Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria

Submitted on: 10/19/2017
Approved on: 03/08/2018

CASE REPORT

Brazilian spotted fever: importance of early diagnosis and treatment

Yasmim de Freitas Vilaça Decaris Veloso[1], Nedstani de Freitas Soares[1], Ana Flávia Quaresma Ragone[1], Karen Anry Chan[1], Paula Marques de Oliveira Martins[1], Fabiana Maria Kakehasi[2], Alexandre Rodrigues Ferreira[3], Adrianne Mary Leão Sette e Oliveira[4]

Keywords:
rocky mountain spotted fever, Rickettsiaceae, child.

Abstract

Brazilian spotted fever is an acute febrile disease caused by the bacterium *Rickettsia rickettsii*, transmitted by the bite of infected ticks, among them *Amblyomma cajennense* is the most important species involved. Although it is an endemic zoonosis in Brazil, especially in the southeast of the country, suspicion is still low and late, which leads to delayed beginning of treatment and may present with high mortality if not readily identified and treated. This case report describes a 10 years old boy, presenting fever, exanthema, headache, myalgia, nausea, vomiting, abdominal pain and meningeal signs, who was treated initially with doxycycline after 8 days of initial symptoms and progressed to death 33 hours after diagnostic suspicion.

[1] MRP 3rd-Year Pediatrics resident at the University Hospital of the School of Medicine of the Federal University of Minas Gerais.
[2] Adjunct Professor IV, Department of Pediatrics, School of Medicine, Federal University of Minas Gerais.
[3] Associate Professor, Department of Pediatrics, School of Medicine, Federal University of Minas Gerais.
[4] Head of the Pediatrics Intensive Care Unit, Intensive Care Pediatrician, University Hospital, Federal University of Minas Gerais.

Correspondence to:
Adrianne Mary Leão Sette e Oliveira.
Unidade de Terapia Intensiva Pediátrica. Avenida Professor Alfredo Balena, nº 110, Santa Efigênia, Belo Horizonte, MG, Brasil. CEP: 30130-100. E-mail: dennelsette@gmail.com

INTRODUCTION

Brazilian Spotted Fever (BSF) is the Brazilian rickettsiosis that has the highest lethality[1]rates. The disease was initially identified in Brazil in 1929, but became a notifiable disease only in 2001, and since 2007 it has been part of the Compulsory Notification Aggravation Information System[2,3]. According to data from the Ministry of Health, 1,688 cases were confirmed between 2000 and 2016 in Brazil, with the highest number of cases (1,239-73%) recorded in the Southeast region, extending to some states in the South, Northeast and Federal District, with an increase in the average lethality rate from 25.7% to 35% in the the periods of 2000-2008 and 2009-2016 respectively[4]. The highest death rates (528/1239 - 42.6%) [4] are also found in the Southeast region. The number of cases are higher between the months of June and October, probably associated to the vector's reproductive cycle, which occurs in less rainy periods[2].

A clinical condition is difficult to diagnose, requiring a high degree of suspicion, especially in its early stages, which presents nonspecific signs and symptoms (fever, headache, myalgia, malaise and vomiting). With tropism for the endothelial cells of capillaries and venule and the reactional inflammatory response, it results in generalized vasculitis leading to thrombosis and hemorrhages. In addition to the initial digestive impairment and the maculopapular and petechial rash, it can evolve to renal impairment (acute tubular necrosis), pulmonary (pulmonary edema, pneumonitis and pleural effusion) and neurological deficits (neurological deficit with encephalitis and meningitis).

The purpose of this case report is to emphasize the importance of early diagnosis and treatment of spotted fever. In the absence of adequate treatment, the patient can progress to severe forms with mortality rates that may reach up to 80%[3,5].

CASE REPORT

This was a 10-year-old male schoolboy, born in Belo Horizonte, Brazil, with a history of high fever (> 38°C) and headache, which started on August 26, 2016. He sought medical services on the 3rd day after the symptoms started, when he diagnosed with sinusitis and was prescribed cephalexin. On the same night, he developed diffuse maculopapular rash in his palm and plantar regions, and intense joint pain in the lower limbs with gait impairment. As he persisted with a high fever, he returned to the emergency room the following day when he was transferred to the hospital on the 5th day of illness. (Hb 13.2 to 11.2 g/dL and platelets 259,800 to 110,000/mm³, respectively), increased C-reactive protein/CRP (23.1 to 96 g/dL) and increased creatinine (1.0g/dL). Dengue was ruled out by the rapid test and serological method. On the 7th day of evolution he presented with diffuse abdominal pain, with ceftriaxone being prescribed under the hypothesis of an acute abdomen - appendicitis, and was transferred to a tertiary care hospital.

Upon admission to the emergency room (PA) of this tertiary care facility, there were clinical signs of septic shock and respiratory failure, when support treatment measures were initiated with fluid expansion with crystalloids, vasoactive amine and he was intubated. Acute appendicitis was ruled out after being assessed by the pediatric surgeon and abdomen ultrasonography. He was anemic (Hb 9.5 g/dL), had significant thrombocytopenia (platelets 43,000/mm³), progressive CRP elevation (257 g/dL) and metabolic acidosis (pH 6.93; HCO3 - 17.3 mmol/L). He developed severe meningeal signs, disseminated petechiae and a crusted lesion in the left popliteal fossa (reported by the mother as being present since 8/20 when she returned from a walk in the city park of the city where he was with his boy scouts group). In view of this outcome, he was transferred to the intensive care unit of the hospital, where he was thought to have hemorrhagic fever, serology was collected and doxycycline initiated by a nasogastric catheter due to the unavailability of chloramphenicol for intravenous administration. On the 9th day of disease progression, chloramphenicol was started, approximately 24 hours after clinical suspicion and admission to the unit.

The child persisted with hemodynamic instability refractory to supportive measures and evolved with multiple organ dysfunction. He remained anuric since admission in spite of high doses of diuretic; hemodialysis was indicated but he died 33 hours after entering the service on the tenth day of evolution. Post-mortem lumbar puncture revealed aseptic meningitis (parameters: protein concentration 710.8 mg/dL, glycemia 104.4 mg/fL, red blood cells 583/mm³, nucleated cells 18/mm³, Segmented 14% Lymphocytes 77% Monocytes 9%; Bacterioscopy did not show bacteria) and the suspicion of Spotted Fever was confirmed by polymerase chain reaction carried out by Fundação Ezequiel Dias/FUNED after the patient's passing.

DISCUSSION

Spotted fever is rickettsiosis caused by Rickettsia rickettsii, in Brazil called Brazilian Spotted Fever (BSF) and in the United States known as Rocky Mountain Spotted Fever (RMSF). In Brazil, the two main vectors of the disease belong to the genus Amblyomma, and A. cajennense, popularly known as star tick, is the most epidemiologically important[6]. The main hosts of the tick are rodents such as capybara and horses, but they can also be found in dogs, cats and birds[7].

R. rickettsii is an obligate intracellular gram negative bacillus that mainly infects vascular endothelial cells, and, less commonly, smooth muscle cells underlying small and medium vessels, causing a systemic vasculitis that occurs early in the disease, causing hemorrhage, microthrombi and increased vascular permeability[8].

The diagnosis of the disease is essentially clinical and epidemiological. The cases may present as oligosymptomatic or develop in a severe and fulminating manner. The incubation

period may vary from 2 to 14 days after the tick bite, with an average of 7 days. The most common clinical manifestations include fever, headache, chills, low back pain, vomiting, abdominal pain, myalgia, arthralgia and rash. The rash appears between the 3rd and 5th day of the disease, it is present in about 80 to 90% of the cases, and its absence seems to be associated with severity. It is typically a non-pruritic maculopapular lesion, initially appearing in the wrists and ankles, with later generalization, being characteristic the involvement of the palms of the hands and soles of the feet. In the most severe cases, limb necrosis may occur[8].

Changes in laboratory tests are nonspecific, but anemia and thrombocytopenia, elevated renal waste and liver dysfunction may be observed[3]. The current gold standard diagnostic method is indirect immunofluorescence (IFR), and antibodies can be detected from the 7th to the 10th day of the disease[9]. Polymerase chain reaction/PCR should preferably be performed within the first 5 days of the disease and prior to treatment onset. Tissue culture for agent isolation requires strict biosafety standards and is routinely unfeasible.

The differential diagnosis of fever and rash is extensive, and during the early stages of the disease, it may be clinically indistinguishable from many viral rashes and other diseases, particularly in children. Brazilian Spotted Fever can be mistaken with simple conditions such as viral gastroenteritis, upper respiratory tract infection, pneumonia, urinary tract infection at the beginning of its presentation and even with other bacterial sepsis, idiopathic vasculitis, meningoencephalitis with the evolution of signs and symptoms. The dermatological classification of the rash, its distribution, and time in relation to the onset of fever, other systemic signs and laboratory tests may help in the differential diagnosis. Epidemiological data such as season, history of tick bites, travels, outdoor activities, exposure to pets or other animals may also be helpful in guiding the diagnosis[9].

Doxycycline is the only drug proven effective for treating all Rickettsioses in all age groups. In the most severe cases requiring hospitalization as presented in this report, chloramphenicol is the drug of choice in Brazil due to the unavailability of intravenous doxycycline. Treatment should be started immediately in people with signs and symptoms suggestive of rickettsiosis.

The delay in starting treatment can lead to severe illness and it is directly related to the need for hospitalization, ICU admission and death.[6,9]

CONCLUSION

In this case report, despite positive epidemiology and characteristic manifestations, such as maculopapular rash in the palmoplantar region, there was a delay in diagnosis with visits to various healthcare services and the patient had systemic involvement. BSF is an acute febrile disease with a high potential for evolution to severe forms, which has nonspecific clinical and laboratory manifestations. The reduction in evolution to severe forms is directly related to clinical suspicion and early institution of adequate antibiotic therapy. Thus, knowledge of the evolution of the disease and epidemiology for early detection and adequate management in order to reduce the high mortality rates of this Brazilian Hemorrhagic Fever is of vital importance.

REFERENCES

1. Greca H, Langoni H, Souza LC. Brazilian spotted fever: a reemergent zoonosis. J Venom Anim Toxins Incl Trop Dis. 2008;14(1):3-18.
2. Souza W. Doenças negligenciadas. Rio de Janeiro: Academia Brasileira de Ciências; 2010.
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Guia de Vigilância Epidemiológica. Brasília: Ministério da Saúde; 2009.
4. Portal da Saúde. Situação epidemiológica – dados – febre maculosa [Internet]. Brasília: Ministério da Saúde; [citado 2017 Maio 15]. Disponível em: http://portalms.saude.gov.br/saude-de-a-z/febre-maculosa/situacao-epidemiologica
5. Couto DV, Medeiros MZ, Filho GH, Lima AM, Barbosa AB, Vicari CFS. Brazilian spotted fever: the importance of dermatological signs for early diagnosis. An Bras Dermatol. 2015;90(2):248-50.
6. Szabó MP, Pinter A, Labruna MB. Ecology, biology and distribution of spotted-fever tick vectors in Brazil. Front Cell Infect Microbiol. 2013;3:27.
7. Milagres BS, Padilha AF, Barcelos RM, Gomes GG, Montandon CE, Pena DC, et al. Rickettsia in synanthropic and domestic animals and their hosts from two areas of low endemicity for Brazilian spotted fever in the eastern region of Minas Gerais, Brazil. Am J Trop Med Hyg. 2010;83(6):1305-7.
8. Secretaria do Estado de Saúde de Minas Gerais (SESMG). Protocolo de Febre Hemorrágicas: Febre Amarela. Dengue. Leptospirose. Rickettsioses. Meningococcemia e Doença Meningocócica. Febre Tifóide. Hantavirose. Hepatites. Malária. Belo Horizonte: Secretaria do Estado de Saúde de Minas Gerais; 2002.
9. Biggs HM, Behravesh CB, Bradley KK, Dahlgren FS, Drexler NA, Dumler JS, et al. Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis - United States. MMWR Recomm Rep. 2016;65(2):1-44.