Spotted Fever Rickettsial Infection in Pregnancy Causing Acute Hepatitis, Fatal Postpartum Hemorrhage and Possible Vertical Transmission

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

We present a rare case of a 31-year-old pregnant mother in 37 weeks of gestation who presented with a 3-day history of vomiting, epigastric pain, and icterus, subsequently diagnosed as a rickettsial disease in pregnancy (with positive IgG titer for SFG) complicated with hepatitis, coagulopathy, pulmonary hemorrhage, and post-partum hemorrhage, who expired despite intensive care management. The newborn baby also had high IgG titer for SFG suggesting a vertical transmission of the disease and recovered following treatment with chloramphenicol. The SFG rickettsial infection can cause diverse clinical manifestations in pregnancy including acute

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2. PRESENTATION OF CASE

A 31-year-old mother of one child in her 2nd pregnancy at 37th week of gestation was admitted with a history of vomiting for 3 days, epigastric pain, loose stools, yellowish discoloration of eyes, and chills without fever or bleeding manifestations. No history suggestive of pre-eclampsia. Her first, second, and third trimesters were uneventful up to 35 weeks of gestation when she was hospitalized and discharged after managing acute gastroenteritis.

On examination, she was icteric, with no pallor in the conjunctiva. The pulse rate was 112 beats /minute with a blood pressure of 110/61 mmHg. The abdominal examination was compatible with 37 weeks of gestation. Right hypochondriac tenderness was detected on palpation. The tendon reflexes were normal. No fetal compromise was detected during the initial assessment.

The investigations revealed- white blood cell count of 14.11x10^9/l (4.5-11 x10^9/l) with 77.9 % neutrophils, hemoglobin 9.5g/dl(12-15.5), and platelet of 35x10^9/l(15-400x10^9). The C-reactive protein was 26.94mg/dl(<5mg/dl) alkaline phosphatase 488U/l (44-147) INR- 3.5 (0.9-1.2)and APTT was 86 sec (control 30). The blood picture was compatible with the liver disease without features of microangiopathic hemolytic anemia. Dengue NS1 antigen was negative. Total bilirubin 231micromol/l(1.7-20.5), Conjugated bilirubin 171micromol/l(<5.1), and unconjugated bilirubin 60 micromol/l, SGPT 18U/l(7-56), SGOT 217 U/l(8-45).

On day 6 in ICU, she developed fresh oral bleeding and chest X-Ray showed features of RHE. She was started on Doxycyclin 100 mg orally 4 times, IM cortisone 250 mg, and IM tranexamic acid. However, on the evening of the same day, she had a sudden gush of vaginal bleeding that required laparotomy with total abdominal hysterectomy with bilateral internal iliac artery ligation to control bleeding. Severe coagulopathy and surgical site oozing persisted despite ROTEM, FBC, and PT/INR-guided massive blood transfusion. Further examination of limbs showed vasculitic macular rash. Based on these new developments, evidence of environmental exposure to tick bites and epidemiological factors possible rickettsial infection was contemplated. Therefore, a blood sample was sent to the Faculty of Veterinary Medicine, the University of Peradeniya where diagnostics are available for testing immunofluorescence antibodies (IFA) for rickettsia. She had a positive (IFA) IgG titer (1:256) for Rickettsia coronii antigen suggesting spotted fever rickettsial infection. Other tests performed to identify infective causes of hepatitis including Hepatitis A, B, C, Leptospirosis yield negative results. She was started on Doxycyclin in addition to other antibiotics and the liver failure regime was continued with coagulation correction.

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suggestive of pulmonary hemorrhages despite repeated correction of coagulation, liver failure regime, and plasmapheresis. The patient’s condition gradually deteriorated with the development of microangiopathic hemolytic anemia, coagulopathy, septic shock, and severe hypoxia despite advanced ventilatory strategies, hemodynamic and organ support. On day 9 in ICU, the patient expired, and the postmortem of the deceased revealed subendocardial hemorrhages in the left ventricle and blood-stained fluid in the pleural cavity with pulmonary hemorrhages and pulmonary edema. The harvested tissues from the brain, liver, lungs, kidneys, heart and skeletal muscle were tested with PCR molecular diagnostics for rickettsial DNA. The PCR was tested positive for spotted fever rickettsiae in the brain and heart.

Concerning the neonate as the baby didn’t cry at birth neonatal resuscitation and intubation were done and was admitted to the sick baby unit (SBU). Her temperature was 36.6°C, and capillary refilling time was 3-4 seconds. She had spontaneous respiration with poor activity and hypotonia. The random blood sugar was 37 mg/dl. The baby needed assisted ventilation for four days. During SBU stay metabolic acidosis was noted and corrected with bicarbonate, moreover, inotropic support was provided with intravenous dobutamine and dopamine. Neonatal convulsions were noted on day 01 and an ultrasound scan brain was performed on the 7th day which showed grade one periventricular leukomalacia. The follow-up scan on day 14 showed prominent third ventricles. In addition, bilious vomiting with poor feed tolerance was noted on day two. There were features of sepsis and broad-spectrum antibiotics were started with intravenous C. penicillin, cefotaxime for 14 days, and intravenous ceftazidime for 7 days. As there was a suspicion of rickettsial infection of the mother, a blood sample of the baby was tested for IFA and found strongly positive IgG (1:256) for R. Coronii antigen suggestive of vertical transmission of rickettsial infection. Thereafter, the baby was treated with IV chloramphenicol for completion of ten days. With chloramphenicol, the baby started improving. The initial high liver function tests (AST 667 & ALT 189 on day one) gradually reduced with treatment (AST of 34.7 & ALT of 13.6). The ultrasound scan of the abdomen and kidney ureter and bladder was unremarkable. The management was further challenged by the hemorrhagic disease of the newborn which appeared on the 6th day with a platelet count of 167x10^6/l and an INR of 1.83, it was managed with IV vitamin K. Ultimately the newborn was discharged in good health from the SBU. Further, follow-up showed normal growth and development of bay under the care of stepmother.

3. DISCUSSION

This case highlights two aspects of spotted fever rickettsial infection namely acute severe hepatitis in the mother and vertical transfer of the infection in the newborn. The initial illness of the mother was just 3 days vomiting and icterus, very suggestive of hepatitis in pregnancy that progressed to develop severe coagulopathy and massive postpartum bleeding. The mother succumbed to the illness and molecular studies detected positive PCR for spotted fever rickettsiae in the brain and heart confirming the diagnosis. There was a delay in diagnosis and treatment with appropriate anti-rickettsial antibiotics as it was a dilemma at the outset heavily considering other causes of hepatitis in pregnancy. However, the newborn baby was lucky to survive even with considerable delay in starting Chloramphenicol despite the baby had hepatic dysfunction, convulsions, and metabolic acidosis. At this juncture, the question arose about how the baby got the rickettsial infection. It may be postulated that it was either transplacental transmission or during labor with direct contact with infected maternal blood. Unfortunately, the placenta was not available for PCR studies and neonatal tissues were not tested for rickettsia.

Commonly, the spotted fever rickettsial infection has a typical picture of cutaneous manifestations with arthritis frequently involving ankle joints [5,6]. Delay in diagnosis could cause fatal multiple organ dysfunction involving liver [7,8]. It is not uncommon to see atypical presentations where typical rash-making dilemmas in diagnosis [5]. Among these presentations, acute hepatitis or liver dysfunction as the primary clinical problem has occurred even though unreported. According to the international literature, both Rocky mounted spotted fever and Mediterranean spotted fever has caused liver dysfunction [7,8]. Spotted fever is a group of infections caused by many species of rickettsial agents distributed widely in the world [1,2]. There may be more than one species of rickettsial agents existing in Sri Lanka causing different clinical manifestations [5,6].
In an endemic setting, pregnant mothers are at risk of spotted fever rickettsial infections where the clinical picture could be atypical. Even in well-known Rocky Mountain spotted fever and its manifestations in pregnancy confines to few reports only [9]. Therefore, our index case is an eye-opener for obstetric practice where treatable infection should not be overlooked. The spotted fever rickettsial infection is treatable if detected early and the most appropriate antibiotic would be Chloramphenicol given intravenously [3]. In Sri Lanka, rickettsial diagnostics are available only in few research laboratories. Despite such constraints, we were able to do both IFA and PCR to confirm the diagnosis.

As tick infestation is common in both domestic and peridomestic animals, tick bites in humans happen both in detected and undetected manner [10]. It is most unlikely that the new borne in this report got the infection from a tick bite. There is a report of newborns catching scrub typhus where authors thought it was due to vector bites after birth [11]. A similar report is available about Japanese spotted fever [12]. As there are hardly any reports about vertical transfer of rickettsial infection in humans, this case could be the first to document a such transmission.

**CONCLUSION**

In conclusion, we wish to highlight the primary hepatic involvement in some cases of spotted fever rickettsial infection, and in pregnancy, it could be overlooked considering other causes [13] leading to maternal death. We postulate possible vertical transmission of the infection to the neonate causing complex morbidity. Experimenting in animal models and more clinical studies are needed to ascertain vertical transmission of rickettsial infections. We stress rickettsial infections are treatable and need extra vigilance for early diagnosis.

**DISCLAIMER**

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

**CONSENT**

As per international standard or university standard, patients’ written consent has been collected and preserved by the author(s).

**ETHICAL APPROVAL**

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

**REFERENCES**


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