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CASE REPORT

Case Series of Pancytopenia Secondary to Pernicious Anaemia

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ABSTRACT

Pernicious anaemia is an autoimmune disorder where vitamin B_{12} deficiency is caused by autoantibodies that interfere with vitamin B_{12} absorption by targeting intrinsic factor or parietal cells or both. It is commonly associated with anaemia, rarely pancytopenia. Here we reported two cases of pancytopenia due to undiagnosed pernicious anaemia. First case was a 26-year-old man presented with lethargy and reduced effort tolerance, associated with postural giddiness and palpitation. Clinically, he was pale with no other findings. On blood investigations, the patient was diagnosed pancytopenia secondary to pernicious anaemia. He was treated with daily subcutaneous injection of vitamin B_{12} cyanocobalamin 1 mg for one week followed by weekly injection for a month and subsequently with lifelong monthly subcutaneous injection. After receiving 2 weeks of B_{12} replacement, his full blood count had normalized and his symptoms resolved. Second case was a 65-year-old man presented with yellowish discolouration of the eyes with lethargy. On examination, he was pale with jaundice. On blood investigations, the patient was diagnosed pancytopenia secondary to pernicious anaemia. He was started with intramuscular injection of 1000 mcg vitamin B_{12} replacement daily for one week followed by monthly for 6 months. After one week of B_{12} replacement, his full blood count had normalized. He was started on lifelong 3 monthly injections of vitamin B_{12} replacement and he remained symptom free. Patients with pernicious anaemia often present with general signs and symptoms which occur insidiously. It is important that early diagnosis is made to avoid harmful complications such as neuropsychiatric disorders.

INTRODUCTION

Pernicious anaemia is an autoimmune-related disorder which mainly affects the elderly population (age over 60). It was first described by Thomas Addison in the year 1855 and subsequently being termed as pernicious anaemia in the year 1872 by Biemer[1]. The word 'pernicious' implies that it was once a harmful and deadly disease without treatment interventions[2]. It is characterized by atrophic gastritis and the destruction of gastric parietal cells causing impairment of intrinsic factor production. As a result, this obstructs the formation of vitamin B_{12} – intrinsic factor complex in the stomach, leading to malabsorption of vitamin B_{12} in the ileum. In humans, vitamin B_{12} is mainly obtained through diet via animal products such as liver, oysters, eggs, etc. In healthy individuals, vitamin B_{12} functions as a co-enzyme in the re-methylation of homocysteine to methionine. Meanwhile, N5-Methyl-tetrahydrofolate is converted to tetrahydrofolate, providing substrates for the replication of DNA in the cells[2]. In vitamin B_{12} deficiency, the above reaction is impaired. This causes the accumulation of N5-Methyl-tetrahydrofolate in the cells, leading to depletion of tetrahydrofolate which is needed for purine and thymidylate synthesis. The clinical features of pernicious anaemia often involve the rapidly dividing cells and organ systems which are metabolically active[3]. Thus, haematological and nervous systems are the two primary systems involved in the disease process. Nowadays, increased cases of pernicious anaemia are being diagnosed, owing to the technological advancement and expertise that we have today. Hence, most of the patients are diagnosed with mild to moderate anaemia. In severe form, patients can present with neuropsychiatric symptoms which are often irreversible[3].

CASE PRESENTATION 1

A 26-year-old Chinese man with no co-morbid, presented with lethargy and reduced effort tolerance for the past three months. This was associated with the presence of postural giddiness and palpitation for a similar period of time. Clinically, he was pale with no jaundice, hepatosplenomegaly or lymphadenopathy. A serial of blood investigations were performed on admission as shown in Table 1. According to blood test and peripheral blood film reports, this patient was diagnosed as pancytopenia secondary to pernicious anaemia. He was treated with daily subcutaneous injection of vitamin B_{12} cyanocobalamin 1 mg for one week followed by weekly injection for a month. After receiving 2 weeks of B_{12} replacement, his repeated haemoglobin count was 13 g/dL, total white cell count 5×10^9/L and platelets 300×10^9/L and all of his symptoms resolved. He was started with lifelong monthly subcutaneous injection.

Table 1 Laboratory results for the patient

Parameters	Results (On admission)	Results (After 2 weeks of B_{12} replacement)	Normal range
Haemoglobin	8.9 g/dL	13 g/dL	13.0 – 18.0 g/dL
Total white cell count	3.41×10^9/L	5×10^9/L	4.0 – 11.0^9/L
Platelet	73×10^9/L	350×10^9/L	$150 – 400 \times 10^9$/L
Mean corpuscular volume (MCV)	100.4 fL	80 fL	76 – 96 fL
Mean corpuscular haemoglobin (MCH)	34.5 pg	30 pg	27 – 32 pg
Red cell distribution width	21.3%	13%	11.6 – 15.0%
Peripheral blood film	Severe pancytopenia with hypersegmented neutrophil seen. No blasts.		
Folate level	22.1 nmol/L	32 nmol/L	7.0 – 39.7 nmol/L
Vitamin B_{12} level	37 pmol/L (Low)	400 pmol/L	145 – 637 pmol/L
Intrinsic factor antibody	Positive		
Parietal cell antibodies	Negative		
Thyroid function test	Normal		
Anti-nuclear antibody	Normal		

CASE PRESENTATION 2

A 65-year-old Chinese man with no co-morbid, presented with yellowish discolouration of the eyes for a month and had a history of lethargy. A serial of blood investigations taken on admission is shown in Table 2. Clinically, he was pale with jaundice. There was no hepatosplenomegaly or lymphadenopathy. According to blood test and peripheral blood film reports, this patient was diagnosed as pancytopenia secondary to pernicious anaemia. He was started with intramuscular injection of 1000 mcg vitamin B_{12} replacement daily for one week followed by monthly for 6 months. After one week of B_{12} replacement, his full blood count had normalized. His repeated haemoglobin count was 12.3 g/dL, total white cell count 4.5/L and platelets 300×10^9/L. His jaundice resolved, and both LDH and indirect bilirubin normalized. He was started on lifelong 3 monthly injections of vitamin B_{12} replacement and he remained symptom free.

Table 2 Laboratory results for the patient

Parameters	Results (On admission)	Results (After 2 weeks)	Normal range
Haemoglobin	6.8 g/dL (Low)	14 g/dL	13.0 – 18.0 g/dL
Total white cell count	3.1×10^9/L (Low)	6×10^9/L	$4.0 – 11.0 \times 10^9$/L
Platelet	50×10^9/L (Low)	342×10^9/L	$150 – 400 \times 10^9$/L
Mean corpuscular volume (MCV)	110.4 fL	80 fL	76 – 96 fL
Mean corpuscular haemoglobin (MCH)	34.5 pg	30 pg	27 – 32 pg
Red cell distribution width	21.3%	13%	11.6 – 15.0%
Thyroid function test	Normal		
Anti-nuclear antibody (ANA)	Normal		
Vitamin B_{12} level	42 pmol/L (Low)	350 pmol/L	145 – 637 pmol/L
Folate level	25 nmol/L	30 nmol/L	7.0 – 39.7 nmol/L
Intrinsic factor	Positive		
Peripheral blood film	Severe anaemia with reticulocytosis, hypersegmented neutrophils seen. No blasts.		
Lactate dehydrogenase (LDH)	1000 U/L (Raised)		114 – 241 U/L
Indirect Bilirubin	100 µmol/L (raised)		6 – 25µmol/L
Alkaline phophatase	Normal		
Alanine transaminase	Normal		

DISCUSSION

In the two cases described above, both patients presented with symptoms of anaemia which occurred insidiously. In the second case, the patient also complained of having jaundice which was likely to be due to ineffective erythropoiesis in the bone marrow. In both cases, diagnosis of nutritional deficiency was suspected when full blood picture showed macrocytic anaemia. Subsequently, serum vitamin B_{12} was found to be low suggesting vitamin B_{12} deficiencies. Vitamin B_{12} deficiency often happens among vegans and patients with pernicious anaemia. In both cases above, they are not vegetarian. Further investigations for pernicious anaemia were worked up. Both showed positive serum intrinsic factor antibody, leading to the diagnosis of pernicious anaemia.

Pernicious anaemia commonly affects the elderly population above the age of 60. However, it does involve younger patients which represent 15% of the cases[2]. This coincides with the first case which the patient was diagnosed at the age of 26 years. Recent hypothesis suggests the role of chronic Helicobacter Pylori infection in the pathogenesis of the disease where autoimmune reaction against the gastric parietal cells was triggered due to molecular mimicry[3]. Pernicious anaemia in adults also associated with other autoimmune diseases, particularly thyroid disease, Addison's disease and vitiligo[3].

Diagnosis of pernicious anaemia requires high index of suspicion. It requires thorough history taking, physical examination and a serial of investigations. The presence of intrinsic factor antibodies in the presence of vitamin B_{12} deficiency confirms the diagnosis of pernicious anaemia. It is present in 50% of patients with pernicious anaemia whereas anti-parietal cell antibodies are present in about 90% of the patients. However, anti-

parietal cell antibodies are not specific in the diagnosis as it is found to be positive in 20% of the population above 60 years[3].

Based on the current knowledge, the sole treatment option for pernicious anaemia is a lifelong parenteral vitamin B_{12} therapy which is available in various forms, namely cyanocobalamin, hydroxocobalamin or methylcobalamin[3]. The recommended dosage is 1000 mcg for once per week for a month followed by monthly injection of the similar dosage for life[4]. Apart from the definitive treatment, patients must also be followed-up regularly for life for regular surveillance of gastric neoplastic lesions and related autoimmune disorders[4].

CONCLUSION

Patients with pernicious anaemia often present with general signs and symptoms which occur insidiously. It is important that all general physicians possess a high index of suspicion when patients present with general symptoms of anaemia. A systematic approach involves careful history taking, thorough physical examination and relevant blood investigations, before a definitive diagnosis is made. It is important that early diagnosis is made to avoid harmful complications such as neuropsychiatric disorders. Furthermore, a long-term joint care with a haematologist is needed to provide high quality of care for the patients.

CONFLICT OF INTEREST

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

CONSENTS

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

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