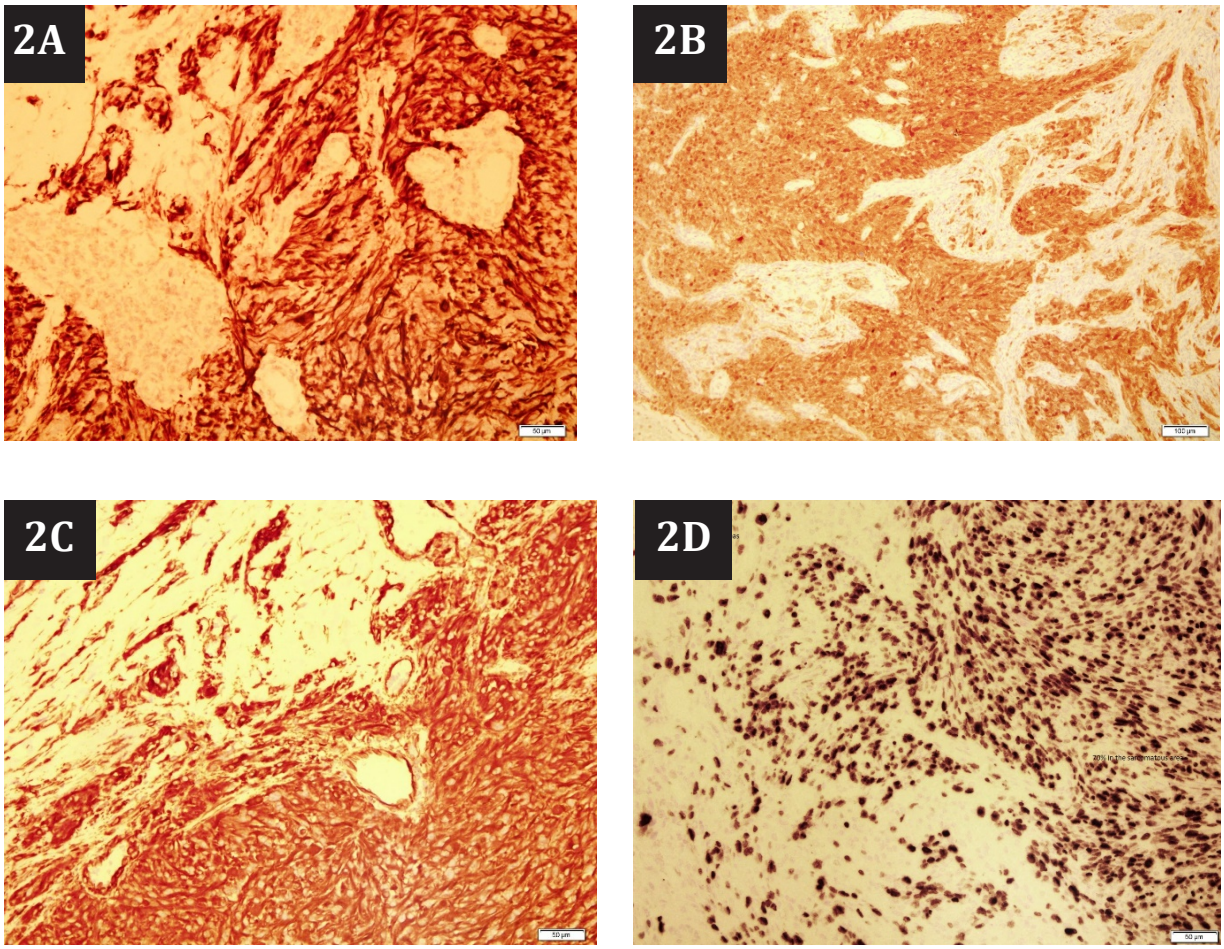

Figure 2 Photomicrograph: Tumour cells are positive for: (2A) GFAP, (2B), S-100, (2C) Vimentin with high Ki-67 proliferation rate, (2D) immunohistochemistry (×20)

The patient recovered well postoperatively and was asymptomatic. He was discharged 4 days after the operation. There was no neurological deficit. Adjuvant three-dimensional conformal radiotherapy (RT) and chemotherapy were given to the patient. He completed 6 cycles of adjuvant chemotherapy and was asymptomatic during follow up with no tumour recurrence. He was planned for surveillance with repeated MRI brain in every six months, or earlier if symptomatic.

DISCUSSION

Gliosarcoma was first described by Stroebe in 1895. It is an uncommon brain tumour and the reported incidence is 1 – 8% of all malignant gliomas and thus represents an exceptionally rare malignancy[1]. Recent genetic studies suggest a monoclonal origin of gliosarcoma and evolution of the sarcomatous component due to an acquisition of a mesenchymal phenotype in a highly malignant astrocytic tumour. Genetic aberrations, clinical features, and prognosis are similar to those of glioblastoma multiforme[5].

Gliosarcoma commonly occurs among elderly with rapid clinical manifestation. However, in this case, the patient is only 28 years old with a 3-year symptom-free interval after the first episode. It is generally supratentorial with the commonest site at the temporal region[1]. As described, the tumour location correlates well with this case. In the literature review, neuroimaging for gliosarcoma may have 2 types; a predominant sarcomatous

component that may mimic a meningioma or with a predominant glial component that gives similar radiological features to those of glioblastoma[2]. In this case, radiological and intraoperative findings were suggestive of an anaplastic convexity meningioma.

It was a challenging case because of the discordance between clinical radiological, intraoperative and microscopic findings in which clinically and radiologically are in favour of benign tumour. A preliminary diagnosis of anaplastic convexity meningioma made the histopathological evaluation more challenging, plus a predominant sarcomatous component was seen microscopically. Extensive immunohistochemical studies had been done to establish the diagnosis of gliosarcoma. Also, the patient's age and atypical clinical presentation made the differential diagnosis in favour of a benign tumour. However, since our patient was a radiographer who had been frequently exposed to radiation, we couldn't rule out the possibility of malignancy.

In general, patients with gliosarcoma that mimics meningioma clinically have longer survival. Those who have tumour-resembling meningioma grossly usually have 16 months of median survival as compared to only 9.6 months in those resembling glioblastoma[4]. In other case series, Salvati et al.[5] highlighted the presence of 2 histological subtypes of gliosarcoma that are gliosarcoma with a prevalence of sarcomatous component and gliosarcoma with a prevalence of gliomatous component. The former has similar surgical and radiological features with meningioma with longer median survival time while the latter is similar to glioblastomas surgically and radiologically[5]. In term of tumour recurrent, patient with predominant sarcomatous component recurred later (mean of 59.7 weeks) as compared to gliomatous predominance with a mean recurrent period of 47 weeks)[5]. It is correlated well with this case as the patient still free from tumour recurrent.

Despite the longer survival time for gliosarcoma mimicking meningioma, primary gliosarcoma, in general, is clinically challenging due to poor prognosis, rarity and limited experience in managing this rare variant[6]. Besides, managing gliosarcoma can be even more challenging if it is extracranial. Gliosarcoma can be extracranial and multifocal with a reported case of the multifocal spinal cord and meningeal involvement of this type of tumour[7]. Therefore, this case is to highlight the presence of this rare variant of a brain tumour and its challenges.

CONCLUSION

In conclusion, individuals with high-risk radiation exposure particularly radiographer as in our case require special attention when it comes to the diagnosis of malignancy. Despite indolent clinical presentations mimicking benign nature of the disease, thorough evaluation has to be made to avoid misdiagnosis and subsequently leading to mismanagement of the patient.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Microsurgical Anastomosis of Median and Ulnar Nerve by Sural Nerve Grafting

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ABSTRACT

The young to the middle-aged group is most affected in peripheral nerve injuries (PNI) and male gender shows predominance among the patients. Upper extremities are most likely to get injured which is three-fourth of total patients. This case report is about repairing of median and ulnar nerve by autologous sural nerve grafting. A 28-year-old man had an alleged history of a stab wound at his right arm 3 months ago. He had clinical features of complete injury of his right ulnar and median nerve. Nerve electrophysiology and magnetic resonance imaging also supported the diagnosis. Neuromas were formed in both the upper ends and the gap between the ends was more than 2 centimetres. The nerve was repaired under an operating microscope by sural nerve and musculocutaneous nerve grafting with very thin monofilament suture. His postoperative recovery was uneventful. Sensory recovery was earlier than motor recovery.

INTRODUCTION

Peripheral nerve injuries (PNI) are gradually increasing in numbers for the last few decades which is nearly 2.8% of all trauma patients[1]. The young to the middle-aged group is most affected and male gender shows predominance among the patients. Upper extremities are most likely to get injured which is three-fourth of total patients. The radial nerve is commonest in upper extremities and the sciatic nerve is commonest in lower limbs to be affected[2]. Modern surgical techniques

like intra-operating electrophysiology monitoring, microscopic neurosurgery and nerve grafting techniques have encouraged surgeons to treat PNI patients more efficiently than before. PNI are classified into five groups according to the severity. Neuropraxia is a less severe type where neurotomesis is the severest. Axonomesis type is also significant but neurotomesis is the type where surgery mostly indicated. High-grade nerve injuries lead to compromising the nerve integrity and suboptimal regeneration and causes Wallerian degeneration. Generally, the regeneration rate of the peripheral nerve is very slow at the rate of 1 millimetre per day[3].

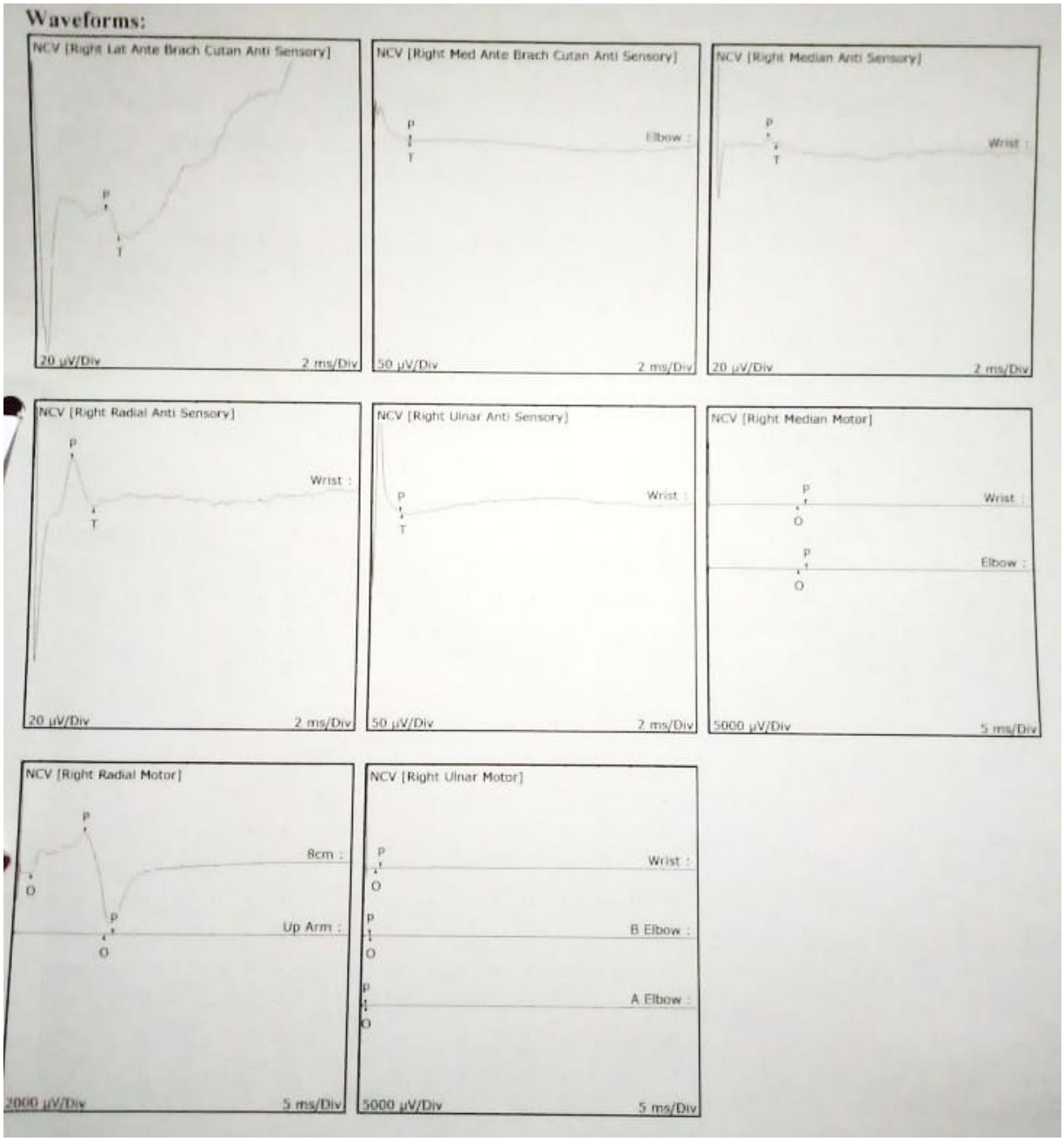
Different surgical options are available for repair of PNI, they are direct end-to-end repair, end-to-side repair, nerve grafting and nerve transfer. Different techniques of nerve anastomosis are epineural repair, grouped fascicular repair and fascicular repair[4]. Autograft has shown a better outcome than the allograft. The common harvesting sites for nerve grafts are sural nerve, lateral antebrachial nerve proximal to the elbow, medial antebrachial cutaneous nerve, a dorsal cutaneous branch of the ulnar nerve and lateral femoral cutaneous nerve[5]. There are many grading systems to assess post-operative nerve repair outcomes. Seddon's grading scale in one of the commonest among the surgeons. It is a four-tier grading includes bad, fair, good and excellent. The assessing parameters are muscle wasting, muscle power (MRS scale), tropic change, sweating, stereognosis, two-point discrimination and temperature sensation[6]. This case presentation is about the surgical technique of Sural and musculocutaneous autograft for a 28-year-old gentleman who suffered from a neurotomesis type of injury to his ulnar and median nerves.

CASE PRESENTATION

This 28-year-old gentleman consulted at neurosurgery outpatient department for his right upper limb weakness and lack of sensation for 3 months. He had an alleged history of stab injury at his inner surface of the upper part of the right arm 3 months ago. He underwent initial toileting and suturing in a local hospital. In course of time, there was no muscle power or sensation improvement achieved. On examination, he was conscious and well oriented. His speech and gait were normal. All cranial nerves were intact. There was an old irregular scar, apparently healed by secondary intention measured 9.5 cm present in the inner aspect of the upper one third-lower two-third junction of his right arm. He had a weakness (0/5) in pronation of the right forearm. He had a claw hand deformity at rest. He had flexion weakness (0/5) at the wrist and medial 3 digits. There was no adduction, abduction, and rotation power of the right thumb. He also had a complete sensory deficit at front of the forearm in the ulnar and median nerve distributing areas and palmar surface of his right hand mostly in the ulnar side in all modules of sensations. His Seddon's grading was bad as his muscle power was 0/5 and had lack of sensation, sweating, stereognosis and two-point-discrimination.

The nerve conduction velocity test reported as evaluation of right median motor nerve showed prolonged distal onset latency (13.8 ms) and reduced amplitude (0.0 mV). The right ulnar motor, the right median sensory and the right ulnar sensory nerves showed reduced amplitude (R0.0, R2.7, R1.3 μV). The conclusion of the report was right brachial plexopathy at the extreme lower end (Figure 1).

Figure 1 The amplitudes of NCV of the upper limb



Magnetic resonance imaging of the right arm revealed complete transection of the right ulnar and median nerve with more than 3 cm gap with neuroma at upper ends of both nerves (Figure 2).

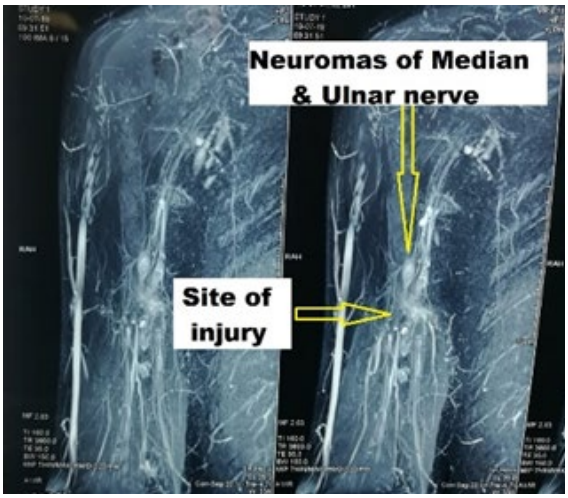


Figure 2 MRI of arm showing the injury site the ends of the injured nerves with neuromas

Poor prognosis and slow recovery were discussed with the patient and relatives. If autograft required then possible complications of donor site was also elaborated. After proper explanation and counselling, he was scheduled for right median and ulnar nerve repair by left sural nerve grafting under general anaesthesia. The scar was measured 60 cm from the tip of the right middle finger. After exposure of the wound, both ends of ulnar and median nerves were identified. The musculocutaneous nerve identified as completely severed. The musculocutaneous nerve had a continuation from the proximal end but the lower end was not well identified. Both the neuromas were dissected shelved off. Dissection and releasing of the fibrous tissue done at both ends of the ulnar and median nerves. After the flexion of the forearm, the distance between the ends of the ulnar nerve was measured 2.5 cm and the gap between the ends of the median nerve was 3 cm. A free auto nerve was harvested from the left sural nerve (Figure 3) measuring 5 cm. A nerve of 3 cm was harvested from the free proximal end of the musculocutaneous nerve. Sural nerve graft was incised into two equal pieces.

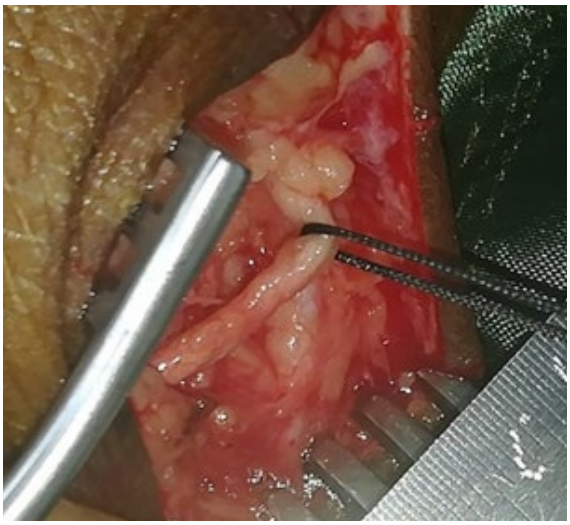


Figure 3 Identifying and harvesting of sural nerve for grafting.

The ulnar nerve was microscopically repaired by two pieces of sural nerves end to end epineural anastomosis with 6-0 sized synthetic, monofilament, nonabsorbable polypropylene suture. The median nerve was repaired with a musculocutaneous nerve graft (Figure 4) by a similar microscopic technique. The wound was closed in layers. Right upper extremity was immobilized in flexion position by a posterior slab.

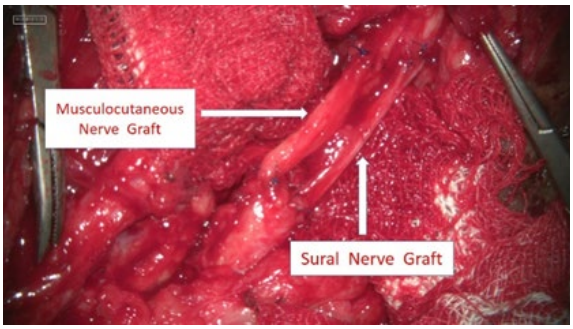


Figure 4 Intraoperative picture showing repair of nerves by grafting.

His postoperative recovery was uneventful. There was no new neurological deficit noticed after the surgery. Touch and temperature modules of sensations of his right hand started appearing and all lateral four finger's power improved to 4/5 when he was examined after 2 months of surgery.

He was able to use his right hand for feeding, dressing and using the toilet after 2 months. A long term follow-up is expected to show more precise postoperative recovery in future.

DISCUSSION

This case report is on a median and ulnar nerve injury patient who underwent repair of the nerves by autograft. The findings of this patient were compared with those of other international cases.

Moneim (1982) published his systemic review on interfascicular nerve grafting[7]. He found that small gap and early repair by direct anastomosis sometimes help in functional recovery. If the lesion is more than 3 weeks old and the gap is more than 2 cm then grafting is ideal. According to his study, he found that if the lesion is above the elbow joint then the chance of regaining the muscle power of the median and ulnar nerve was poor. After grafting of nerve, recovery of median nerve function was proven better than ulnar nerve when operated at the same site of arm or forearm. Dorsal cutaneous nerve separating from the main trunk using as graft showed a better result than other grafts. In this case, the gap was more than 2 cm in case of both the nerves. The injury was 3 months old.

Young et al. performed their study on the effectiveness of nerve grafting who underwent median, ulnar and digital nerve surgery[8]. A total of 38 patients included in the study among where 11 patients had the median nerve, 7 patients had the ulnar nerve and 33 had digital nerve graft. They have also compared the prognosis between grafted and non-grafted patients. It was concluded that sensory function improvement was significantly better in grafted patients in comparison to the non-grafted patients in case of ulnar nerve injuries. Ulnar nerve patient's motor recovery was as similar to the direct repair patients. Median nerve grafted patients had a significantly better result than the non-grafted patients. In this case, sensory has recovered earlier than motor but there was ulnar or median nerve predominance.

Mohseni et al. reported their study on different types of nerve repairs with their result[9]. The study included 85 adult and 65 paediatric patients. The follow-up period was between 2 – 10 years. Primary repaired patients obtained better result than grafting or delayed repaired patients. Younger patients showed a better outcome than older patients. The patient of this study was adult who required a graft and eventually showed a good result.

Yang et al. published one of the largest meta-analysis studies on nerve repair in 2011 which included 33 studies and 1531 cases[10]. They did not find any significant difference in the postoperative outcome between the median and the ulnar nerves (odds ratio = 0.98). Sensory nerves achieved a better satisfactory recovery than motor nerves after nerve repair surgery ($P < 0.05$). In the cases of nerve gap less than 5 cm, there was no statistical difference in outcome between the direct repair and the autologous nerve graft patients. According to the study, the median nerve with sensory impairment had the best postoperative prognosis, while ulnar nerve with motor power damage showed worse prognosis. In this case, both ulnar and median nerves were repaired for the same patient and the gap was less than 5 cm. A longer period follow-up may highlight more information regarding optimum recovery. The study of Yang et al.[10] did not show similarity with this study as we could not establish any comparative study between grafting and direct closure cases.

CONCLUSION

Few international studies had a similar result to this study. On the other hand, few had contradictory results. A comparative study of large case number with significant test could have highlighted a better result about

the preferred surgical option. As far surgical technique is a concern, a sural nerve grafting could be a preference of grafting.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written consent was obtained from the patient to publish the case with some related pictures. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Frontonasal Dysplasia in Yangon, Myanmar

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Keywords: frontonasal dysplasia, midline facial cleft, congenital anomaly, Myanmar

ABSTRACT

Frontonasal dysplasia (FND) is an uncommon congenital anomaly affecting the eyes, nose and forehead. In this case report, a baby of a 22-year-old mother was diagnosed with a midline facial cleft, bifid nose and hypertelorism during an ultrasound scan at 29th week of gestation. Besides a history of miscarriage on first pregnancy, no other abnormalities findings were found in laboratory or radiological examination of the newborn. Counselling about abnormality and psychological support were given by both obstetrician and neonatologist during the antenatal period. The patient delivered vaginally at 36th week with spontaneous labour and no complication was observed. Further interventions including corrective treatment have been planned as they often interfere with important functions such as breathing and feeding. Thus, the paediatric surgical team decided to do the operation when the baby reaches one year old as then tissues have been developed to 90% of their eventual form to give optimal treatment results. Further life expectancy depends on the severity of the malformation and whether or not surgical intervention can improve the associated health problems. This case report raises the importance of awareness on the nutritional value of pregnant mothers especially carotene and folic acid intake which may be associated with the organ maldevelopment. Overall, this report outlined the management of this rare condition experienced by the patient, particularly in a resource-limited setting like Yangon in Myanmar and also reviewed the literature about the presentation and classification of this condition.

INTRODUCTION

Frontonasal dysplasia (FND) is a very rare congenital anomaly affecting the eyes, nose and forehead[1]. Approximately 100 cases have been reported so far in the literature[1, 2]. This is an interesting case report as the average global prevalence rate is one in every 700 population, wherein in Myanmar one in every 800 to 1,000 babies every year according to the health report of Central Women's Hospital of Yangon in 2015[3]. The underlying causes of this condition are nutritional deficiency, including folic acid requirement[4]. Due to the facts that most of the affected individuals are often associated with the lack of health knowledge, unbooked pregnancies and poor quality of diet, including vitamin supplements during the antenatal period[5, 6]. This is an interesting clinical case in a resource-limited country like Myanmar to achieve optimal patient care and to avoid complications of FND if left untreated, such as feeding, speech and language delay or difficulties, dental and ear infections, hearing loss due to the risk of middle ear fluid formation as well as psychological problems in the affected individuals.

FND can have a variety of phenotypes[7]. However, the classical definition of FND is based on Sedano et al.[6] and Sedano and Gorlin[8]. The diagnostic criteria include at least two of the following features[8, 9], such as (1) anterior cranium bifidum occultum, (2) v-shaped or widow's peak of frontal hairline, (3) true ocular hypertelorism (IP distance >97th centile), (4) broadening of nasal root, (5) lack of nasal tip formation, (6) median facial cleft (nose and/or upper lip and palate) and (7) unilateral or bilateral clefting of the alae nasi. Besides, the severity of the malformations can determine the life expectancy of affected individuals. In some cases, both the front and back parts of the palate are open and have problems with breathing, feeding and speaking clearly in later life. They also might have hearing problems and ear infection.

FND is an autosomal recessive disorder[10]. In the majority of cases, it is caused by a gene mutation. Some common examples of gene mutation reported, including *ALX3* that causes FND type 1[11] and Homeobox Protein Aristaless-Like 4 (*ALX4*) gene can lead to FND type 2[12]. Additionally, a gene mutation on Homeobox Protein Aristaless-Like 1 (*ALX1*) causes FND type 3[11] has also been reported. Lastly, the mutation of both Eph-related receptor tyrosine kinases (*EFNB1*) and Zinc Finger SWIM-Type Containing 6 (*ZSWIM6*) genes can manifest to craniofrontonasal syndrome (CFNS) FND and acromelic frontonasal dysplasia (AFND), respectively. However, in some cases, such as oculo auriculo frontonasal syndrome (OAFNS) and AFND, the associated genes causing the syndromes remain unknown[10].

Each subtype of FND has its distinct phenotypic features (Table 1), and the phenotypes can generally be subdivided into six. CFNS phenotypes are more distinct in females, including severe hypertelorism, a bifid nasal tip, coronal craniosynostosis, malformations of the clavicle, longitudinally grooved nails and thick hair[10].

Table 1 Phenotypic classifications of the face in FND

Sedano-Jirásek classification	Characteristics	Causes of gene mutation
FND type 1	Hypertelorism, median nasal groove, and absent nasal tip	Homeobox Protein Aristaless-Like 3 (ALX3)
FND type 2	Hypertelorism, median groove or cleft face, with or without lip or palate cleft	Homeobox Protein Aristaless-Like 4 (ALX4)
FND type 3	Hypertelorism and notching of alae nasi	Homeobox Protein Aristaless-Like 1 (ALX1)
Acromelic frontonasal dysplasia (AFND)	Hypertelorism, median groove or cleft face, with or without lip or palate cleft and notching of alae nasi	Eph-related receptor tyrosine kinases (EFNB1) and Zinc Finger SWIM-Type Containing 6 (ZSWIM6)

For the FND1 phenotypes, it is characterised by short medial nasal region with a broad columella that attaches to the widely spaced nasal alae producing a distinctive concave shape to the nasal tip and a long philtrum with raised and fleshy lateral margins[10, 11] in addition to the CFNS prominent characteristics.

Besides, several characteristics attributed to frontorhiny type 2 (FND2) include hypertelorism, severely depressed nasal bridge, malar flattening, bifid nasal tip, cleft palate alae, craniosynostosis and hypoplastic clavaria, resulting in extensive brain abnormalities, including agenesis of the corpus callosum[11].

CASE PRESENTATION

The condition was noted on ultrasound scan showing a midline facial cleft, bifid nose and hypertelorism during a routine antenatal follow-up at 29th week of gestation (Figure 1). A history of miscarriage was reported in the mother's first pregnancy. The mother's fasting glucose level of 4.3 mmol/L and two hours postprandial of 6.2 mmol/L were within the normal range. Besides, other clinical and laboratory findings were not suspicious of any abnormalities. Genetic testing was not performed to confirm the karyotypes of the baby due to lack of facility in Yangon, Myanmar. As a standard guideline to prevent the complication of iron deficiency anaemia, ferrous fumarate tablets and Obimin AZ® were given orally to the mother. Moreover, extensive counselling, including psychological support, was given to the parents by both obstetrician and neonatologist throughout the antenatal period. Ultimately, the baby was delivered by spontaneous vaginal delivery at 36th week without any complications. The vital signs were stable and APGAR score was 5, 7 and 10 at 1, 5 and 10 minutes respectively. Ocular hypertelorism and a central cleft involving the nose, upper lip and palate were observed (Figure 2). The antenatal ultrasound diagnosis of midline facial cleft with hypertelorism, in this case, was confirmed following delivery of the baby. Moreover, cranial ultrasound and MRI also confirmed the defect and excluded other associated abnormalities.

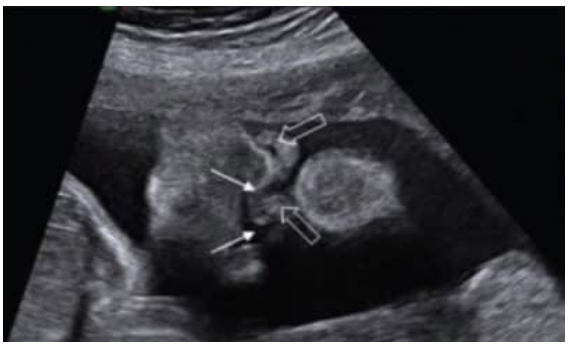

Figure 1 Ultrasound examination at 29th week of gestation showing a midline facial cleft, bifid nose and hypertelorism

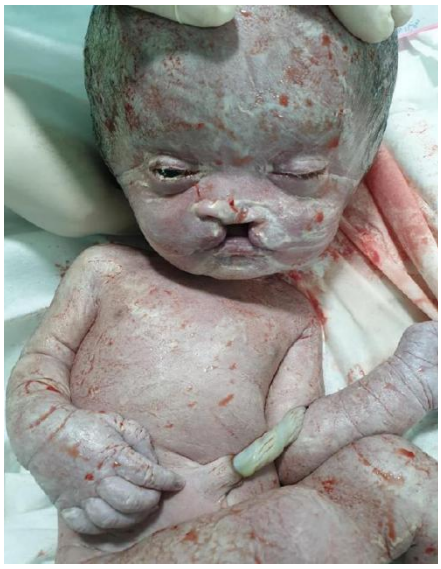

Figure 2 Frontal view showing ocular hypertelorism and a central cleft involving the nose, upper lip and palate.

DISCUSSION

According to Sedano's classification, this case is an example of type 3 FND[6]. The baby may require correction of hypertelorism in the future, whereby surgery is usually performed between 6 and 8 years of age because the cranial vault and the orbits are about 90% of their final size at that time. The paediatric surgical team has planned a primary surgery for the baby after the age of one year. The procedure is important because if the condition is left untreated, it could lead to many consequences, including speech delay. Furthermore, it helps to facilitate the child to adapt and integrate better in the family, society and school. Further correction surgery like rhinoplasty and cleft lip repair might also be needed. The baby is under currently under regular follow-up.

Frontorhiny type 3 (FND3) phenotypes are characterised by hypertelorism, a wide nasal base, isolated nasal alae, malformed orbits, microphthalmia, cleft primary and secondary palate as well as low-set and posteriorly rotated ears[10, 12]. While AFND phenotypes are characterised by hypertelorism, median cleft face, bifid nasal tips, widely spaced nasal alae, parietal defects and limb abnormalities (polydactyly, tibial hypoplasia and talipes equinovarus)[13, 14]. In some patients, it is manifested as marked mental retardation and brain malformations, including hydrocephalus, agenesis of the corpus callosum, interhemispheric lipoma and periventricular nodular heterotopia[15]. Lastly, OAFNS has several distinct phenotypic features, including microtia, preauricular tags, hemifacial microsomia and epibulbar dermoids[16].

Hypertelorism is the main and invariable component of FND. It is the main feature that differentiates FND from holoprosencephaly with median facial cleft[17]. FND can be an isolated feature or may be associated with other malformations, such as distal limb abnormalities including syndactyly, polydactyly, clinodactyly, tibial/fibular hypoplasia, acrocallosal syndrome or oral-facial-digital syndromes[9].

This case report is interesting as it happened in the economically deprived population in Yangon, Myanmar. Though, there is no obvious background condition that can lead to maldevelopment of the organs, the possibility of carotene and folic acid deficiency can be associated.

CONCLUSION

The described baby developed a congenital anomaly of FND type III. The baby is planned for correction of hypertelorism as well as a surgical intervention to avoid speech problems and psycho-social impact. This case report is important to emphasize the awareness of the nutritional value in pregnancy to the clinicians and population as a whole.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written consent was obtained from the patient to publish the case with some related pictures. A copy of the written consent is available for review by the Chief Editor.

ACKNOWLEDGEMENTS

The authors would like to thank the patient for her cooperation in consenting to write and publish this case report. Our highest gratitude to the Director of North Okkalapa General and Teaching Hospital, Yangon, Myanmar for the support in this case report.

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SHORT COMMUNICATION

Telomere and a Final Verdict for Cellular Senescence

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Keywords: telomere, cellular senescence, eukaryotic cells, tumourigenesis

ABSTRACT

Telomeres are specialized DNA complexes found at the end of all chromosomes. Human, as a member of eukaryotic cells, requires telomeres to maintain the length and the stability of chromosomes. Telomeres lose their non-coding DNA sequence to protect the genetic information on the chromosomes. Shortening of telomeres occurs in most somatic cells after sufficient cell division in a human lifetime. Normal haemopoietic cells or stem cells possess telomerase enzyme to restore telomeres and allow further replication. Telomere dysfunction is the origin of several degenerative disorders and also predispose to cancer. Roles of telomere in carcinogenesis and ageing related disorders are reviewed.

INTRODUCTION

Telomeres are repetitive (TTAGGG) DNA-protein complexes at the ends of chromosomes. Shortening of telomere is one of the mechanisms of replicative senescence[1]. During replication of somatic cells, a portion of telomere is not duplicated and it becomes shorter. Telomerase enzyme is a specialised RNA-protein complex which is composed of reverse transcriptase (hTERT) and an RNA subunit (hTER)[2]. Telomerase can use its RNA as templates to add nucleotides to the end of chromosome preventing the shortening. Normal somatic cells do not express it; hence have limited replication capacity resulting in replicative senescence activation.

Telomere and Cancer

Majority of cancer cells express telomerase to maintain chromosome length to become immortal. This activity is crucial for the survival of cancer cells[3]. In other instances, telomeres in cancer cells become extremely short and form *t*-stumps. Many chromosomal instability characteristics of human cancer cells result from *t*-stumps. In tumour cells positive for telomerase, these short *t*-stumps are generated, stabilized or protected from elimination by the hTERT[4]. Several methods measure telomere length (TL) namely: quantitative polymerase chain reaction, terminal restriction fragment length analysis, quantitative fluorescent in situ hybridization, telomere dysfunctional induced foci analysis, single telomere length analysis, telomere shortest length assay[5]. Telomere Restriction Fragment (TRF) analysis is the gold standard for measurement of telomere[6].

Telomere length and telomerase activity play important role in tumourigenesis and immortality of cancer cells. Studies showed short or eroded telomeres accounted for ~73% of the 125 colorectal cancers (CRCs) analysed whereas ~27% of the tumours showed unchanged or elongated telomeres. The survival rate is better in length-maintained colorectal cancers compared to those with eroded or shortened telomeres[7]. Cancer cell expresses constitutive telomerase reverse transcriptase (TERT) expression. Overexpress TERT is seen in many cancers including colorectal cancer[8], bladder cancer[9], ovarian and lung cancer[10].

Downregulation of telomere-related genes is useful in gene therapy for cancers. Knockdown of telomerase RNA (hTER) leads to rapid growth inhibition of cancer cells[11]. Efforts to target telomerase showed that the activity of tumour telomerase becomes attenuated resulting in reduced survival of cancer cells[12]. Personalised genetic therapies which modify inhibitory effects of telomerase are reliable alternatives for effective treatment of cancer in the future.

Telomere and Degenerative Diseases

Telomere attrition is responsible for degenerative or ageing disorders[13]. There is an association between short leukocyte telomere length and cardiovascular risk factors, such as smoking, obesity, and hypertension[14]. Germline mutation of TERT is associated with idiopathic pulmonary fibrosis, emphysema and dyskeratosis congenita[15, 16]. Telomere length seems to have a key role in cardiovascular disease contributed by vascular ageing[17]. Induction of telomerase gene expression benefits regeneration after cardiac injury by inhibiting the apoptosis of cardiac myocytes. Also, a similar study showed survival of vascular lining endothelial cells and smooth muscles preventing the age-related disorders[13]. Autopsy findings revealed significantly short telomere in the hippocampus of major depressive disorders suggesting the evidence of stress-mediated accelerated cellular ageing in depression[18]. Telomere attrition was seen in the beta cell of the pancreas in type 2 diabetic patients with poor glycaemic control autopsied pancreas[19]. Some factors, such as oxidative stress, result in the accelerated shortening of telomere and diminish the survival of cells leading to cardiomyopathy and atherosclerosis[20]. Defect telomerase RNA is associated with aplastic anaemia[21]. Experimental study on Tert-gene knock out mice treated with Tert-gene therapy showed an increase in peripheral blood count and bone marrow haemopoietic cells in previously aplastic marrow[22]. In advanced liver cirrhosis and idiopathic pulmonary, the fibrotic process can be reversed by transfer of telomerase gene[23]. Experimental expression of telomere maintenance genes or telomerase is helpful for diseases associated with shortening of telomere. Non-integrative expression of these genes does not promote oncogenesis[24]. However, the potential risk of carcinogenesis by upregulation of telomerase should be studied in long term basis[25].

CONCLUSION

Telomere shortening is a natural process that all somatic cells must undergo. Some exceptional cells such as marrow stem cells and haemopoietic cells have their mechanism to maintain their telomere length to sustain their function throughout life. Modification of telomere-related genes is helpful in anti-ageing, antifibrotic or anticancer therapies. Further research on the mechanism of telomere related tumour genesis and its relationship with genomic change is essential for clinical application. Modifying genes that control telomerase and its use as a therapy has a significant role in comprehensive control of tumour progression in a variety of neoplasms.

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CLINICAL QUIZ

Eyelid Abscess with Dacryocystitis due to *Burkholderia pseudomallei*

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QUESTION

A 24-year-old female complained of a 2-week history of fever and right-eye swelling. There was no ocular pain, blurring of vision, or history of prior trauma to the affected eye. On examination, she was febrile and not in respiratory distress. The right lower eyelid appeared swollen with skin erythema (Figure 1), while the visual acuity was normal. The white cell count was 14.8 × 10^3/μL (normal range = 4 – 10 × 10^3/μL). Her liver and renal function tests were within the normal range. The abdominal ultrasonography revealed multiple splenic microabscesses, while chest radiograph was normal. Contrast-enhanced computed tomography of the orbit showed a right lower eyelid abscess with extension into the right nasolacrimal duct (Figure 2). Incision and drainage of the eyelid abscess were performed and the culture of the pus, as well as the blood, yielded *Burkholderia pseudomallei*. She received intravenous ceftazidime 2 g every 8 hours for 4 weeks, followed by oral trimethoprim-sulfamethoxazole for 20 weeks' duration. The right eyelid abscess and splenic microabscesses resolved completely post-treatment. Please interpret the figures and suggest the provisional diagnosis.

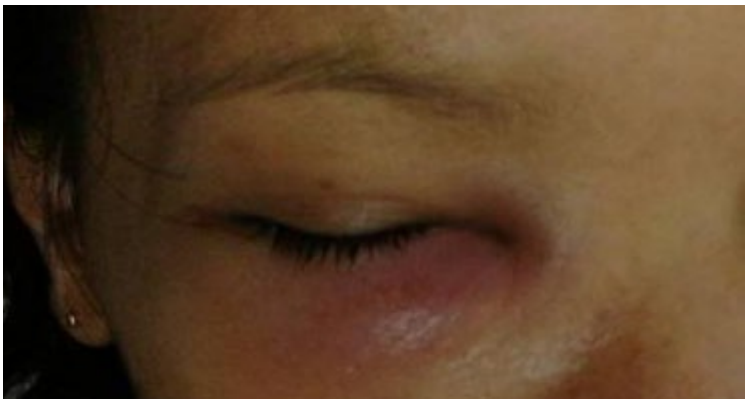

Figure 1 Swollen right lower eyelid with skin erythema

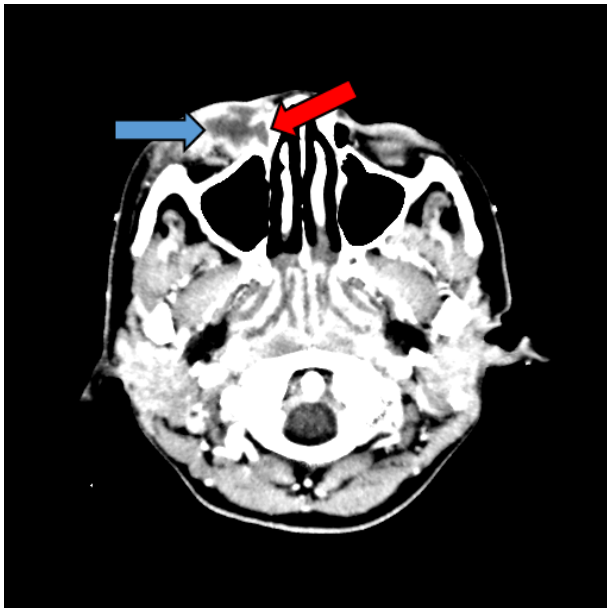

Figure 2 CT of the orbit shows right lower eyelid abscess (blue arrow) with extension into the right nasolacrimal duct (red arrow)

Please find the answer in the next issue.

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CLINICAL QUIZ

Intramural Gas: Would it be Life-threatening?

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ANSWER

The CECT scan of the abdomen at axial and coronal views show gas bubbles tracking along the inner wall of the ascending colon and hepatic flexure, which is separated from the intraluminal gas within the bowel. These intramural gas bubbles appear to be outlining the bowel wall circumferentially. The bowel wall appears to be thickened however the inner mucosa is not enhanced. There are no ascites in the images provided. The colon of the hepatic flexure and transverse colon appears dilated. No significant atherosclerotic plaque in the visualised arteries. Based on the clinical presentations and CECT features in Figure 1 and Figure 2, the best diagnosis for him is benign pneumatosis intestinalis (PI) secondary to obstructed low rectal cancer. He was subjected for a trephine transverse colostomy to relieve the obstruction with simultaneous transanal rectal mass biopsy. Once the histology is available, he subsequently will be referred for concurrent chemo-radiotherapy as neoadjuvant treatment and later for a low anterior resection, provided that it is a localized disease.

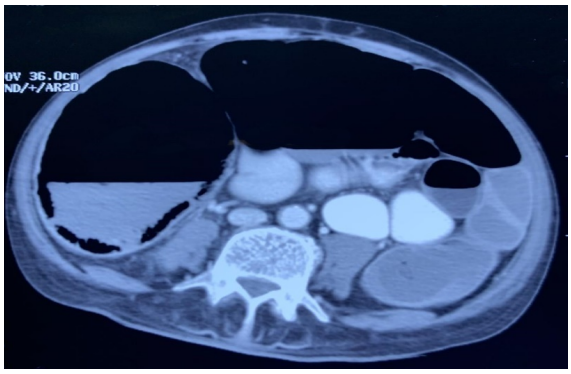

Figure 1 Axial image of CECT of the abdomen

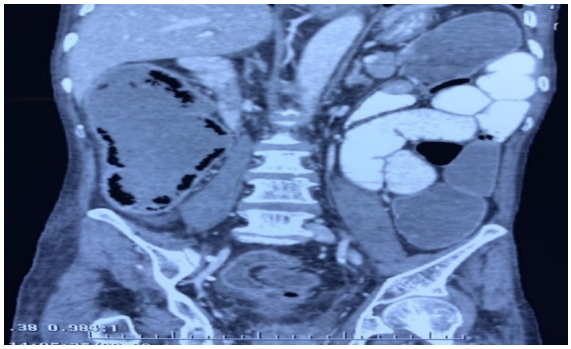

Figure 2 Coronal image of CECT of the abdomen

PI is defined as a presence of gas in the bowel wall[1, 2]. Two main theories have been postulated namely mechanical and bacterial theories. The first theory is suggested after gas dissection into the bowel wall from either the intestines or lungs via the mediastinum. Meanwhile, the latter occurs after gas-forming bacilli entering the submucosa through mucosal rents or increasing the mucosal permeability and producing gas within the bowel wall. CECT is the most sensitive imaging modality for identification of PI[2].

PI can be categorised into two, either benign or life-threatening causes[2]. It is always a diagnostic dilemma to differentiate between those two in a radiological perspective. Worrisome CT imaging features for PI includes soft tissue bowel wall thickening of more than 2 mm, peri-intestinal soft tissue fat stranding, free peritoneal fluid, abnormal bowel wall enhancement, presence of atherosclerosis and vascular occlusion[3, 4]. However, imaging features which include the greater extent of pneumatosis, normal bowel wall and pneumomediastinum favour to benign causes of PI[3]. Essentially it is important to determine benign against life-threatening PI, particularly colonic perforation because the treatment is significantly different. The correlation with clinical history, physical examination, and laboratory test results are the best indicator for subsequent management as well as to avoid unnecessary intervention.

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GOOD TO READ

The Possible Culprit of Obesity in Malaysia – *'Pisang Goreng'*!

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Obesity has become a global health issue, not to mention Malaysia, which topped over the list of countries in Asia. On World Health Day in 2019, the World Health Organization (WHO) announced that 64% of the male population and 65% of the female population in Malaysia are either obese or overweight[1]. The ringing of alarm is tremendously loud in the silence. Depending on each of us, this can be an issue that we laugh over or a kind but severe urge for us to take a step backwards, observe, and self-reflect.

Malaysia is well known for its wide variety of local cuisine, which delights both the tourists and the locals. The ubiquitous accessibility of cheap and succulent food, especially snacks, can be the culprit of the rising prevalence of obesity in Malaysia. In 2013, the Harvard School of Public Health had addressed on toxic food environment being one of the factors of obesity[2]. In Malaysia, there are several studies on overweight and obesity based on the food environment by settings – families[3], neighbourhoods[4], school[5,] and worksites[6]. What if Malaysians are being brought up in a way that is way too close to banana fritter locally known as '*pisang goreng*' in every stage of their life from being children to adults, adding extra kilograms on the weighing scale? A study done in Mexican cities found that body-mass-index is significantly associated with the availability and accessibility of the food[7].

According to Guidance on Calories for 200 Types of Food[8] produced and published by the Ministry of Health of Malaysia, one piece of '*pisang goreng*' at 65 g contains 129 calories. Having two small cute pieces of them is almost equivalent to a plate of chicken rice at 250 g – is not it daunting to know this fact? In Malaysia, the vendors of '*pisang goreng*' had six customers in 2 hours[9], yet we do not know how many pieces of '*pisang goreng*' will be taken away by each customer. The only thing we can be sure of is that the person will probably take away with more than two pieces of '*pisang goreng*' since they are always sold in bulk.

Imagine that it is 4.00 p.m. now. Somehow the stomach is reminding that it has cleared off the havoc from lunch and cannot be readier to embrace some snacks. So, what is the first thing that comes to mind? Indulging with '*pisang goreng*' with its crispy covering and sweet, soft, and hot filling along with a cup of iced coffee when you are sitting in the air-conditioned room is undoubtedly a more comfortable choice than working out on your clumsy body and sweating. What is more, this privilege can be enjoyed by anyone regardless of their income, as '*pisang goreng*' is not only cheap but also handy to grab in every little corner of Malaysia. Banana fritter is inevitably the best option if someone is looking for cheap yet yummy food that keeps the tummy full when he is on a tight budget.

It may seem unfair to point our fingers towards something innocent and lifeless as such '*pisang goreng*', but the fact that Malaysia is rife with cheap but delicious local snacks is one of the aspects upon which we need to reflect. Self-control is essential, but when it has come to a point when the citizens are no longer paying attention to pieces of advice given by the government and selectively choose to neglect the comorbidities and the economic burden that potentially come together with obesity – tackling other aspects for possible changes may help. It is time to make a difference before we persistently top over other countries for the coming decades.

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