Case Report/Relato de Caso

Severe coinfection of melioidosis and dengue fever in Northeastern Brazil: first case report

Coinfecção grave de melioidose e dengue no Nordeste do Brasil: primeiro caso

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ABSTRACT

This report focuses on a fatality involving severe dengue fever and melioidosis in a 28-year-old truck driver residing in Pacoti in northeastern Brazil. He exhibited long-term respiratory symptoms (48 days) and went through a wide-ranging clinical investigation at three hospitals, after initial clinical diagnoses of pneumonia, visceral leishmaniasis, tuberculosis, and fungal sepsis. After death, *Burkholderia pseudomallei* was isolated in a culture of ascitic fluid. Dengue virus type 1 was detected by polymerase chain reaction in cerebrospinal fluid (CSF); this infection was the cause of death. This description reinforces the need to consider melioidosis among the reported differential diagnoses of community-acquired infections where both melioidosis and dengue fever are endemic.

Keywords: Melioidosis. Dengue fever. Coinfection.

RESUMO

Estudo de caso fatal de coinfecção de melioidose e dengue grave em um motorista de 28 anos, residente no município de Pacoti, nordeste do Brasil. O paciente apresentou inicialmente sintomas respiratórios com evolução por 48 dias. Foi internado em três diferentes unidades de saúde com suspeitas de pneumonia, leishmaniose visceral, tuberculose e sepse fúngica. Após o óbito, a cultura de líquido ascítico identificou a bactéria *Burkholderia pseudomallei.* O vírus da dengue tipo 1 foi detectado por PCR no líquor do paciente. Esta descrição reforça a necessidade de considerar a melioidose entre os diagnósticos diferenciais de infecções comunitárias onde as duas doenças são endêmicas.

Palavras-chaves: Melioidose. Dengue. Coinfecção.

INTRODUCTION

Melioidosis was first diagnosed in Ceará in 2003[1,2], and so far, 17 cases have been confirmed. Recent studies indicate that the disease is endemic in northeastern Brazil[3,4]. Dengue fever is also endemic in this region, with cases reported since 1986 and widespread outbreaks occurring in 1994, 2003, 2008, and 2011, most significantly affecting the younger portion of the population[5,6]. This is a report on a fatality involving severe dengue fever and melioidosis in a 28-year-old truck driver residing in Pacoti in northeastern Brazil. He exhibited long-term respiratory symptoms (48 days) and underwent a wide-ranging clinical investigation at three hospitals, after initial clinical diagnoses of pneumonia, visceral leishmaniasis, tuberculosis, and fungal sepsis.

CASE REPORT

On June 5th, 2010, the patient began to exhibit a daily evening fever, a persistent dry cough, malaise, and hyporexia. A physical examination revealed nothing abnormal. He was initially diagnosed with pneumonia 7 days after the onset of symptoms, and azithromycin was administered for 5 days (500mg 1x/d) followed by amoxicillin/clavulanate for another 7 days (800/125mg 3x/d). An initial investigation indicated pancytopenia with hemoglobin at 12.5g/dL (13.5-17.5g/dL), leukocytes at 2,700/mm^3 (4,000-10,000/mm^3), and platelets at 113,000/mm^3 (130,000-400,000/mm^3). However, a chest x-ray indicated nothing abnormal. The patient's symptoms worsened, and in the middle of July, he was transferred to Fortaleza, capital of the State of Ceará, for further diagnosis. He had lost 5kg since the onset of clinical symptoms. A complete blood count (CBC) revealed hemoglobin at 10.5g/dL (13.5-17.5g/dL) and leukocytes at 2530/mm^3 (4000-10,000/mm^3), including neutrophils at 2,251/mm^3, lymphocytes at 225/mm^3, and platelets at 104,000/mm^3. A chest x-ray indicated a small opaque area in the right pulmonary hilum. Sputum samples tested negative for acid-alcohol-resistant bacillus (BAAR). An abdominal ultrasound scan revealed mild splenomegaly with no textural alterations. On July 10th, a high-resolution computed tomography indicated a thick-walled cavitary lesion surrounded by satellite nodules and a "tree-in-bud" pattern located in the upper section of the inferior lobe of the right lung. On July 12th, as tuberculosis was suspected, tuberculosis treatment was initiated (rifampin, isoniazid, pyrazinamide, and ethambutol). The patient's condition, however, did not improve, and he was hospitalized in Fortaleza on July 19th. A bronchoscopy was executed, and a bronchoalveolar lavage culture isolated *Aspergillus spp*. On July 24th, he was transferred to another hospital, as he was experiencing persistent daily fever (38.5 to 39ºC), coughing with hyaline expectoration, respiratory discomfort, and bloatedness. A CBC revealed the following: hemoglobin, 9.83g/dL; Ht, 19.8%; leukocytes, 1,200/mm^3, including, neutrophils, 882/mm^3, lymphocytes, 279/mm^3, and platelets, 76,100 cells/mm; blood urea, 27mg/dL; creatinine, 0.9mg/dL; sodium, 123mg/dL; potassium, 4.2mg/Dl; AST, 547U/L (15-37U/L); ALT, 267U/L

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(30-65 U/L); LDH, 2,843U/L (24-480 U/L); and total bilirubin, 1.99mg/dL (0.2-1.0mg/dL). The patient tested negative for HIV and for hepatitis B and C. Tuberculosis treatment was discontinued due to an increase in liver enzymes, and treatment with amphotericin B (50mg 1x/day) was initiated after a diagnosis of fungal sepsis. After hospitalization, the patient's symptoms continued and worsened to include abdominal bloating, nausea, vomiting, and insomnia. A physical examination revealed continued fever, jaundice (+/4+), diaphoresis, severe dyspnea, tachycardia (HR=95bpm, RR=21ppm, ABP 121x78mmHg), palpation of the abdomen showing abdominal distention, a palpable liver, occupied Traube's space, and edema in the lower limbs. A chest X-ray showed an unspecified infiltration. A CBC revealed the following: hemoglobin, 9.5g/dL; Ht, 27.7%; leucocytes, 2,790/mm^3; platelets, 65,100/mm^3; blood urea level, 47mg/dL; creatinine level, 1.0mg/dL; AST, 861U/L; and ALT, 319U/L. Seventy-two hours after hospitalization, the patient developed respiratory distress with a drop in oxygen saturation, hypotension, abdominal discomfort, jaundice, and mental confusion. The following were found: arterial blood gas, pH 7.21 (7.35-7.45); PO2, 82mmHg (80-100mmHg); PCO2, 15mmHg (35-45mmHg); bicarbonate, 8.4mEq/L (22-26mEq/L); and StO2, 93.9%. Amphotericin B was discontinued and caspofugin (50mg 1x/d), imipenem (1g 2x/d), and teicoplanin (400mg 2x/d) were administered. Vigorous intravenous hydration with a crystalloid solution was maintained.

Thereafter, the patient developed hemodynamic instability and severe dyspnea, and endotracheal intubation was executed, along with the administration of vasoactive drugs. He was transferred to the Intensive Care Unit and died the same day. After death, *Burkholderia pseudomallei* was isolated in a culture of ascitic fluid. Dengue virus type 1 (DENV-1) was detected by polymerase chain reaction (PCR) in cerebrospinal fluid (CSF) during autopsy, and this infection was reported as the cause of death.

DISCUSSION

Melioidosis has a broad clinical spectrum, from asymptomatic infection, localized acute or chronic suppurative infection, and latent chronic infection, to severe forms that include fulminant pneumonia and sepsi[7]. Cavitary pneumonia accompanied by weight loss, often confused with tuberculosis, is another clinical presentation of melioidosis[7,8]. The patient presented symptoms of chronic melioidosis with prolonged fever and lung involvement simulating pulmonary tuberculosis. The patient's symptoms probably worsened after dengue infection, which probably began four days prior to death. The clinical presentation had 40 days of evolution and involved pancytopenia, which simulated other infections. The warning signs of dengue hemorrhagic fever could not have been suspected during the evolution of the patient's condition, as they are non-specific and they also occur in other serious infections.

This case serves as a pertinent reminder of the constant need to consider melioidosis among the differential diagnoses of many community infections in Brazil. It also proves the necessity of investigating coinfections with dengue fever, a prevailing and serious public health issue in Brazil. On the other hand, the clinical manifestations of dengue fever, especially when the disease evolves into its serious hemorrhagic form, may also be similar to those of acute melioidosis.

The Epidemiological Surveillance of Ceará has a protocol with the Central Laboratory of Public Health of Ceará State Virology Section and the Death Verification Service (DVS), where in all the cases referred to the DVS that present bleeding, pleural effusion, or other manifestations suggestive of hemorrhage, even when dengue is not suspected, material (blood, cerebrospinal fluid, and viscera) is harvested and sent to Central Public Health Laboratory of Ceará (LACEN) where PCR and viral isolation are performed[9]. It is a routine for suspected cases in Ceará to go through Epidemiological Surveillance and DVS. As the patient presented at the end of a frame compatible illness during the autopsy and the pathologist acknowledged signs suggestive of bleeding, biological material was collected and forwarded to LACEN for laboratorial investigation.

Due to the prevalence of dengue fever, coinfection with melioidosis may occur independently of whether the latter has an acute or chronic clinical presentation. In the case under consideration, the patient had a chronic illness of unknown etiology. The fact that his clinical evolution worsened considerably immediately prior to death may have been due to a worsening chronic condition or a superimposed acute infection. A laboratory diagnosis involving the isolation of *Burkholderia pseudomallei* and DENV-1 confirms that the bacterial infection had a superimposed viral infection. Three important aspects make this noteworthy: 1) melioidosis should always be considered in differential diagnoses involving community-acquired infections in Brazil, where patients have a background of exposure to soil and water; 2) the clinical history of dengue fever, especially when it evolves into serious forms, may also simulate an acute melioidosis infection; and 3) dengue fever is a prevalent and serious health problem in the country, so the possibility of coinfection with melioidosis should always be taken into consideration. Moreover, a description of coinfection of dengue fever and melioidosis in Thailand[10] supports the application of this recommendation in other countries where both diseases are endemic.

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