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Case Report

Cryptogenic organizing pneumonia in hypothyroid patient: A case report

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Abstract

A 43-year-old female having hypothyroidism presented with fever, dry cough, loss of weight and appetite, dyspnoea on exertion since last 4 weeks with no past history of tuberculosis or pneumonia. General examination and vitals were normal with oxygen saturation of 97% on room air. Blood investigations showed leucocytosis, raised ESR and raised CRP levels. Chest computed tomography (CT) scan showed patchy scattered areas of consolidation in peripheral sub pleural location and in peri-bronchiolar location in both lung fields with ground glass opacity. Lung biopsy specimen gross showed multiple whitish soft tissue and microscopic examination revealed presence of intra-alveolar fibro mucoid plug with mild to moderate interstitial infiltrates of lymphocytes, few plasma cells and neutrophils which supported the diagnosis of cryptogenic organizing pneumonia. The patient was treated with oral prednisone with a dose of 0.4mg/kg/day for 15 days resulting in complete resolution of respiratory symptoms. A rare case of co-existence of hypothyroidism and COP is presented here as thyroid disorders may have some role in etiology of COP which is a diagnostic challenge in itself.

Keywords: Cryptogenic organising Pneumonia, hypothyroidism, HRCT, lung biopsy.

Introduction

Cryptogenic organizing pneumonia (COP) is a form of idiopathic interstitial pneumonia characterized by lung inflammation and scarring that obstructs the small airways and alveoli. It may present as flu like illness with cough, fever, malaise, fatigue and weight loss. It usually affects adults in midlife 40-60 years of age with no specific underlying cause. (1) The first case of COP was reported in 1983 by Davidson et al (2) followed by detailed study by Epler et al in 1985 (3).

Diagnosis of COP is difficult challenge as its diagnosis by exclusion of other causes of organizing pneumonia. Other forms of organizing pneumonia may result from infection (bacteria, viruses, parasites, or fungi); drugs; or a reaction to radiation therapy for breast cancer. Organizing pneumonia can also be associated with specific disorders such as certain connective tissue disorders, blood malignancies (cancers), or ulcerative colitis. (4) Diagnosis can be helped by HRCT and lung biopsy. HRCT may show bilateral diffuse alveolar ring-shaped opacities with ground glass opacities and biopsy shows histopathological findings in alveolar spaces, alveolar ducts and insterstitial lung. Lack of specific clinical

manifestation, clinical biomarkers and precise imaging features, makes COP a difficult idiopathic condition to be diagnosed and distinguished from community-acquired pneumonia.

Hypothyroidism can be a risk factor many disease, though it has not been previously reported to be associated with COP, here we present a case of COP in hypothyroid patient. Patients with hypothyroidism accompanied with COP are considered more critical and complicated cases which demands detailed investigation and better therapeutic management practices.

Case Presentation

A 43-year-old female suffering from fever, dry cough, loss of weight and appetite, dyspnea on exertion lasting for 4 weeks duration without any apparent cause was presented to the hospital. Patient does not have any significant past of family history of such disease but she was diagnosed with hypothyroidism. She also had past history of hysterectomy before 2 years. No past history of tuberculosis or pneumonia was present and she was a non-smoker and non-drinker.

On examination at initial admission, pulse rate was 67/min, blood pressure was 120/70 mm of Hg and oxygen saturation was 97% on room air. Blood investigations revealed normal haemoglobin level 13.8 gm%, elevated white blood cell count 12.9 K/cu.mm, with higher percentage (73%) of neutrophils and (24%) lymphocytes. The platelet count was 281K/cu.mm, erythrocyte sedimentation rate was 68 mm/h and C reactive protein was 3.2 mg/L which were significantly higher than the normal range.

Chest x-ray showed prominent broncho-vascular markings in both lower para cardiac area. Chest Computed Tomgraphy (CT Scan) imaging revealed patchy scattered areas of consolidation predominantly in peripheral sub pleural location and in peri-bronchiolar location in both lung fields spraying anterior segment of right upper lobe and lateral segment of right middle lobe. Chest CT imaging also indicated area of ground glass opacity surrounded by consolidation noted in apico-posterior segment of left upper lobe. Pulmonary function tests indicated mild restrictive ventilatory defect and moderate diffusion abnormality. Blood and sputum cultures for bacteria and mycobacterium were found to be negative. Also purified protein derivative test was negative. Furthermore, analysis for rheumatoid factor, antinuclear antibodies and cytoplasmic and perinuclear antineutrophilic cytoplasmic antibodies were all found negative.

Bronchoscopy was performed but no masses, haemorrhage or stenosis were observed. Blood and lavage fluid analysis were negative for tumour-associated markers. On cytological examination no malignant cells were observed in lavage fluid. Biopsy was performed from right upper lobe; lung biopsy specimen gross showed multiple whitish soft tissue- 0.2 cm to 0.3 cm and microscopically showed lung tissue with intraalveolar fibromucoid plug and mild to moderate interstitial infiltrates of lymphocytes, few plasma cells and neutrophils. Initially the focus of diagnosis was centred towards pulmonary infection considering the symptoms and causative agents but lung biopsies and histopathologic review confirmed the diagnosis of cryptogenic organising pneumonia.

Treatment

Oral prednisone with a dose of 0.4mg/kg/day was immediately started on diagnostic confirmation of COP for 15 days. CT examination during the treatment revealed clinical improvement in patient with progressive disappearance of intra-

alveolar fibromucoid plug. The condition of the patient continued to improve steadily over the hospitalization period followed by her discharge with tapered dose of 5 mg/day oral prednisolone for next 10 months. Patient was functionally normal after 12 months of complete follow up and treatment.

Discussion

Cryptogenic organizing pneumonia is still a difficult case to diagnose. Its presentation varies from mild symptoms of upper respiratory tract infection to severe breathlessness and hypoxia with picture similar to pneumonia. Exact etiology of the disease is not known and diagnosis is always by exclusion. Here we present a case of COP in hypothyroid patient.

With recent advances in clinical and radiological fields COP is classified as interstitial lung disease. Histopathologically it is characterized by formation of loose plugs of granulation tissues engulfed by fibroblasts, myofibroblast and Masson bodies blocking alveoli, respiratory bronchioles and distant airspaces. COP involves formation of clusters of fibrinoid inflammatory cells with no specific cause and is initiated as response to lung injury followed by reaction of alveolar epithelium producing granulation tissues. (5)

Many a times, COP diagnosis is confused with radiation pneumonitis. Earlier reports on effects of radiation on lungs suggest that radiation therapy causes a potential complications like lungs inducing radiation pleuropulmonitis followed by chronic radiation fibrosis during treatment of patients with breast or lung carcinoma or mediastinal neoplasms. Radiation therapy has been long known to induce an inflammatory reaction in lungs which has similar pathological features as organizing pneumonia. (6) A similar study was done recently wherein a female patient with adenocarcinoma after radiation therapy presented with a biological inflammatory syndrome suffering from dyspnoea with chest imaging revealing migratory multiple alveolar opacities. On performing transbronchial lung biopsies Intra-alveolar granulation tissue were observed which clearly indicated typical cryptogenic organizing pneumonitis. (7)

A previous cytological and immunological study of bronchoalveolar lavage of COP patients revealed a specific pattern which was distinctive from patients with idiopathic pulmonary fibrosis, chronic eosinophilic pneumonia and extrinsic allergic alveolitis. The marked features were abnormal increase in lymphocytes, moderately neutrophils, eosinophils and mast cells along with foamy macrophages and plasma cells in BAL. A similar observation with BAL analysis was made in present study also. Even it was established by previous study that there was decrease in CD4/CD8 ratio with increase in activated T-cells specifically expression of human leucocyte antigen-DR and normal percentage of CD57+ cells. (8)

In multiple studies it is observed that presentation of clinical symptoms, laboratory results, respiratory function test findings and cytological analysis of bronchoalveolar lavage fluid indicate no significant difference between cases of idiopathic COP and other lung disease. A study by S Cazzato et al, suggested transbronchial lung biopsy coupled with BAL as initial diagnostic approach for COP patients. It was concluded that combination of both the procedures improves diagnostic yield with 86% sensitivity. BAL in combination with trans- bronchial biopsy (TBB) can be useful to exclude other disorders arising due to infectious disease. (9)

The presentation of our case is similar with that reported classically in literature. Bilateral-peripheral consolidation and ground glass opacities confined to lower lung lobe were the most common radiological findings in patients with COP

which was consistent with previous reported literatures. Lower lobe of the lung was the common site of lesions detected in our study which was also reported by previous study indicating predominance of lesions in the lower lung areas in patients with COP. (9) Elevated ESR with increased inflammatory cytokines were commonly observed in patients with COP. This was similar to previous studies where majority of cases have reported elevated levels of CRP which are synthesized by liver during inflammation. (10, 11) Only difference in this case was co-existance of hypothyroidism which is not reported previously. Exact association and reason for such coexistence needs to be explored. Thyroid hormones play variety of functions in body and rarely associated with COP. Previous autoimmunity study observed that patients with chronic lymphocytic thyroiditis commonly manifesting as local inflammatory response are rarely affected with COP which is infrequently reported. Few cases demonstrating symptoms of COP are concomitantly affected with auto-immune thyroid disease. A similar case was presented by Litao Guo et al in a 49-year-old female suffering from COP with increased thyroid gland. On performing thyroid ultrasound and thyroid function tests diagnosis of Hashimoto's thyroiditis was confirmed indicating it involvement in development of COP. (12) A study by Watanabe K et al, presented 4 cases where patients with thyroid disease were associated with COP. It was observed that one patient diagnosed with COP had a past history of hypothyroidism and surgery for thyroid cancer in which the clinical manifestation of COP was found to be related to multiple myeloma. Another reported reason for clinical manifestation of COP was due to administration of thiamazole drug. Chronic thyroiditis was also found to be associated with development of COP in patients as reported by Cohen et al which also suggests the importance of association between COP and chronic thyroiditis. The results of present study were found to be in consistence with previous study observations. (13-16)

In conclusion, COP presents a diagnostic challenge to most treating doctors. Clinical and radiological findings do not suffice accurate diagnosis of COP but they can show the direction and help in excluding other similar conditions. A definitive confirmation of diagnosis needs transbronchial biopsy (TBB) and BAL which provides elements to predict response to therapy. Open lung biopsy should be practiced less frequently in cases where transbronchial biopsy (TBB) and BAL are not specific and distinctive. Thyroid disorders may have some association with COP but not clearly understood. Corticosteroids are hallmark in treatment of COP resulting in rapid clinical, radiological and functional improvement. However, it does not result in complete resolution and commonly leads to relapse when discontinued but overall, long-term prognosis for people with cryptogenic organizing pneumonia (COP) is generally good.

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