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CASE REPORT

Acute Q fever and pulmonary tuberculosis in pediatric age: a case report

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Abstract

In pediatric age groups, fever of unknown origin composes a diagnostic challenge due to its multiple possible etiologies. A high percentage of those cases is caused by infections. In this article, we describe the clinical case of an adolescent with atypical pneumonia caused by simultaneous infection of *Coxiella burnetti* and *Mycobacterium tuberculosis*. In children, tuberculosis is a known cause of prolonged fever and high mortality. Diagnosis of Q fever is less prevalent, but its importance has been highly increasing. The clinical picture outlined here improved after pursuing the treatment for acute Q fever. Nevertheless, it is essential to emphasize the importance of identification and treatment for both infections. This association is rare since this is the third case reported in the literature and the first one in pediatric age.

Keywords: Fever of unknown origin. Pediatrics. Q Fever. Tuberculosis. Zoonoses. Case reports.

Febre Q aguda e tuberculose pulmonar em idade pediátrica: um caso clínico

Resumo

A febre de origem desconhecida representa um desafio diagnóstico, com múltiplas possíveis etiologias em idade pediátrica. Uma grande percentagem dos casos é de causa infeciosa. Neste artigo descrevemos o caso clínico de um adolescente com pneumonia atípica causada por infeção simultânea por *Coxiella burnetii* e *Mycobacterium tuberculosis*. Em idade pediátrica, a tuberculose é uma reconhecida causa de febre prolongada e elevada mortalidade. O diagnóstico de febre Q é menos prevalente, mas tem assumido importância crescente. O quadro clínico exposto evoluiu favoravelmente após tratamento dirigido para a febre Q aguda, mas salienta-se a importância da identificação e tratamento de ambas as infeções. Esta associação é rara, sendo este o terceiro caso reportado na literatura e o primeiro em idade pediátrica.

Palavras-chave: Febre de origem desconhecida. Pediatria. Febre Q. Tuberculose. Zoonoses. Caso clínico.

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Keypoints

What is known

– Most cases of fever of unknown origin are caused by infections. In children, tuberculosis is a known cause of prolonged fever and high mortality. Diagnosis of Q fever is less prevalent.

What is added

– Even in the absence of epidemiological context, it is important to consider the diagnosis of Q fever and tuberculosis. Notified cases of Q fever underestimate the prevalence of this diagnosis. Reported simultaneous infection by *C. burnetti* and *M. tuberculosis* is rare.

Introduction

Fever is one of the most common signs of illness in children[1]. When it has a prolonged course and its cause is not identified after anamnesis, detailed physical exam, and initial investigation, we are in the presence of fever of unknown origin (FUO)[1]. This entity can be caused by multiple disorders, infectious diseases being the most frequent etiology. Atypical pneumonia can be one of the causes and its clinical, analytical and imagiological manifestations often do not predict the diagnosis[1,2].

Previously considered a rare disorder, limited to certain population groups, Q fever has assumed increasing importance as a cause of FUO[3]. Since its introduction as a notifiable disease in Portugal, only 217 cases have been reported in 15 years[4]. However, serologically, there was a much higher number of infections[5].

Pulmonary tuberculosis can also cause prolonged fever[1]. Due to the immaturity of their immune system, 40% of infected children develop the disease, which explains the higher prevalence of this diagnosis[6,7].

Case report

We report a case of a 12-year-old male adolescent, previously healthy and with history of tuberculosis vaccine, resident in a suburban area in Bordeaux, France. He denied any contact with animals, ingestion of unpasteurized foods or epidemiological context of disease.

Observed at his local hospital with two days of fever, dry cough and headache, he was diagnosed with pneumonia and discharged home with amoxicillin. Due to sustained fever after 72 hours on this antibiotic, clavulanic acid was added to the treatment.

In Portugal, due to persistent fever on day-four of amoxicillin/clavulanic acid, he was taken to the emergency department. His physical examination was significant for crackles at the base of the right lung on pulmonary auscultation, but showed hemodynamic stability, good general state, no signs of respiratory distress and adequate peripheral oxygen saturation in ambient air.

An analytical study revealed 21210 leukocytes/uL with 17070 neutrophils/uL and C-reactive protein of 105.8 mg/L, with no other abnormalities. Chest radiography showed hypotransparency in the right lung base. An ultrasound confirmed this consolidation and discarded any associated complications.

On the suspicion of atypical pneumonia, he was admitted for intravenous antibiotic therapy with ceftriaxone.

As the fever persisted on day three of admission, analytical and imagiological evaluation was repeated, showing maintained leukocytosis and C-reactive protein elevation, sedimentation rate of 56 mm/h and bilateral interstitial infiltrates on chest radiograph. Clindamycin and azithromycin were added to the therapeutics.

After a week of hospitalization and sustained fever, a thoracic computed tomography was requested, revealing extensive areas of parenchymal consolidation, with bibasal predominance but also affecting the upper segments, multiple cavitated areas and diffuse tree-in-bud pattern.

It was decided to extend the etiological study, suspend ongoing therapeutic and start doxycycline. After eight days of treatment, the patient became apyretic.

Blood cultures on day nine and day seventeen of disease, virological examination of nasopharyngeal aspirate and *Legionella pneumophila* urinary antigen were negative. There was no serological evidence of acute CMV, EBV, parvovirus B19 or *Brucella* infection. *Coxiella burnetti* serologies revealed IgG phase II > 800, fulfilling diagnostic criteria for acute Q fever. From the study directed to *Mycobacterium tuberculosis*, *Mantoux* test was negative, IGRA was positive and molecular biology and culture in bronchoalveolar lavage were positive.

Considering the diagnosis of acute Q fever, an echocardiogram was performed, showing no abnormalities, and antibiotic therapy was maintained for 14 days. In the face of the concomitant diagnosis of pulmonary tuberculosis, the patient was referred to the regional referral center and is currently undergoing targeted therapy.

Discussion

In this article, we describe a case of concomitant acute Q fever and pulmonary tuberculosis, two disorders

of challenging diagnosis in the absence of evident epidemiological context.

Q fever is a zoonosis with a worldwide distribution caused by the bacterium *C. burnetii*, whose main route of human transmission is inhalation of aerosols contaminated with excreta from farm animals[8]. Although in the present case no direct contact with possible reservoirs was identified, the outbreak of acute Q fever in the Netherlands between 2007-2010 indicated that this is not required, since the bacterium has a highly resistant sporiform phase in its life cycle, which can cause infection within 2 km of the infectious source[8,9].

The transmission of *M. tuberculosis* occurs by inhalation of aerosolized particles and the diagnostic suspicion arises, in most cases, from contact with a patient with active tuberculosis[1,6]. Although, in this case, the epidemiological history was negative, the clinical course and imagiological findings made this a mandatory differential diagnosis.

It is difficult to distinguish which of the infections was responsible for the patient's symptoms. The clinical presentation of acute Q fever is highly variable, the infection being asymptomatic in 50% of cases, with an even higher percentage in pediatric age[8]. Among symptomatic patients, the most frequent presentation is a self-limited febrile illness, associated with findings of pneumonia or hepatitis[8]. The diagnosis is made, in the first two weeks of the disease, by detection of bacterial DNA in the blood by PCR or, later, by detection of high or quadrupled IgG phase II titers in relation to the previous sample by indirect immunofluorescence[8]. The clinical response to doxycycline, the first-line therapy in children over eight years of age, suggests that the fever was the result of *C. burnetii* infection[8]. Thus, and considering that infections are one of the most immunologically disturbing events in pediatric age, we can interpret pulmonary tuberculosis as a consequence of the reactivation of the latent bacillus in a previously balanced immune system[10]. Regardless of the infection that determined the patient's clinical picture, we highlight the importance of identifying and treating both diseases. Despite the good prognosis of acute Q fever, with a reported mortality of less than 2% and development of persistent disease in only 5% of cases, chronic infection, in most cases in the form of endocarditis, implies a challenging treatment with high mortality[8]. Tuberculosis is the tenth leading cause of death worldwide, with 16% of all deaths occurring in children[11].

Simultaneous infection by these two microorganisms is rare, this being the third case reported in the literature and the first case described in pediatric age[12,13]. In adulthood, this co-infection also caused prolonged fever, associated with hepatitis in the case of Sumida et al.[12] and atypical pneumonia in the report by Simões et al.[13]

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Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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