



CASE REPORT

Cavitary legionella pneumonia in a patient with immunodeficiency due to Hyper-IgE syndrome

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KEYWORDS

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Summary We report about a 35-year-old man with a cavitary legionella pneumonia who had a history of chronic eczematoid lesions since infancy, recurrent skin and lung infections and a very high total IgE level. We carried out further investigations and made a diagnosis of a primary immunodeficiency classified in the Hyper-IgE syndromes. Cavitation of legionella pneumonia may become fairly common in immunocompromised patients, while is found rarely among immunocompetent hosts.

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Legionella species are an important but often not early recognized cause of pneumonia. Usually legionellosis infection occurs after persons have breathed mists that come from a water source contaminated with the bacteria. *Legionella* has been associated with a broad spectrum of disease, from mild influenza-like symptoms to severe cavitating pulmonary disease, which more commonly occurs in patients with a compromised immune status or other underlying disease. Herein we present a case of cavitary *Legionella pneumophila* in a young man with a rare primary immunodeficiency classified in the Hyper-IgE syndromes.

Case report

A 35-year-old man, working in the last 4 months for a company which was restructuring a sewage pipeline, was admitted for high fever, confusion, disorientation, breathlessness and hemoptysis. He had complained of non-productive cough, fever, diffuse myalgia and breathlessness with wheezing for almost a week. He was diagnosed flu syndrome with acute exacerbation of bronchial asthma and given symptomatic (paracetamol) and antiasthmatic (a 3 days course of 16 mg of prednisolone, inhaled fluticasone 1 g and salmeterol 100 µg daily and inhaled salbutamol 200 µg as needed) therapy. The patient's medical history included allergy to house dust mite with persistent allergic rhinitis and mild persistent bronchial asthma. He had undergone house dust mite specific immunotherapy for 5 years in the past with only partial resolution of rhinitic symptoms. Asthma was effectively controlled with inhaled fluticasone 500 µg and salmeterol 100 µg daily. He had

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also a history of chronic eczematoid lesions since infancy diagnosed as atopic dermatitis and treated with topical steroids and cycles of PUVA therapy, recurrent infections such as skin abscesses and candidiasis, bronchitis and pneumonia (5 episodes in the last 10 years treated empirically, 3 of those requiring hospitalization). He had a very high total IgE level (ranging from 5000 to 15,000 IU/mL in few measurements) believed to be caused by his atopy and therefore not controlled over time.

On chest physical examination he had scattered wheezing on both hemithorax, fine inspiratory crackles and bronchial breath sounds in the upper left lobe, cardiac exam was normal with a tachycardic heart rate (100 p/min), respiratory rate was 25 breaths/min, oxygen saturation of 92%, no lymphadenopathy, normal jugular venous pulsation, no peripheral oedema. Abdomen examination was normal. Mental status exam revealed confusion and disorientation, while cranial nerve, coordination, sensory, motor and gait exams were normal. He had particular facial traits characterised by large head circumference, prominent forehead, broad nasal bridge and mild prognathism.

Blood gas findings were pH 7.41, PaO₂ 75 mmHg, PaCO₂ 36 mmHg, HCO₃ 25 mmol/L. Laboratory analyses revealed an erythrocyte sedimentation rate of 56, WBC 17,000 per mm³ with 72% neutrophils, a mild eosinophilia of 7% (eosinophil counts 1200 mm³), AST 50 U/L, ALT 75, LDH 1100 U/L, CK 390 U/L with isoenzyme MB < 5% of total, aldolase 86 U/L, mild proteinuria. Total IgE levels were 38190 IU/mL. ECG was normal. Chest X-ray showed an area of consolidation in the left upper lobe and shadowing of the right upper lobe (Fig. 1). Chest CT scan revealed cavitation of the previously identified left lung infiltrate (Fig. 2).

Mantoux test and QuantiFERON-Gold TB test were negative. Skin prick test, specific IgE and precipitins for aspergillus antigens were negative. Cultures from BAL samples were negative for mycobacteria and fungi (including aspergillus). BAL samples in the affected area allowed the identification of Gram negative bacilli which failed to grow in routine aerobic and anaerobic cultures.

The *Legionella* urinary antigen was positive and legionella colonies were isolated from a BAL sample after 7



Figure 1 Chest radiography showing a left upper lobe consolidation and right upper lobe shadowing.

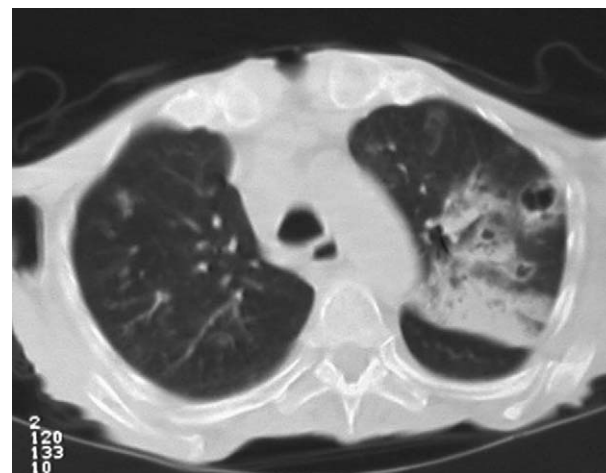


Figure 2 Computed tomographic imaging demonstrating progressive cavitation of the infiltrate in the left upper lobe.

days of culture on a buffered charcoal yeast extract (BCYE) agar. Seroconversion was also demonstrated by indirect immunofluorescent antibody (IFA) against *L. pneumophila* serogroup 1, with a titer rising from 1/128 on day 5 to 1/652 on day 15 from admission.

The patient started empirically intravenous piperacillin–tazobactam (4 g/0.5 g die) and levofloxacin (500 mg die), then was treated with intravenous rifampicin (600 mg die) and azitromycin (500 mg die) for 2 weeks, both switched to a 2 weeks oral course as outpatient and made a complete recovery. We carried out an immunophenotypic analysis of peripheral blood lymphocytes demonstrating a significant reduction of CD¹⁶⁺–CD⁵⁶⁺ NK lymphocytes and B activated lymphocytes. Moreover the in vitro production of INF γ by cultures of peripheral blood mononuclear cells stimulated by PHA and the flow cytometric analysis of INF γ intracellular expression by CD4 T cells were significantly lower than controls. Studying the patient's family medical history, we found a first grade cousin with multiple similar findings.

Discussion

In this case the atypical legionella pneumonia with cavitary infiltrates likely developed due to the primary immunodeficiency characterizing the patient Hyper-IgE syndrome. The Hyper-IgE syndromes are multisystem disorders including not only immune system deficits and extreme elevations of serum IgE (>2000 IU/mL), but also abnormalities of the soft tissues, skeletal and dental systems.^{1,2} Typical anomalies of the head, face and skeleton, recurrent lung and skin infections, chronic generalized eczematoid dermatitis are common,^{1,2} but exist also additional variants.² The etiology of the Hyper-IgE syndromes is still unknown. Studies of these syndromes focused on the immune system have revealed defective granulocyte chemotaxis,³ abnormalities in T-lymphocyte subgroups,^{4,5} decreased production of or responsiveness to cytokines such as interleukin-4 and interferon- γ .^{6,7} Pedigrees' studies of patients with these syndromes have demonstrated an autosomal dominant inheritance with varying expressivity.¹ An autosomal recessive inheritance and sporadic cases have

also been described.² Unlike patients with autosomal dominance inheritance and sporadic cases, those with autosomal recessive inheritance lack skeletal or dental involvement and do not develop lung cysts, while they are susceptible to molluscum contagiosum and other viral infections and may develop severe neurological complications.² In this patient the abnormal elevation of IgE had been superficially attributed to atopy and was not further investigated, despite the presence of relevant susceptibility to infections.

Legionella pneumonia chest radiographic findings usually include unilateral or bilateral patchy or nodular pulmonary infiltrates, which may progress to either lobar or consolidating, as in the classic pyogenic pneumonia, and cavitation is found rarely among immunocompetent hosts.^{8–12} It has been described in infancy¹³ and early childhood.¹⁴ In immunocompromised patients cavitation may become fairly common, establishing difficulty in differential diagnosis for pathogens causing cavitary necrosis such as mycobacteria, fungi, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella* and anaerobes. Cavitary legionella pneumonia has been associated with corticosteroid or immunosuppressive therapy,^{15,16} solid organ transplant,^{17–19} and HIV infection.²⁰ *L. pneumophila* may produce a broad spectrum of clinical disease depending on environmental conditions, individual risk factors as well as individual underlying health disorders, and the radiographic findings may be atypical, particularly in immunocompromised hosts.

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