CASE REPORT

Cryptogenic organising pneumonia presenting with bilateral hilar and mediastinal lymphadenopathy

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Dr Mehmet Fatih İnci,
drfatihinci@gmail.com**SUMMARY**

Cryptogenic organising pneumonia is not considered in the differential diagnosis of bilateral hilar and mediastinal lymphadenopathy. We submitted a patient presenting with bilateral hilar and mediastinal lymphadenopathy. We suspected diagnosis of sarcoidosis, but the patient was diagnosed as cryptogenic organising pneumonia with the histological result. This is the second case report of cryptogenic organising pneumonia presenting with bilateral hilar and mediastinal lymphadenopathy.

BACKGROUND

Organising pneumonia is a pathological diagnosis defined by intra-alveolar buds of granulation tissue consisting of fibroblasts and myofibroblasts embedded in loose connective matrix, especially consisting of collagen. Cryptogenic organising pneumonia (COP) is a disease that occurs in the absence of any aetiology.¹ The three main imaging characteristic patterns of COP are multiple alveolar opacities (typical COP), solitary opacity (focal COP) and infiltrative opacities (infiltrative COP). Other rare presentations were multiple masses or nodules, bronchocentric consolidation, irregular lines or bands and perilobular opacities. Lymphadenopathy has been very rarely associated with COP. We describe a case of COP presenting bilateral hilar and mediastinal lymphadenopathy. To best of our knowledge, this case is the second one in literature.

CASE PRESENTATION

A 38-year-old woman presented with persistent dry cough, loss of weight and appetite, intermittent low-grade fever, fatigue, weakness, and dyspnoea on effort lasting 4 weeks duration. In the history, 2 years ago with similar symptoms, she was admitted to our clinic and with findings of erythema nodosum and bilateral hilar lymphadenopathy, and was diagnosed as sarcoidosis and started on prednisone treatment with dose of 1 mg/kg and continued for 12-month period. After the treatment, she had no symptoms along 10-month period. We did not have any of the previous roentgenograms and reports because of archival storage issue problems. On admission, there was no history of orthopnoea, paroxysmal nocturnal dyspnoea, exposure to toxic gas or organic dust or joint pain. She was a non-smoker and non-drinker.

INVESTIGATIONS

Physical examination was normal, blood pressure was 135/80 mm Hg, and oxygen saturation was

96% on room air. Laboratory data showed: white cell count, 11.1 K/ μ L, with 74% granulocytes and 17% lymphocytes; haemoglobin, 13.2 g/dL; platelet count, 364 K/ μ L; erythrocyte sedimentation rate 66 mm/h and C reactive protein 32 mg/dL; Ca, 9.9 mg/dL. Pulmonary function tests were measured with a ZAN 500 pulmonary function device (nSpire Health GmbH, Oberthulba, Germany) and verified a mild restrictive pattern and corrected diffusing capacity of the lungs for carbon monoxide value was 77%. A chest radiograph showed bilateral hilar enlargement, nodular infiltration in bilateral upper and middle lung zones, and consolidation at left lower lobe (figure 1). CT scan showed extensive bilateral hilar and mediastinal lymphadenopathy with areas of peripheral consolidations and nodules (figure 2). Differential diagnosis included sarcoidosis, tuberculosis, interstitial lung disease, autoimmune and collagen-vascular disease, viral infections, lymphoma or malignancy. An antibiotic regimen of doxycycline and ampicillin-sulbactam was given but did not respond. Blood and sputum cultures for bacteria and mycobacterium were negative. Also purified protein derivative test was negative. Analyses for rheumatoid factor, antinuclear antibodies and cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies were all negative.

Flexible bronchoscopy was performed but findings were not diagnostic. Two years ago, our patient had been diagnosed as sarcoidosis on clinical and radiological grounds. An open lung biopsy

Figure 1 A chest radiograph showing bilateral hilar enlargement, nodular infiltrates in bilateral upper and middle zones of the lungs and consolidation at left lower zone.

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Figure 2 CT scan showing bilateral hilar and mediastinal lymphadenopathies (A), with areas of peripheral consolidations and nodules (B).

was thought and performed from lingula segment of left upper lobe. The biopsy showed plugs of granulation tissue (fibroblast and lymphocytes in an oedematous or myxoid stroma) in the lumens of bronchioles, alveolar ducts and adjacent alveoli and also showed rounded nodules of granulation tissue in alveolar spaces called as Masson bodies (figure 3). This confirmed the diagnosis of cryptogenic organising pneumonia.²

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of COP includes diseases like community-acquired pneumonia, idiopathic interstitial pneumonias, hypersensitivity pneumonitis and chronic eosinophilic pneumonia and sarcoidosis.^{1 3} In our case, with the persistence of symptoms and lack of response to antibiotics, we diverged from bacterial or viral pneumonia. COP is a subgroup of idiopathic interstitial pneumonias. Sometimes small organising pneumonia areas are seen within another kind of disease such as non-specific interstitial pneumonia or idiopathic pulmonary fibrosis.³ We excluded the diagnosis of idiopathic interstitial pneumonia with clinicopathological collaboration. COP has similar clinical and radiographical presentation to that of subacute hypersensitivity pneumonitis. We excluded the disease because of absence of a known exposure to an aetiological agent and absence of poorly formed granulomas on lung biopsy. Chronic eosinophilic pneumonia can have a similar clinical and radiographical presentation to COP. In chronic eosinophilic pneumonia, blood eosinophilia is usually higher than 1500/mm³ and bronchoalveolar eosinophilia is higher than 25%. In our case blood eosinophilia was within normal range. Also in histopathological patterns, significant eosinophilic infiltration is seen and the eosinophilic infiltration is often accompanied by foci of necrosis and proteinaceous debris, termed eosinophilic microabscesses.^{1 3} Sarcoidosis has the characteristic morphological feature of the non-caseating granuloma of the lung and may have similar clinical and radiological presentation to COP. Histopathologically, the sarcoid granuloma contains epithelioid cells, frequently multinucleated giant cells and often has

cytoplasmic inclusions, such as asteroid bodies, Schaumann bodies and birefringent crystalline particles. By these findings we excluded all other diseases and established the diagnosis of COP.

TREATMENT

Oral prednisone (dose of 0.5 mg/kg/day) was started. Within 8 weeks, clinical improvement was observed and lymph nodes disappeared radiologically. The prednisone dose was gradually tapered and stopped at the end of fifth month (figure 4).

DISCUSSION

COP, formerly called as idiopathic bronchiolitis obliterans organising pneumonia, is a distinct clinical situation with major appearances of pneumonia, rather than a primary airway disorder. Once a diagnosis of COP is suspected, obtaining lung tissue for histopathological study is necessary.⁴ The pathogenesis of the pathological lesions of COP has been reported as early injury phase, second proliferative phase, third mature phase and resolution phase. COP is an exceptional model of an inflammatory lung disease with intra-alveolar fibrosis, that is, completely reversible with corticosteroid therapy. The diagnosis of COP depends on demonstration of the typical histological features in a patient with a compatible clinical and radiographic pattern. It is characterised by the presence of buds of granulation tissue consisting of fibroblasts–myofibroblasts surrounded by connective tissue especially collagen within the alveoli, protruding into the small bronchiole and alveolar ducts. Masson bodies containing a mixed cell population with lymphocytes, plasma cells, mast cells, monocytes and fibroblasts within the lumen of an alveolar duct may also present.^{1 2 5} In our patient histopathological investigation showed similar findings. Clinical features of COP are non-specific, with the progressive onset of mild fever, cough, malaise, anorexia, weight loss and mild dyspnoea. The mean age of onset of COP is 50–60 years, with rare cases reported in children. There is no sex predilection. COP is more common in non-smokers or ex-smokers, especially in female

Figure 3 Low power shows plugs of granulation tissue in bronchioles, alveolar ducts and alveoli (A) (H&E×40); high power shows mason bodies that are rounded nodules of granulation tissue in alveolar spaces (B) (H&E×200).

Figure 4 A chest radiograph showing an ill-defined consolidation at left lower zone.

patients.¹ The laboratory findings are non-specific and present leucocytosis and neutrophilia in half of the patients, an increased C reactive protein in 70–80% and an increased sedimentation rate in 84%.⁶ Our patient was female, non-smoker, and had similar clinical and laboratory presentations.

The most common radiographic abnormalities in COP patients are patchy migratory airspace opacities that are often multiple and bilateral. Their size varies from a few centimeters to a whole lobe, and an air bronchogram is often seen in consolidated opacities. Alveolar infiltrate can begin as focal lesions but usually become bilateral over time with predilection for presenting at periphery and lower lobes. Interstitial infiltration, honeycombing, cavities and pleural effusions are other rare presentation form of the disease.^{4–7} An evaluation of the literature revealed that on radiological imaging, occurrence of mediastinal lymphadenopathy has very rarely been associated with COP. A retrospective study conducted to determine prevalence of mediastinal lymphadenopathy in COP from University of British Columbia determined that COP may be associated with enlarged mediastinal lymph nodes but usually only one or two nodal stations are enlarged.⁸ Varma *et al*⁹ reported the first case of COP presenting with bilateral hilar and mediastinal lymphadenopathy and our case is the second COP case.

In COP, spontaneous remission is rarely seen. The use of corticosteroid does not always result in complete resolution and relapses are common.¹⁰ Most of COP patient respond to corticosteroid within several days and the response may be

dramatic. In our case clinical situation at both 2 years ago and present applications was either associated with activation and remission of COP or our patient was first recovered from sarcoidosis and then COP. Eventually, our patient gave good response to corticosteroid treatment and recovered.

In conclusion; this is the second case of COP presenting bilateral hilar and mediastinal lymphadenopathy. This case supported that COP previously called as bronchiolitis obliterans-organising pneumonia, can look like sarcoidosis both clinically and radiologically. COP must be incorporated in the differential diagnosis of bilateral hilar and mediastinal lymphadenopathy.

Learning points

- ▶ Cryptogenic organising pneumonia (COP) can look like sarcoidosis both clinically and radiologically.
- ▶ Lymphadenopathy has been very rarely associated with COP.
- ▶ COP must be incorporated in the differential diagnosis of bilateral hilar and mediastinal lymphadenopathy.

Contributors HK wrote the manuscript and followed the case. MT performed open lung biopsy and HS pathological investigation. MFI commented on the radiological images. All authors read and approved the final manuscript.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Cottin V, Cordier JF. Cryptogenic organizing pneumonia. *Semin Respir Crit Care Med* 2012;33:462–75.
- 2 Epler GR, Colby TV, McCloud TC, *et al*. Bronchiolitis obliterans organizing pneumonia. *N Engl J Med* 1985;312:152–8.
- 3 <http://www.uptodate.com/contents/cryptogenic-organizing-pneumonia?source=preview&anchor=H11162171&selectedTitle=1~99#H11162171> (accessed time 22 April 2013).
- 4 Cordier JF. Cryptogenic organising pneumonia. *Eur Respir J* 2006;28:422–46.
- 5 Kuhn C, McDonald JA. The roles of the myofibroblast in idiopathic pulmonary fibrosis. Ultrastructural and immunohistochemical features of sites of active extracellular matrix synthesis. *Am J Pathol* 1991;138:1257–65.
- 6 Izumi T, Kitaichi M, Nishimura K, *et al*. Bronchiolitis obliterans organizing pneumonia: clinical features and differential diagnosis. *Chest* 1992;102:715–19.
- 7 Ujita M, Renzoni EA, Veeraraghavan S, *et al*. Organizing pneumonia: peribubular pattern at thin-section CT. *Radiology* 2004;232:757–61.
- 8 Niimih H, Kangey EY, Kwong JS, *et al*. CT of chronic infiltrative lung disease: prevalence of mediastinal lymphadenopathy. *J Comput Assist Tomogr* 1996;20:305–8.
- 9 Varma S, Gupta S, Elsoueidi R, *et al*. Bilateral hilar lymphadenopathy in a young female: a case report. *J Med Case Rep* 2007;1:60.
- 10 Drakopanagiotakis F, Polychronopoulos V, Judson M. Organizing pneumonia. *A J Med* 2008;335:34–7.

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