Case Report

Placental Histopathological Examination in Foetal Sepsis

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ABSTRACT

Intrauterine infection has emerged to be the main and frequent cause of premature delivery and foetal demise. Microorganisms gain entry into the amniotic cavity via ascending route, haematogenous dissemination, retrograde seeding from peritoneal cavity and accidental introduction during invasive procedures. This is a case of foetal loss in utero from a twin pregnancy due to intrauterine sepsis diagnosed through placenta examination. Both maternal and foetal evidences of inflammatory response were demonstrated in the placenta on histology. Microscopically, there were acute chorioamnionitis and villitis as well as abundant gram positive cocci in the foetal blood within placental villous capillaries. The presence of intravascular bacterial organism provides evidence for a conclusive diagnosis of intrauterine sepsis, particularly where the placenta or foetal blood microbiological cultures results are not available or equivocal. More attention should therefore be given when sampling, as pathological evidences of underlying foetal compromise or death could be provided by well-represented placental tissue samples.

Keywords: foetal loss, intrauterine sepsis, villitis, chorioamnionitis

INTRODUCTION

Intrauterine infection has emerged to be the main and frequent cause of premature delivery and foetal demise. Microorganisms enter into the amniotic cavity via ascending route, haematogenous dissemination, retrograde seeding from peritoneal cavity as well as accidental introduction during invasive procedures[1, 2]. More often microbiological laboratory investigations are being done on the suspected cases to determine the causative microorganism. However, as an additional investigation, placenta histopathological evaluation on well-represented samples could be helpful in understanding and ascertaining the cause of foetal death which will be of value in the management of future pregnancies. We present a case of intrauterine sepsis with foetal loss diagnosed through placenta examination.

CASE PRESENTATION

A 31-year-old lady, G2P1 with a twin pregnancy at 20 weeks and one day of gestation presented to the emergency department with one day history of leaking liquor and low grade fever. She also gave a history of previous mild episode of per vaginal bleeding at 2 months of gestation and was prescribed a hormonal medication. The bleeding ceased subsequently and she had stopped taking the medication 2 weeks later. However, she started to have vaginal spotting for the past 3 days prior to admission. There was no history of trauma or abdominal pain. Foetal scan showed growth parameters appropriate for gestational age in both twins and the placenta was monochorionic and diamniotic. Her first child was born four years ago by caesarean section due to poor progress of labour. The previous pregnancy was complicated by late onset pregnancy induced hypertension requiring antihypertensive during labour. The daughter is alive and in good health. On physical examination

her pulse rate was 120 beats per minute and blood pressure was 130/80 mmHg. Both foetal heart beats were detected. Her liquor was clear and the membrane was ruptured. Laboratory investigations showed elevated white cell count (17.75×10^9/L), predominantly of neutrophils. However subsequently in the ward, she developed chills and rigors with temperature of 38.5°C. The twins were spontaneously delivered at 20 weeks and 4 days of gestation with no sign of life. The liquor was foul-smelling.

Microscopic examination of the placentas showed acute chorioamnionitis and funisitis. There were acute villitis (Figures 1a and 1b) with abundant neutrophils within the intervillous spaces of the placenta. Numerous bacterial colonies were present within the foetal villous capillaries (Figures 2a and 2b) in both placentas which were shown to be gram positive cocci. Group B *Streptococcus* was isolated from high vaginal swab and *E.coli* from maternal blood culture. She was treated with parenteral ampicillin and metronidazole.

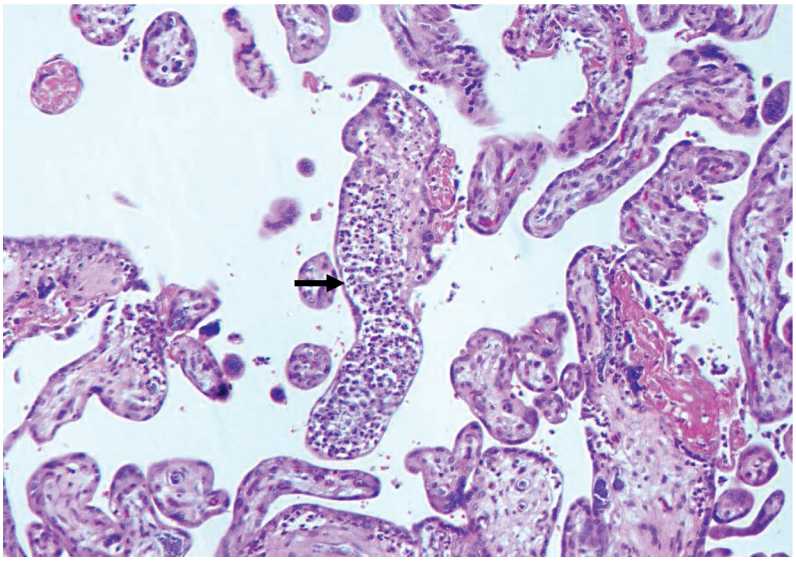

Figure 1a Photomicrograph: Architecture of placental villous tissue. The arrow indicates acute villitis. (Haematoxylin and Eosin stain, ×100 magnification)

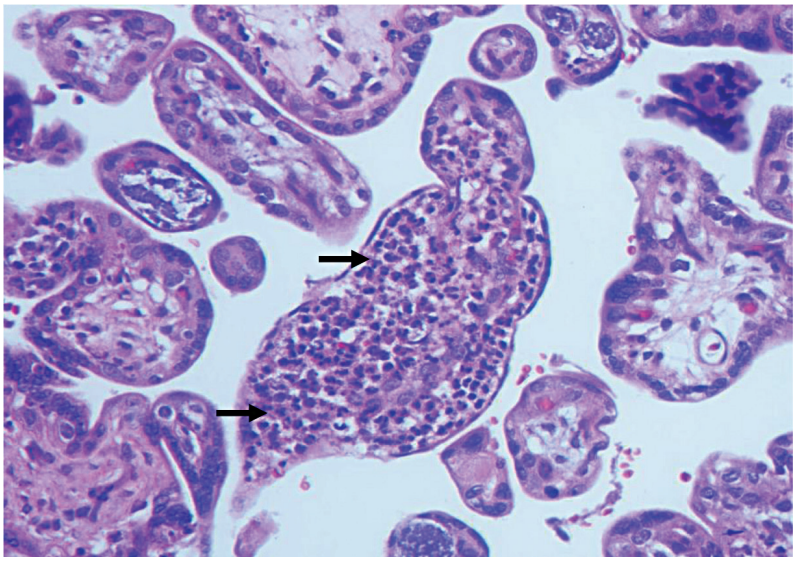

Figure 1b Photomicrograph: Architecture of placental villous tissue. The arrows indicate dense intravillous neutrophils infiltrates. (Haematoxylin and Eosin stain, ×200 magnification)

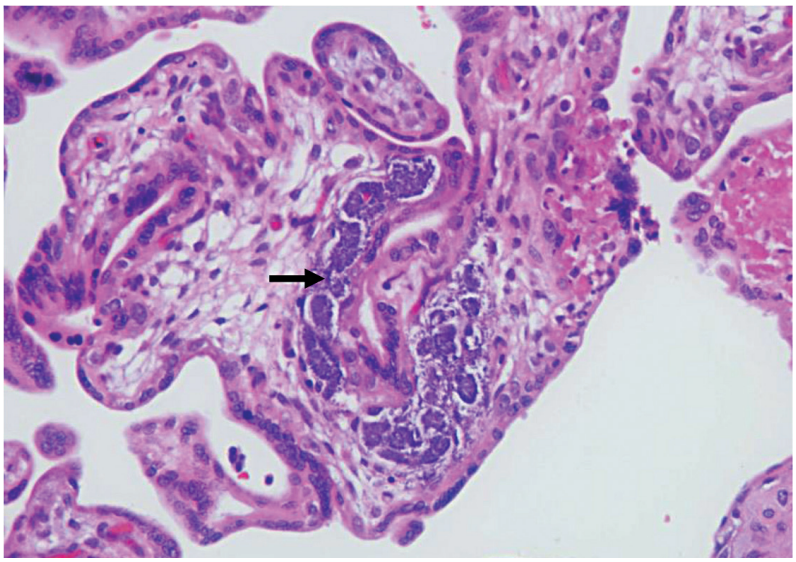

Figure 2a Photomicrograph showing placental villi with intravascular bacterial organism within the foetal villous capillaries as indicated by the arrow. (Haematoxylin and Eosin stain, ×200 magnification)

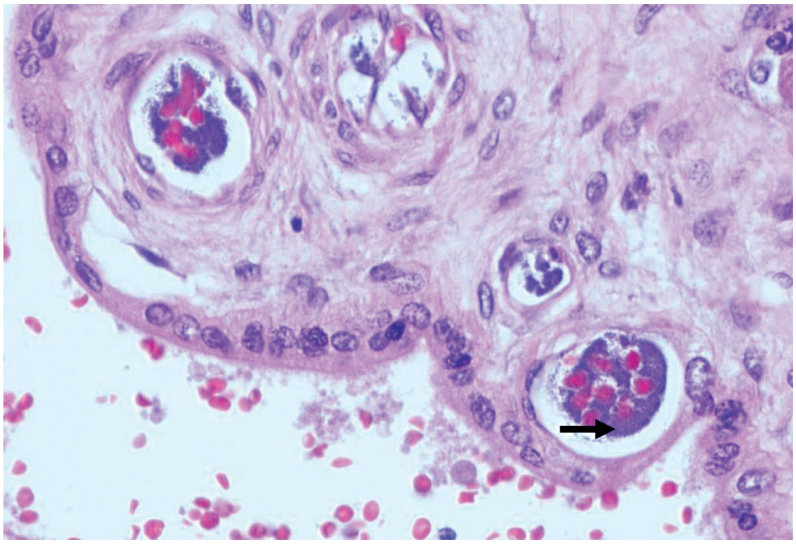

Figure 2b Photomicrograph showing foetal villous capillaries with presence of intravascular bacterial organism as indicated by the arrow. (Haematoxylin and Eosin stain, ×400 magnification)

DISCUSSION

Infection is a well-recognized cause of spontaneous miscarriages and perinatal mortality. The placenta and amniotic membrane are the two important structures preventing the access of organisms to the foetus[1]. A breach in these barriers may lead to amniotic and intrauterine infection. Prematurity, foetal or neonatal sepsis and other related perinatal morbidity are some of the known complications associated with intrauterine infection.

The most common route of intrauterine infection is through ascending infection from the cervicovaginal flora[2]. Microorganisms may also be transmitted to the foetus by haematogenous dissemination, retrograde seeding from peritoneal cavity as well as accidental introduction during invasive procedures[1, 2]. Almost 40% of all premature births are due to intrauterine infection and chorioamnionitis[3]. However, many of the mothers with intrauterine infection are asymptomatic.

Acute chorioamnionitis is an acute inflammatory reaction characterized by presence of neutrophils infiltrates. It usually starts at the point of membrane rupture where it is first exposed to the pathogenic organisms[3]. The other parts of placenta tissue which include chorionic plate, subchorionic space as well as the umbilical cord are also involved depending on the progression of the inflammatory response. Acute chorioamnionitis on histopathology demonstrates evidence of both maternal as well as foetal inflammatory responses[1, 4]. The neutrophils originate from two sources; maternal and foetal. Neutrophil infiltrates in the foetal membrane, subchorionic intervillous spaces and in the maternal blood vessels of deciduas are of maternal origin, while neutrophils seen within the umbilical cord or in the chorionic plate vessels are of foetal origin[4]. The emigration of neutrophils is often in the direction towards the source of infection in the amniotic cavity[1, 4]. In the umbilical cord, neutrophilic emigration takes place in the umbilical vein before the arteries, towards the amniotic surface (funisitis)[4]. The presence of funisitis and inflammation in the foetal vessels signify that the foetus has mounted an immune response[1]. In maternal inflammatory response, the neutrophils migrate from the maternal blood vessels into the deciduas. The resulting deciduitis and decidual bleeding often manifest clinically as vaginal bleeding followed by rupture of membranes[1, 5].

The most significant and important complication of ascending amniotic infection is foetal infection. Aspiration of infected amniotic fluid may cause intrauterine pneumonitis[4]. Foetal sepsis and meningitis are other common sequelae observed during perinatal period[6]. It is reported that 23.5% of chorioamnionitis was detected histopathologically in those with negative amniotic fluid culture[7]. Thus, histopathological evaluation of placental tissue is important and would be helpful in suspected chorioamnionitis with negative culture results[8]. This would capture those cases with subclinical or 'silent' acute chorioamnionitis.

Intrauterine infections are associated with a selected group of high virulence infecting organisms, such as Group B *Streptococcus* (GBS), *Escherichia coli*, *Ureaplasma* sp., *Fusobacterium* sp. and anaerobes[9]. When significantly high quantities of these organisms are present, an inflammatory response will be elicited leading to systemic signs of infection. When maternal and/or neonatal bacteremia complicates intrauterine infection, the two organisms most commonly isolated are the group B *Streptococcus* (GBS) and *Escherichia coli*[9]. These microorganisms are found colonized in the maternal genitourinary tract. Both are important leading causes of neonatal sepsis[3].

GBS commonly causes asymptomatic bacteriuria in pregnant women[6]. Neonates born to colonized mothers are at risk of developing GBS disease. Ascending intrauterine infection usually gives rise to early-onset invasive GBS disease, sometimes resulting in foetal demise[3]. This is in contrast to much later onset of disease when the exposure to GBS is acquired at birth. Microscopic findings of acute villitis and the presence of large colonies of GBS bacteria within the foetal villous capillaries indicate an underlying foetal sepsis[3]. Amongst the gram negative bacilli, *E.coli* is also an important cause of neonatal sepsis. In this case the underlying maternal *E.coli* bacteraemia could have increased the risk of invasive intrauterine GBS infection as demonstrated in the histopathological findings.

The entry of microorganisms into the amniotic cavity is associated with high concentrations of pro-inflammatory cytokines in the amniotic fluid. Examples of the cytokines are interleukin-1, tumour necrosis factor, interleukin-6, interlukin-8 and a gelatinase, matrix metalloproteinase-9[10]. It was also found that funisitis and chorionic vasculitis are associated with elevated foetal blood level of interleukin-6[11]. Current researchers are focusing on the effects of these elevated cytokines on foetal tissue and infant morbidity[4]. Some studies emphasized on the associations of elevated cytokines with cerebral palsy, asthma and autism[12, 13].

Routinely, a positive foetal blood culture result is required to confirm the diagnosis of intrauterine sepsis as the cause of foetal demise. In this case, both maternal and foetal evidences of inflammatory response were demonstrated on placenta histology. The demonstration of gram positive cocci through placenta examination provided a definitive evidence of underlying intrauterine sepsis, although placenta and foetal blood culture were not available or inconlusive[14].

Placenta is an invaluable source of information and its histological evaluation is of equal importance to other ancillary investigations. This is especially so when it concerns intrauterine death of a foetus. For Muslim mothers, adequate tissues sampling are necessary before the placenta is returned to them for burial purposes. This is to ensure that all lesions are being represented for determining a more definite underlying cause of foetal compromise or demise.

CONCLUSION

This case illustrates the importance of examination of placenta tissue in cases of foetal losses. Both maternal and foetal evidences of inflammatory response were demonstrated in placenta on histopathological examination. The demonstration of gram positive cocci within the foetal blood through placental examination provides a definitive evidence of underlying intrauterine sepsis. Pathological evidences of underlying foetal compromise or death could be provided by well-represented samples of placental tissue. Examination of placenta tissue is of equal importance to other investigations as it may provide the only evidence of foetal infections.

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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 written consent is available for review by the Chief Editor.

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