Case Report

An unusual case of fatal pulmonary hemorrhage in pregnancy

N. L. A. Dissanayake[1], Dushantha Madegedara[2]

[1]Senior Registrar in Respiratory Medicine, [2]Consultant Respiratory Physician, Teaching Hospital, Kandy, Sri Lanka

ABSTRACT

Rickettsial diseases are common in Srilanka. The spotted fever group of rickettsiae presents in many ways, including very severe disease causing significant morbidity and mortality. A regional variation of the *Rickettsia conorii* subspecies and differences in clinical presentations are reported. This case describes disseminated *Rickettsia conorii* infection in a pregnant woman presenting with endocarditis.

KEY WORDS: Endocarditis, pregnancy, pulmonary hemorrhage, *Rickettsia conorii*, zoonotic infections

Address for correspondence: Dr. Dushantha Madegedara, Consultant Respiratory Physician, Teaching Hospital, Kandy, Sri Lanka.
E-mail: dmadegedara@yahoo.com

INTRODUCTION

Rickettsia are obligatory, intracellular, small gram-negative bacteria associated with eukaryotic hosts. They are traditionally divided into three groups: the spotted fever group, the typhus group and the scrub typhus group. The spotted fever results from a large group of tick-, mite- and flea-borne zoonotic infections that are caused by closely related rickettsiae. *Rickettsia conorii* has been identified as the agent causing Mediterranean spotted fever (MSF). A variety of geographically distinct types of *R. conorii* have been described that cause variable clinical presentations different from typical MSF. The *R. conorii* complex includes *R. conorii* subsp. *indica* which causes "Indian tick typhus". Fatal outcomes are common in severe disease.

CASE REPORT

A 27-year-old primigravida with a 16–week history of amenorrhea and respiratory failure was transfered to a tertiary care center. She had high-grade fever for 8 days prior to the transfer and had developed an erythymatous maculopapular rash on day 4 of the illness, involving the trunk initially, later extending to the palms and soles [Figure 1].

A persistant dry cough, not associated with hemoptysis, was noticed on day 5. She developed a progressively worsening dyspnea with bilateral ankle edema not associated with oliguria or orthopnea. Her condition deteriorated rapidly, warranting intubation for respiratory failure and transfer to a tertiary care center.

On admission to the tertiary care center ICU, her oxygen saturation was 95% with an FiO_2 of 0.5. The blood pressure was 86/44 mmHg while on Dobutamine and Dopamine. The patient also had tachycardia (128 beats/min) without any significant ST segment changes on the ECG.

The patient was pale, anicteric and had no lymphadenopathy. The lungs had bilateral diffuse coarse crepitations. Cardiac murmurs were not audible. Central venous pressure was normal. The examination of the abdomen revealed a 1-cm, firm hepatomegaly with mild ascites.

The chest X-ray showed bilateral difffuse opacitites [Figure 2]. The blood urea measured 8.7 mmol/dl with a serum sodium of 140 meq/l and a pottasium of 5.0 meq/l. Full blood count showed neutrophilia of 78% in a total of 14.4×10^9 l^{-1}. Hemoglobin was 7.4 g/dl with a mild thrombocytopenia of 160,000μl^{-1}. The blood picture revealed normochromic normocytic anemia with no evidence of disseminated

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.83979

intravascular coagulation (DIC). The international normalized ratio (INR) was 0.96. The serum glutamate oxaloacetate transaminase (SGOT) activity was 42 U/l and serum glutamate pyruvate transaminase (SGPT) activity was 28 U/l. Urine examination revealed + protienuria. It was negative for blood or organisms. The C-reactive protein (CRP) level was 6 mg/dl and the antinuclear antibody (ANA) was negative. The results for blood, urine and tracheal aspirates revealed no significant growth. The HIV serology and tracheal aspirates for H1N1 were negative. A 2D echocardiogram was not performed due to the lack of a portable machine.

The patient was started on oral azithromycin, IV cefotaxime, IV hydrocortisone 50 mg 6 hourly. IV chlorampenicol was ordered.

The patient's condition deteriorated rapidly on day 3 of ICU stay and needed adrenaline, noradrenaline, dobutamine and vasopressin to maintain a blood pressure of 70/50 mmHg. The saturation was maintained at 90% with an FiO_2 of 0.96. A repeat X-ray of the chest showed increased opacities of the lung.

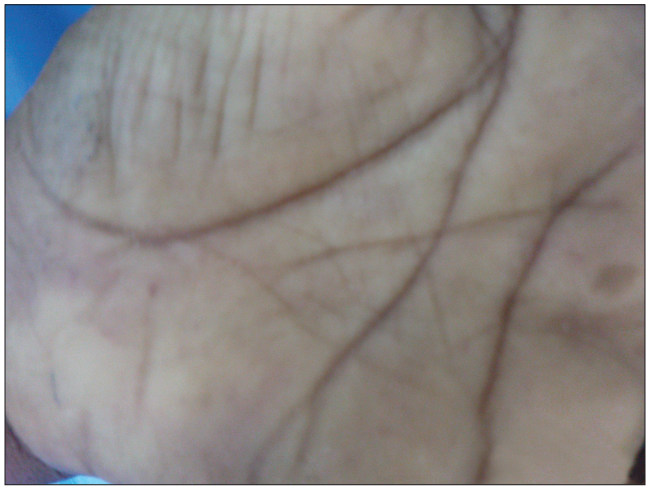

Figure 1: Erythematous maculopapular rash in a hand

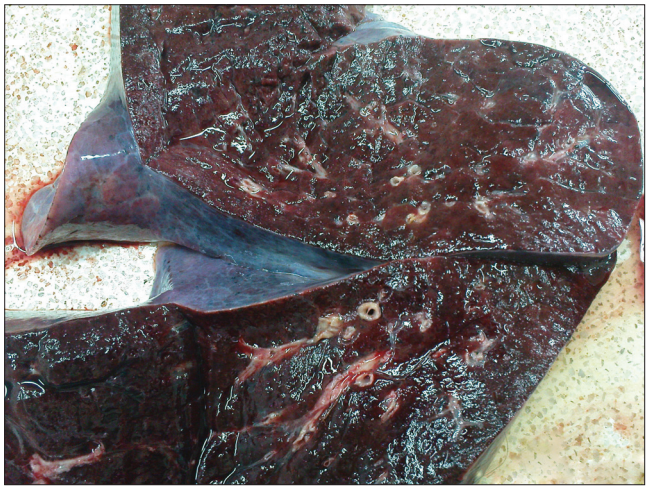

Figure 3: The grossly hemorrhagic lung

The urine output dropped and the urine microscopic examination revealed granular casts and dysmorphic red blood cells. Blood urea rose to 12.9 mmol/dl and the electrolytes showed pottasium level of 5.6 meq/l. Hemoglobin dropped to 7.1 g/dl and platelets to 85,000μl^{-1}. The total white count rose to 35×10^9 l^{-1} with 90% neutrophilia. The blood picture did not reveal DIC.

The serology report for *R. conorii* showed a titer of 1/512.

On the 4th day at the ICU and 12th day of the disease, she devoloped anuria with further increase in blood urea and serum creatinine. She was hemodynamically unstable with a blood pressure of 60 mmHg even with total inotrope support. She died later that day from cardiac arrest.

The post-mortem revealed a grossly hemorrhagic lung [Figure 3]. The liver was enlarged and fatty with hemorrhagic spots. Endocardium of the heart showed vegitations on a narrowed mitral valve [Figure 4]. The kidneys were of normal size, but the cortico-medullary demarcations were less clear. The spleen as well as the adrenals were congested. The brain was normal.

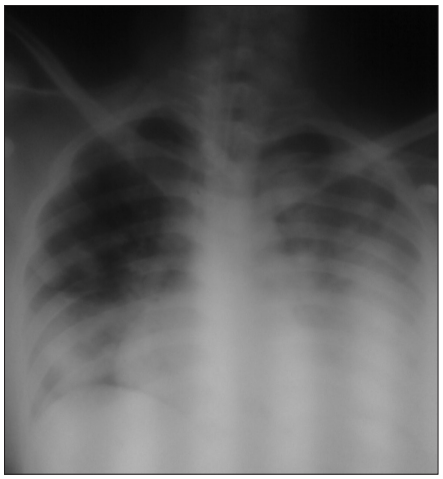

Figure 2: Chest X-ray on day 1 at ICU, showing diffuse bilateral opacities

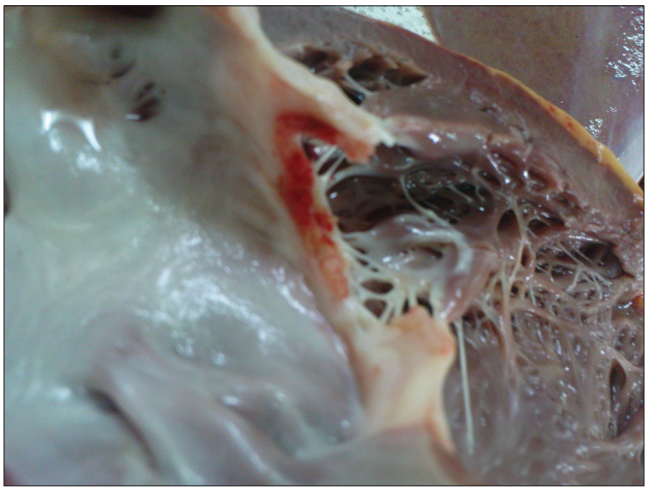

Figure 4: The heart showing narrowing and vegetations at the mitral valve

The histology of the lung showed gross hemorrhage and foci of pneumonia. The vegetations of the heart were reported as fibrinous with entrapped white cells, but with no bacteria or fungi. Histology of the liver revealed centrilobular necrosis with a tendency to confluence, and a mild fatty change. Tubulointerstitial nephritis was identified in the kidney.

A final diagnosis of disseminated *R. conorii* infection with pulmonary hemorrhage, endocarditis and tubulointerstitial nephritis was made.

DISCUSSION

R. conorii is an obligate, intracellular, slow-growing, gram-negative bacterium belonging to the spotted fever group of Rickettsiae. It is the cause of MSF, also known as boutonneuse fever. Unusual rickettsial strains related to *R. conorii* have been described as belonging to an "*R. conorii* complex" which includes the Indian tick typhus rickettsia (ATCC VR-597) with *R. conorii* subsp. *indica* being the causative agent.[1] It is transmitted to humans through the bite of dog ticks (*Rhipicephalus sanguineus*) widely prevalent among the "old world". It is also known to be transmitted by *Haemaphysalis* ticks, especially in Pakistan and Kenya.[2] The worldwide incidence of these *R. conorii*-mediated diseases is increasing.

The infection is transmitted via larvae and nymphs, and the tick bite is usually not felt.[3] The minimum infectious dose is less than 10 organisms. The incubation period ranges from 3 to 15 days depending upon the route of rickettsial entry and the rickettsial load.[4] After introduction into the skin at the site of the tick bite or through the conjunctiva contaminated by blood or excretions from an infective tick, the primary multiplication occurs. In the skin, the localized multiplication of the rickettsiae in the endothelial cells of the capillaries leads to the formation of a raised red papule. The inflammation and thrombosis of the affected capillaries lead to necrosis of the center of the papule and the formation of the typical red lesion with a black center, the "tache noire". This is followed by the spread of infection through lympho-hematogenous routes throughout the body, causing disseminated vascular lesions in multiple organs.[2] About 6% of the cases are severe, and fatal cases occur even in young, healthy adults, with a reported death rate of about 2.5%.[5] Old age, alcoholism and glucose-6-phosphate dehydrogenase (G6PD) deficiency are known risk factors for severe disease. Pregnancy has not been reported as a risk factor.

The patient described here is from Kotagla, a tea estate village in central Sri Lanka. The patient reported a history of significant exposure to stray dogs, abundant in any Sri Lankan village, but not of any tick bites. Most infected individuals do not remember being bitten by a tick. The absence of the tachy noire is significant in this case as the clinical diagnosis of MSF (caused by *R. conorii* subsp. *conorii*) relies on the triad of fever, tache noire, and rash. However, the absence of tache noire has been noted in Israeli spotted fever caused by *R. conorii* subsp. *israelensis*.[1] As the probability of the infective subspecies in this patient is high, this may explain the absence of tache noire.

In spotted fevers, the fever starts after an incubation period of 7 days followed by a febrile period (up to 40°C, usually continuous) associated with a maculopapular rash. Our patient had the typical clinical picture of high fever followed by a rash. The papules of the rash are first noticed on the 3rd to 5th day of illness, and they come out in crops and are palpable as small nodules in the skin. In severe cases, the macules are prominent on the skin and have a dusky cyanotic appearance.[6] Characteristically, the rash involves the palms of the hands, the soles of the feet and, to a lesser extent, the face. In this patient, the rash involved the palms and soles, sparing the face, and was of dusky cyanotic appearence with prominant macules.[2,7,8]

The cough and the dyspnea reported in our patient were relatively rare in a case series of MSF, with a representation of 10% and 21%, respectively.[7] Severe pulmonary hemorrhage has been associated with *R. conorii* infection. Hepatomegaly is present in 13% and splenomegaly in 6% of patients.[3,7] Hepatocellular necrosis has been described as a complication of the infection. Renal insufficiency is a known complication in around 6% of the patients and is caused by tubulointerstitial nephritis.[5] Myocarditis had been obseved in 11% of patients and might explain the severe tachycardia with poor response to inotropes in this patient.

The diagnosis of *R. conorii* infection in this patient is justfied as there is a compatible clinical picture along with a single titer of >1/512.[9]

Endocarditis is not described as a complication of *R. conorii* infection. Identifying *R. conorii* as the causative organism of endocarditis in this patient is supported by the absence of previous heart disease and lack of clinical features to suggest subacute bacterial endocarditis on admission and during prenatal clinics. The vegetations isolated from this patient as well as the blood cultures did not reveal bacteria or fungi. Possibility of marantic or connective tissue assosiated endocarditis was excluded at postmortem.

Serological diagnosis is usualy delayed, causing a delay in treatment in many intances. This patient was correctly started on oral azithromicin and intravenous chlorampenicol at the tertiary hospital. A diagnostic scoring system with microbiological, epidemiologic, and clinical parameters has been proposed for MSF and it had shown good sensitivity and specificity.[6]

This case highlights the need of clinical suspicion of uncommon diseases based on the geographic and

socioeconomic background of a patient. Relatively benign diseases may have severe manifestations resulting in fatality; therefore, physicians should consider there factors for early diagnosis and intervention.

REFERENCES

1. Giammanco GM, Vitale G, Mansueto S, Capra G, Caleca MP, Ammatuna P. Presence of Rickettsia conorii subsp. israelensis, the causative agent of Israeli spotted fever, in Sicily, Italy, ascertained in a retrospective study. J Clin Microbiol 2005;43:6027-31.
2. Gear JH. Other spotted fever group rickettsioses: Clinical signs, symptoms and pathophysiology. In: Walker DH, editor. Biology of Rickettsial Diseases. Boca raton, Florida, USA: CRC Press, Inc.;1988.p.101-13.
3. Mert A, Ozaras R, Tabak F, Bilir M, Ozturk R. Mediterranean spotted fever: A review of fifteen cases. J Dermatol 2006;2:103-7.
4. Azad AF, Radulovic S. Pathogenic Rickettsiae as Bioterrorism Agents. Ann N Y Acad Sci 2003;990:734-38.
5. Bentov Y, Sheiner E, Kenigsberg S, Mazor M. Mediterranean spotted fever during pregnancy: Case presentation and literature review. Euro J Obstet Gynecol Reprod Biol 2003;107:214-6.
6. Wu JJ, Huang DB, Pang KR, Tyring SK. Rickettsial infections around the world, part 1: Pathophysiology and the spotted fever group. J Cutan Med Surg 2005;9:54-62.
7. Raoult D, Tissot Dupont H, Caraco P, Brouqui P, Drancourt M, Charrel C. Mediterranean spotted fever in Marseille: Descriptive epidemiology and the influence of climatic factors. Eur J Epidemiol 1992;8:192-7.
8. Kaplan LI. Other spotted fevers. Clin Dermatol 1996;14:259-67.
9. Bernabeu-Wittel M, Del Toro MD, Nogueras MM, Muniain MA, Cardenosa N, Marquez FJ, *et al*. Seroepidemiological study of Rickettsia felis, Rickettsia typhi, and Rickettsia conorii infection among the population of southern Spain. Eur J Clin Microbiol Infect Dis 2006;25:375-81.

How to cite this article: Dissanayake N, Madegedara D. An unusual case of fatal pulmonary hemorrhage in pregnancy. Lung India 2011;28:205-8.
Source of Support: Nil, **Conflict of Interest:** None declared.