Pancreatitis, hypereosinophilia and bilateral pulmonary infiltrates as presentation of acute Q fever

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Abstract

Q fever, caused by *Coxiella burnetii*, is a poorly recognized zoonotic infection given its polymorphic clinical presentation. The diagnosis should not be missed to treat in the acute phase and thus prevent major complications of the chronic phase.

We describe a case of acute Q fever with pancreatitis, hypereosinophilia and pulmonary infiltrates.

Keywords: Coxiella, hypereosinophilia, intracellular bacteria, pancreatitis, Q fever

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Brief report

A 30-year-old woman born in Morocco and living in Switzerland for 9 years was admitted to the emergency room for dyspnea and fever. Her past medical history was relevant for latent tuberculosis that was treated a few years ago and an episode of pancreatitis (score Balthazar C) of unclear origin one month earlier. A CT scan was performed and revealed multiple bilateral nodular infiltrates (Fig. 1). Laboratory tests showed a white blood cell (WBC) count of 15.3 G/l of cells with 5.97 G/l eosinophils (39%), C-reactive protein (CRP) 50 mg/l and alkaline phosphatase 149 U/l, whereas other biological parameters, including creatinine, liver function tests and lipase/amylase were within the physiological range of values. The patient did not mention exposure to animals or consumption of raw-soft cheese.

In view of this lung infiltrate, a bronchoalveolar lavage (BAL) was performed and demonstrated significant alveolar eosinophilia (75.5%). Histology of a transbronchial biopsy showed an eosinophilic alveolar infiltrate without granuloma or fibrosis. Blood cultures and culture of expectorations remained sterile. Direct examination of stools, as well as serology panel for helminths, were negative. The immunological work-up with anti-nuclear antibodies (ANA), anti-neutrophil-cytoplasmic antibodies (ANCA) and tryptase was also negative. The diagnostic work-up was completed by serology for HIV, Cytomegalovirus, Epstein-Barr virus, *Brucella*, *Bartonella* and *Treponema pallidum*, which were all negative. Immunofluorescent serology for *Coxiella burnetii* was positive for phase II IgG titers (1:256) and IgM titers (1:256), while phase I IgG titers were below the threshold of significance (1:32) [1], which was consistent with acute Q fever. These results were confirmed by a chemiluminescent immunoassay (CLIA) with an index of phase II IgM and IgG at 1.29 (positive) and 0.957 (limit), respectively (cutoff 0.9 – 1.1). Specific *C. burnetii* PCR [2] in the blood (EDTA) and bronchoalveolar lavage fluid were both negative (positive control and inhibition control were both positive as expected). A treatment of doxycycline 100 mg bid was introduced for a duration of 14 days for the treatment of acute Q fever, with

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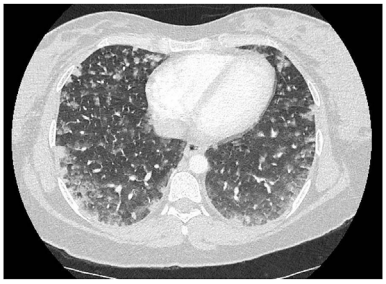

FIG. 1. CT scan revealing diffuse peripheral pseudonodular consolidations associated with patchy ground-glass attenuation, following a mostly centrilobular subpleural pattern. These findings open a large differential, including endobronchial infection, vascular infection, as well as allergic or inflammatory disease.

rapid improvement of all the symptoms, resolution of the radiological infiltrate, as well as the correction of the laboratory tests (WBC 6.3 G/l with 1.89 G/l eosinophils). Repeated *C. burnetii* serological testing at 14 days from the initial diagnosis also showed a significant decline of phase II IgM titers (1:64) and persistently high IgG titers (1:256).

Discussion

Q fever is a worldwide zoonosis caused by *Coxiella burnetii*, obligate intracellular bacteria that infect cattle, sheep, goats, and also cats, rabbits and dogs [1,3]. Human infections occur after inhalation of contaminated aerosols or after ingestion of unpasteurized milk or raw-soft cheese [1,3]. About 60% of infected persons will remain asymptomatic [1]. Presentation is very variable, ranging from a flu-like syndrome to atypical pneumonia, granulomatous hepatitis, or even pancreatitis and meningoencephalitis [1,3,4]. Pregnancy, immunosuppression or heart valvulopathies are predisposing for chronic Q fever that may occur months to years after infection [1,5]. Endocarditis is the most common manifestation of chronic Q fever and is associated with high mortality rates (25–60% without treatment) [5].

Our patient's presentation was atypical due to extensive bilateral lung infiltrates and hypereosinophilia suggestive of an auto-immune disorder (e.g. vasculitis) or severe pneumonia with consecutive perivascular inflammation. A parasitic infection (e.g. nematodes-associated Loeffler syndrome) was also suspected and excluded. The diagnosis of acute Q fever was finally established based on the serological pattern and after exclusion of other infectious and non-infectious etiologies as mentioned above. The rapid favourable evolution without any corticosteroid-based treatment (or other immunomodulating therapy) also strongly speaks against eosinophilic pneumonia or similar auto-immune disorders.

C. burnetii infection can be associated with hypereosinophilia in the peripheral blood smear [6,7], as well as in pleural effusion, as previously reported [8]. One likely explanation is that the infection induces the production of chemokines (eotaxins), which are responsible for the recruitment of eosinophils [6,9]. A third unusual presentation of acute Q fever is acute pancreatitis, which has been described in some cases [4]. In the present case, the initial clinical presentation with acute pancreatitis of unclear origin, which preceded the symptoms of eosinophilic pneumonia, could probably be attributed to acute Q fever.

Altogether the patient presented with an unusual triad of bilateral pneumonia, hypereosinophilia and pancreatitis, which have all been reported in subjects with acute Q fever. The co-occurrence of such severe pneumonia mimicking a lung vasculitis and the documentation of eosinophils in the lung suggest that hypereosinophilia has played a role in the pathogenesis of the disease. Thus, based on this unusual triad and positive serology, the diagnosis of acute Q fever is very likely.

In case of suspected *Coxiella* infection, diagnosis is based on serology and PCR [2,3]. PCR on blood and lower respiratory tract samples is highly specific and has excellent sensitivity, especially if it is performed in the early phase of the infection [2,10]. However, PCR detecting bacterial DNA can be falsely negative once antibody seroconversion has occurred [5,10]. Therefore, serology remains a reference standard for the diagnosis of Q fever. Despite negative PCRs, our patient's serology was positive with phase II titers, which confirmed the suspected diagnosis.

The standard treatment for acute Q fever is doxycycline at 200 mg/day for 14 days. The alternative in case of allergy or contraindications (e.g. pregnancy) is cotrimoxazole. After the antibiotic treatment, a follow up should be carried out at three and six months with serologies in order to document a possible transition to chronicity, which would necessitate a prolonged treatment [1].

Conclusion

In the presence of pancreatitis and/or hypereosinophilia, Q fever should be suspected, at least in endemic countries, during outbreaks or in the presence of a lung infiltrate.

Transparency declaration

No conflict of interest.

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