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Case report

Mycoplasma pneumonia with persistent lymphadenopathy and severe cold agglutinin haemolysis

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ABSTRACT

Mycoplasma pneumonia is an atypical pneumonia commonly affecting young patients with generally mild clinical course. We present a case of a 66-year-old female presenting with weight loss, night sweats and low-grade pyrexia. She acquired symptomatic haemolytic anaemia requiring blood transfusion, markedly raised erythrocyte sedimentation rate (ESR) to 114 mm/hr and extensive peri-hilar lymphadenopathy on computed tomography (CT) scan. After excluding malignancy and granulomatous diseases, she made good recovery although a 4 week follow-up CT scan showed persistent but resolving lymphadenopathy. We discuss the considerations for blood transfusion in cold agglutinin disease, and the investigations for immunological manifestations in Mycoplasma pneumonia.

1. Introduction

Mycoplasma pneumonia is one of the most common causes of community acquired atypical pneumonia, which rarely requires hospitalisation. It predominantly affects children and teenagers with gradual onset of headache, malaise and low-grade fever. Extra-pulmonary manifestations occur in 5–10% of patients, including skin (Stevens-Johnson syndrome, erythema multiforme), gastrointestinal (abdominal pain, diarrhoea), neurological (encephalitis, meningoencephalitis), and cardiac (arrhythmia, myocarditis). Cold agglutinin haemolysis associated with IgM reaction against erythrocyte I antigen commonly occurs in 50–75% patients after 1–2 weeks of infection, however it is usually not clinically significant and severe anaemia has only been described in paediatric cases or patients with sickle cell disease. This case highlights the management of severe anaemia associated with haemolysis, and characterises the immunological manifestations of mycoplasma pneumonia, especially in elderly patients.

2. Case presentation

A 66-year-old lady presented with three-week history of night sweats, low-grade pyrexia and weight loss. She also had progressive dyspnoea on exertion over 3–4 weeks and non-productive cough that failed to respond to a seven-day course of oral amoxicillin. Her medical history included well controlled asthma, migraine, hypothyroidism and a tonsillectomy as child, with no hospitalisations. She is a non-smoker with minimal alcohol consumption, and no recent travel abroad. On examination she had a low grade pyrexia (37.9 °C). Respiratory examination revealed respiratory rate of 24 breaths/min; oxygen saturations were 97% on air. There were minimal coarse crackles in the right lung base and subclavian lymphadenopathy. Cardiovascular, abdominal and neurological examinations were unremarkable. Rectal examination showed no evidence of melena.

Full blood count revealed normocytic anaemia with a haemoglobin of 70 g/L (baseline haemoglobin 136 g/L), white cell count of 17.3×10^9/L (Neutrophil counts 14.7×10^9/L) and mildly raised C-reactive protein (74 mg/L). Platelet counts was also elevated (667×10^9/L). Erythrocyte sedimentation rate (ESR) was markedly elevated at 114 mm/hr. Her bilirubin was also slightly raised (29 μmol/L) with a low albumin (28 g/L), liver and renal function tests were otherwise unremarkable. A chest radiograph showed bilateral small pleural effusion.

In light of the persistent cough, night sweats, weight loss and significantly raised ESR > 100mm/hr, initial differential diagnosis included infective (e.g. tuberculosis), inflammatory (e.g. polymyalgia rheumatica, rheumatoid arthritis) and malignant (e.g. lymphoma, multiple myeloma) aetiology.

CT scan showed extensive mediastinal lymphadenopathy, with the largest lymph node seen in the paratracheal region measuring

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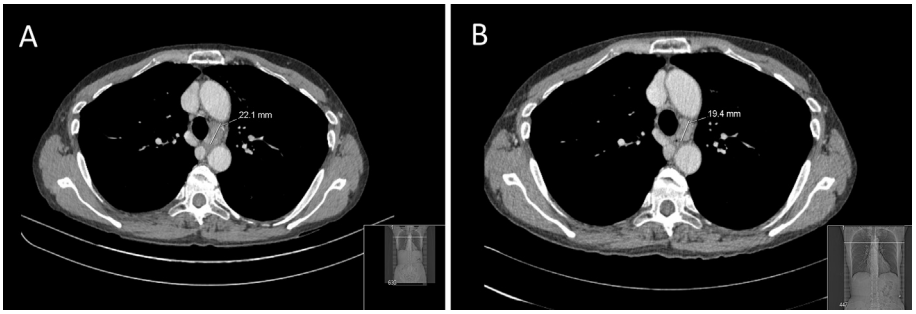

Fig. 1. Mediastinal lymphadenopathy associated with Mycoplasma pneumonia at presentation and 1 month follow up.

22 mm and additionally in the subclavian, pretracheal and paratracheal distribution (Fig. 1). No pulmonary masses were found. Broncho-alveolar lavage showed no acid-fast bacilli on smear, and no growth after 6 weeks of culture. No malignant cells were detected on cytology. Myeloma screen was negative with normal serum immunoglobulins and absence of Bence Jones protein in urinalysis. Serum calcium was also within normal range (2.13 mmol/L).

A haemolysis screen revealed raised lactate dehydrogenase (643 IU/L) and reticulocytes (9%, absolute count 292 $\times$ 10^9/L). Iron, folate and Vitamin B12 level and thyroid function test were all within normal range. Direct antiglobulin test (DAT) was positive for complement C3d, and negative for IgG, consistent with cold agglutinin haemolysis. Blood film confirmed multiple cold agglutinins, large platelets and target cells. Serology showed positive IgM for Mycoplasma pneumonia, and there was >4 fold increase in IgG between the initial sample and convalescent sample.

The patient was initially treated with intravenous (IV) fluids and empirical broad-spectrum IV pipercillin-tazobactam as well as oral clarithromycin for the atypical presentation. Given her symptomatic anaemia, two units of warm packed red cells was transfused. Her observations post-transfusion remained stable, apyrexial with no further significant haemolysis, and she was discharged with oral clarithromycin.

The patient was followed up in respiratory clinic one month following hospitalisation, and found to have a normal clinical examination. Interval CT scan showed improving but persistent lymphadenopathy (Fig. 1). Endobronchial ultrasound (EBUS) was therefore performed for mediastinal lymph node biopsy, which showed fragments of blood clots with lymphocytes/anthracotic lymphoid tissue. No malignant cells were seen. The patient remained symptom-free in two month follow up.

3. Discussion

We report a case of Mycoplasma pneumoniae infection presenting with few pulmonary signs and symptoms, but with marked haemolytic anaemia requiring transfusion, persisting lymphadenopathy and significantly raised ESR.

Pneumonia caused by Mycoplasma usually takes a benign self-limiting course, affecting mostly 5–20 year old patients [1]. It is rare for it to require hospital admission, as in our patient, and there are relatively few cases reported of morbidity and mortality attributable to Mycoplasma pneumonia, with most caused by respiratory failure. Mycoplasma has both pulmonary and extra-pulmonary manifestations. The latter is seen in up to 25% of patients with the infection [2], and includes skin, central nervous system and cardiac features, as well as haematological and immunological, both of which were prominent features in our patient [3–5].

Haemotological manifestations associated with Mycoplasma infections include subclinical haemolytic anaemia most commonly [6], as well as thrombocytopenia, haemophagocytosis, and hypercoagulability [7]. Cold agglutinins are IgM antibodies, and bind to red blood cell (RBC) I/i antigens in the cooler peripherally circulating blood. Subsequently in warmer parts of the circulation, complement fixation and activation occurs and the agglutinins detach. Haemolysis then results in a number of ways. Direct RBC lysis occurs by complement membrane attack complex, opsonised RBCs are also removed from the circulation by the reticuloendothelial system and finally agglutinated RBCs occlude the small vessels and contribute to mechanical lysis [8].

To our knowledge, only one adult case of haemolytic anaemia in Mycoplasma infection requiring transfusion has been reported, which had a fatal outcome [9]. Transfusion must be used sparingly in such instances, because transfused RBCs will be exposed to cold agglutinin autoantibodies, which could propagate further lysis reactions. This can be avoided by using “in line” blood warmers and keeping the patient warm to reduce elimination of the transfused erythrocytes by the autoantibodies [10].

Significant immunological manifestations of Mycoplasma were also exhibited in our patient. Such excessively raised ESR is extremely uncommon, and one study calculated the mean ESR in their sample population of children infected with Mycoplasma was 49 mm/hr [11]. Such widespread large lymphadenopathy are very uncommon in Mycoplasma infections, with only a few case reports documenting this finding. Lodi et al. detail a 48 year old male with several lymph nodes up to 50mm [9], whilst the remaining reports detail paediatric cases with lymph nodes up to 18mm [4,12].

Despite the unusual haematological and immunological manifestation of Mycoplasma infection, and the need for blood transfusion in haemolytic anaemia, our patient made a full recovery following thorough investigation to exclude tuberculosis and malignancy.

4. Conclusions

Mycoplasma pneumonia infection could present with persistent lymphadenopathy and significantly raised erythrocyte sedimentation rate (ESR). Despite mild pulmonary signs, it could be complicated with severe haemolytic anaemia in elderly patients. Direct antiglobulin (DAT) is useful in identifying cold agglutinin haemolysis, and if transfusion is indicated, warm packed red cells should be used to prevent further advertent haemolysis due to cold agglutinin antibodies.

Conflict of interests

None.

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