Group A *Streptococcus* puerperal sepsis with invasive neonatal infection: A fatal case

Siti Hafsyah Mohd Hariri, MBBS[1,2], Nor Rosidah Ibrahim, MBBS[2,3], Noraida Ramli, MBBS[2,3], Ahmad Amir Ismail, MMed[2,4], Anani Aila Mat Zin, MPath[2,5], Khalid Hajissa, PhD[1,6], Zeehaida Mohamed, MPath[1,2]

[1]Department of Medical Microbiology and Parasitology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, [2]Hospital Universiti Sains Malaysia, Universiti Sains Malaysia Kampus Kesihatan, Jalan Raja Perempuan Zainab 2, Kota Bharu, Kelantan, [3]Department of Pediatric, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, [4]Department of Obstetrics and Gynaecology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, [5]Department of Pathology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, [6]Department of Zoology, Faculty of Science and Technology, Omdurman Islamic University, Omdurman, Sudan

SUMMARY

Neonatal invasive Group A *Streptococcus* (GAS) infection is a rare occurrence nowadays. Prior maternal vaginal colonization is an important factor in early neonatal disease. We report a case of invasive and fatal infection in a neonate. At Day 1 of life, a term baby was found to be lethargic, with poor feeding, and later became unresponsive. Consequently, the baby was immediately brought to the Emergency Department of Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan via ambulance. Despite the active resuscitation efforts in the hospital, the baby died. An autopsy was carried out to determine the cause of death. The mother was noted to have puerperal pyrexia secondary to vaginal discharge. Her high vaginal swab culture was positive for GAS. GAS was also isolated from the intracardiac blood, pleural fluid, peritoneal fluid, and umbilical swab of the baby, giving evidence to the aetiology of the mortality. Vaginal colonization of GAS is an important factor for high morbidity and mortality for both mother and infant due to its invasiveness and virulence.

KEYWORDS:
Streptococcus pyogenes, Group A Streptococcus, GAS, neonate, puerperal sepsis

INTRODUCTION

Streptococcus pyogenes, also known as Group A *Streptococcus*, is a Gram positive, beta-haemolytic bacteria, and a significant human pathogen capable of causing broad range of infections from mild infections such as pharyngitis and impetigo to severe infections like necrotizing fasciitis and streptococcal toxic shock syndrome (STSS). An immune-mediated non-pyogenic complications such as acute rheumatic fever, post streptococcal acute glomerulonephritis, and post streptococcal reactive arthritis are also parts of the disease spectrum. In the United States, the incidence of Group A *Streptococcus* postpartum infection is 6 per 100 000 live births with 2% maternal mortality.[1] It is estimated that there is a 20-fold increased risk of invasive GAS in pregnant women compared to non-pregnant women.[2] The reported prevalence of vaginal-rectal colonization of GAS during pregnancy is very low as compared to Group B *Streptococcus*, 0.03% and 20% respectively.[3] Due to the rarity of GAS vaginal colonization and its low incidence of postpartum infection, a screening-based approach is not commonly done. We report here a case of invasive neonatal streptococcal disease resulting in a neonatal death and simultaneously illustrated a classical case of puerperal sepsis in her mother.

CASE PRESENTATION

A term baby girl, birth weight of 2.46 kg, was delivered by spontaneous vaginal delivery with an Apgar score of 9 in 1 minute. The baby was discharged home the next day. However, at home, the baby was not breastfeeding well throughout the evening until night. At 26 hours of life, the baby became more lethargic and grunting, hence brought to a hospital. Upon arrival at the Emergency Department of Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan, the baby was unresponsive with neither spontaneous breathing nor heart rate detected. Cardiopulmonary resuscitation was immediately commenced and the baby was intubated. The blood sugar level was low 2.3mmol/L hence 12 mL D10% bolus and 60 mL normal saline were administered intravenously. However, after 30 minutes of resuscitation, there was no return of spontaneous circulation and the baby succumbed. The baby was subjected to post-mortem examination due to undetermined cause of death.

At post-mortem examination, the external appearance of the baby was unremarkable. However, upon opening of the thoracic cavity, there was a diffuse area of patchy light brown discolouration over the inferior part of the right upper and middle lobe of the lungs. The pleural cavity was filled with a significant amount of thickened and cloudy fluid. There was presence of dilated alveolar air spaces at the periphery of the left lung with area of petechiae seen on the surface of the superior part of the left upper and lower lobes. The brain, lung and liver tissues were sent for histopathological examination. The histopathology result of the lung tissue showed scattered cocci-shaped bacteria and patchy intra-alveolar fibrinopurulent exudates with associated septal wall necrosis (Figure 1) as well as evidence of congestion in the background. Sections from the brain and liver showed

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Corresponding Author: Prof. Dr. Zeehaida Mohamed
Email: zeehaida@usm.my

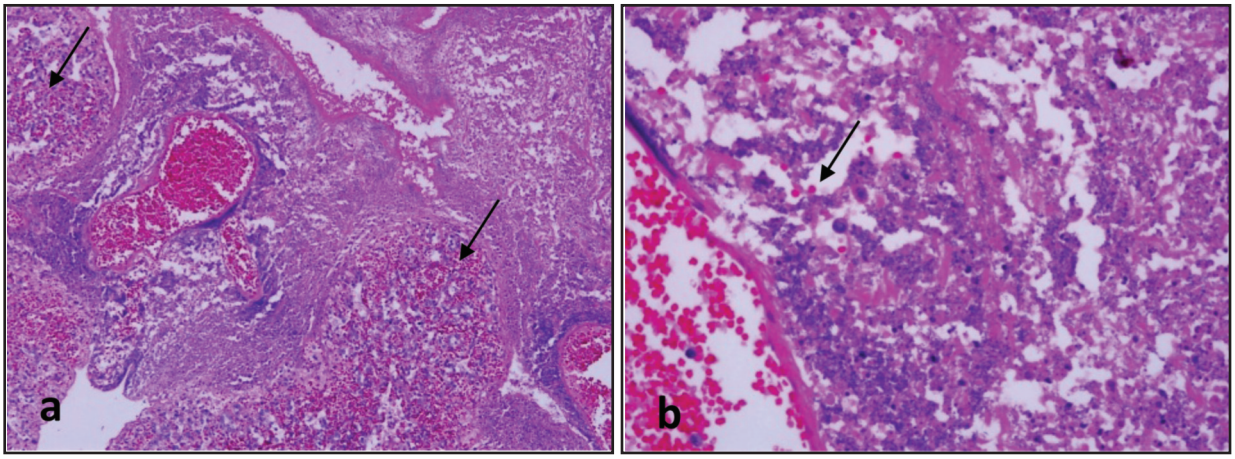

Fig. 1: Histopathological images showing fibrinopurulent exudates and scattered cocci-shaped bacteria (arrows) (a) Haematoxylin and Eosin (H&E) stain, magnification x 100, (b) H&E stain, magnification x 400.

congested tissues with no evidence of infection. Bacterial cultures of the peritoneal fluid, pleural fluid and intracardiac blood were positive for Group A *Streptococcus*.

Retrospectively, the baby was born to a 24-year-old housewife, a primigravida at 37 weeks' period of amenorrhoea. Apart from symptoms of labour, she also complained of vaginal itchiness associated with vaginal discharge for 6 days. She had a risk factor for gestational diabetes mellitus (DM) with family history of DM and hypertension. However, her oral glucose tolerance test (OGTT) done twice were normal. Her body mass index (BMI) at booking was 34.6.

She was admitted in the active phase of labour. On vaginal examination, her cervix was effaced with 5cm dilatation. Per speculum examination revealed minimal vaginal discharge and high vaginal swab sample was taken for culture. Later, she experienced spontaneous rupture of membrane with clear liquor, and labour progressed well in five hours without any complications. Finally, she delivered a baby girl via spontaneous vaginal delivery. Postpartum, she was afebrile, able to tolerate orally and was discharged home with her baby girl in the afternoon.

At day three postnatal, the mother experienced fever associated with chills and rigors for two days. There was no other symptom such as abdominal pain or foul smelly vaginal discharge. She visited local health clinic and was referred to a tertiary hospital for puerperal pyrexia. Her temperature was 39.9°C and tachycardic with heart rate of 148 bpm. However, other vital signs were stable. Transabdominal sonography was unremarkable. Her arterial blood gas showed respiratory alkalosis and the full blood count examination showed an elevated total white count of 22 x 10^9/L, with 90% neutrophils, haemoglobin level of 11.9 g/dL and platelet count 244 x 10^9/L. Her C-reactive protein (CRP) was more than 200 mgL. Her renal profile and coagulation study were normal. Her high vaginal swab culture was positive for Group A Streptococcus. However, the blood culture did not grow any organism. She was treated with IV piperacillin-tazobactam and clindamycin for 10 days and was discharged well. On the next clinic visit, she had no further complaints and was discharged from follow-up.

DISCUSSION

Neonatal infections are commonly caused by Group B *Streptococcus* and *Escherichia coli*. Group A *Streptococcus* is a rare causative agent but the infection can be invasive and fatal.[4] Invasive Group A streptococcal disease was defined as isolation of GAS from a normally sterile sites such as blood, CSF, joint, pleural and peritoneal fluid. The incidence of invasive neonatal GAS infection in the United Kingdom was 1.5 per 100 000 person years while in the United States of America, an increasing incidence of invasive GAS infections in children from 0.16 to 0.37 per 1000 admissions was observed within the 7-year period.[4,5]

The major virulence factor for GAS infection is M protein, encoded by emm gene. More than 125 emm gene types have been discovered, with certain types causing specific diseases. The predominant M serotypes causing invasive infections are M1 and M3 types. M protein is a major surface antigen that is capable of inhibiting the immune response and interferes with phagocytosis.[6]

Almost half of infants less than 3 months or early neonatal sepsis diagnosed with invasive GAS infection are severely ill, with the most common clinical presentation were respiratory distress, bacteraemia and non-specific signs of sepsis with rapid deterioration and high mortality similar to this case.[4,6] The overall mortality rate was as high as 31%.[6] Vertical transmissions via ascending spread from the vagina colonized by *Streptococcus pyogenes* during delivery is a possibility in this case. As reported by a previous study, vertical transmission accounted for 75% cases of early onset neonatal GAS disease.[6]

The management of severe invasive GAS disease involves mainly specific antimicrobial therapy, supportive treatment with fluid and electrolytes, minimizing or neutralizing the toxin effects and other measures on specific situation for example controlling the source of infection by extensive

surgical debridement in deep-seated abscess. Penicillin remains the treatment of choice and no resistance strain to this antibiotic has been encountered yet. The addition of clindamycin is beneficial especially in the case of streptococcal toxic shock as it can suppress exotoxin and M-protein production by GAS. Besides, it has longer half-life with no antagonist effect with penicillin.[7]

Unlike *Streptococcus* Group B that is common in causing neonatal sepsis, more extensive screening measures and aggressive maternal prophylaxis has been adopted as compared to maternal GAS, which is rarely detected due to its low prevalence of vaginal colonization, and rarely cause maternal and neonatal disease. So far, there has been no specific guidelines and recommendations on chemoprophylaxis for maternal GAS vaginal colonization or asymptomatic carriage. However, considering its nature of invasiveness and interaction with immunocompromised host, resulting in high morbidity and mortality, a more aggressive approach and intrapartum antibiotic prophylaxis should be considered whenever GAS is isolated from pregnant women.

Puerperal sepsis due to GAS infection may present with two or more of the following clinical manifestations: pelvic pain, fever, abnormal vaginal discharge, abnormal smell/foul odour discharge or delay in uterine involution.[7] Some of the identified host risk factors for perinatal infections are prolonged ruptured of membranes or prolonged labour, pre-existing comorbidities such as malnutrition, diabetes, severe anaemia, obesity, prior vaginal infections as well as repeated vaginal examinations and Caesarean section.[2] In our case, the mother had no identified risk factors except maternal obesity. It was postulated that women who are obese had elevated levels of inflammatory cytokines and monocytes, resulting in chronic state of inflammation causing the immune systems to be less responsive to the threat of infection and diminished their ability to mount an acute cytokines response to an infection.[8]

The less severe clinical presentation of the mother raised possibility of prior colonization or state of asymptomatic carriage before the onset of delivery as most patients with GAS colonization are asymptomatic. GAS can become the colonizer of oropharyngeal tract, vagina and even skin. The mechanism of colonization is poorly understood, it is suggested that GAS virulence factors and certain mutations leads to its ability to escape phagocytosis, simultaneously increasing its capacity in adherence to host cells.[9] In this patient (mother), the most striking symptom that she presented was per vaginal discharge several days before labour. Although this may appear common among pregnant ladies, this history should not be taken lightly. A study on pregnancy-related *S. pyogenes* revealed that 38.5% of patients with early puerperal sepsis presented with purulent vaginal discharge. GAS was isolated from the genitourinary tract in 76.9% of the cases, suggestive of prior vaginal colonization.[1] In conclusion, although routine screening for asymptomatic vaginal GAS carriage in pregnancy may not be indicated, isolation of GAS from vaginal specimens should prompt early clinical management and antimicrobial therapy to both mother and infant. However, this requires high degree of suspicion with optimum approach and management. Although it is quite challenging to differentiate normal leucorrhoea of pregnancy with pathological vaginal discharge in pregnancy, measures should be taken to suspect and detect GAS, so that an appropriate treatment can be initiated to prevent any devastating complications during the postnatal period.

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CONSENT

Written informed consent was obtained from the patient for publication of this case report and all accompanying images.

CONFLICT OF INTEREST

The authors state that there is no conflict of interest to declare.

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