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Case Report

Cryptogenic organising pneumonia- Atypical presentation

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ABSTRACT

Organizing pneumonia is an interstitial lung disease that affects the distal bronchiole, respiratory bronchiole, alveolar ducts, and walls. To diagnose cryptogenic organising pneumonia, other aetiologies, such as inflammatory infections, connective tissue disease, drug responses, pulmonary infarction, and organ transplantation need to be ruled out. Radiological and histological progress in this disease will help to understand the disease in a better way. Early diagnosis of organizing pneumonia is important because of a good prognosis if it is treated earlier. But atypical clinical and radiological presentation will lead to difficulty in diagnosis and delay in treatment. Here we report two atypical presentations of organizing pneumonia cases to highlight the importance of upfront aggressive multimodality diagnostic approaches to rule out rare causes of cavitating lesions.

1. Introduction

Cryptogenic organizing pneumonia (COP), the idiopathic form of organizing pneumonia (OP) (formerly called bronchiolitis obliterans organizing pneumonia), is a type of diffuse interstitial lung disease that affects the respiratory bronchioles, distal bronchioles, alveolar walls, and alveolar duct. In OP alveolar wall is the primary area of injury. It's a different clinical entity with inflammatory pneumonia rather than a primary airway disorder, thus the omission of the term 'bronchiolitis obliterans' from the name.

The histopathologic findings characteristic of COP includes an excessive proliferation of granulation tissue, which comprises loose collagen-embedded myofibroblasts and fibroblasts, mainly involving alveoli and alveolar ducts, with or without intraluminal polyps of bronchi.[1]

Organizing pneumonia is classified as interstitial lung disease because it can be associated with interstitial infiltrate.[2] In addition to the cryptogenic form, organizing pneumonia can be seen in secondary causes like connective tissue diseases, malignancy, a variety of drugs, and other interstitial pneumonia. Hence all these should be ruled out before diagnosing COP.[3] We herein share our experience of Organizing pneumonia mimicking like lung malignancy.

2. Case Details

2.1. Case 1

A 50-year-old female, a nonsmoker presented with dry cough and breathlessness for 3 months duration. Breathlessness was initially of grade I Modified Medical Research Council (mMRC) and it progressed over time to grade III mMRC. The patient had no history of haemoptysis,

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fever, loss of appetite, weight loss, skin rashes, joint pain, regurgitation, or myalgia. No history of tuberculosis or antituberculosis drug (ATT) intake. She had a blood pressure of about 110/70 mm of Hg and pulse rate of 98/minute, respiratory rate of around 22/minute, oxygen saturation was 96% in room air by pulse oximetry. On respiratory system examination, bilateral normal vesicular breath sounds with no added sounds. Other system examination was found to be normal.

Chest X-ray showed ill-defined and irregular nodular opacities in the mid, and lower zones of the right lung and lower zone of the left lung. She was further evaluated by contrast-enhanced computed tomography of the thorax which revealed multiple pulmonary nodules in bilateral lungs (right>left) largest measuring 2.1 cm X 2.1 cm in the lateral segment of the right lower lobe, few nodules in lateral and anterior segments of the right lung lower lobe. No abnormality was found in abdominal and pelvic CT.

Laboratory investigations on admission showed: erythrocyte sedimentation rate (ESR) 32 mm in first hour, white blood cells (WBC) 5 X 10^9 cells, DLC (neutrophils 55%, lymphocytes 34%, monocytes 6%, eosinophils 2% and basophils 3%). Creatinine was 85 mmol/mL-1, and blood urea nitrogen (BUN) was 0.33 mg/mL. Pulmonary function tests indicated a mild restrictive defect with a normal CO transfer. Arterial blood gas analysis showed PH-7.41, PCO2-39mm Hg, PO2-86 mm Hg, and HCO3-22 mEq/L. six-minute walk test (6MWT) suggestive of exertional desaturation from 96% to 88% and has walked for 370 meters. Anti-neutrophilic antibodies (ANA) and Anti-neutrophilic cytoplasmic antibodies (ANCA) were negative. Microbiology specimens (blood and sputum cultures) were negative. Serum tumor markers were done to rule out malignancy and metastases. Fibreoptic bronchoscopy revealed no abnormality. Bronchial washing and biopsy were normal. As Fibreoptic bronchoscopy is non-diagnostic, CT-guided biopsy was taken from a lateral segment of the right lower lobe. Histopathology showed alveolar air spaces with few Masson bodies made of myxoid connective tissue forming polypoid structures in air spaces suggestive of cryptogenic organizing pneumonia. On immunohistochemistry, tumour markers were negative and fungal stains were negative. The patient was started on 1mg/kg/day of prednisolone for four weeks after which the patient showed clinical improvement along with radiological resolution and so steroids gradually tapered over the next two months. No exertional desaturation in follow-up 6MWT and has walked for 450 meters. While on tapering doses of steroids, the patient developed increased breathlessness of mMRC grade 3 for which a repeat chest x-ray was taken which showed new consolidation changes associated with previous nodular opacities. Sputum stain for acid-fast bacilli was positive for mycobacterium tuberculosis and the patient was started on ATT along with tapering of steroids. The patient is still under follow up showing both clinical and radiological resolution post-ATT. (Figure 1)

2.2. Case 2

A 37-year-old male with no comorbidities presented with complaints of cough with scanty whitish expectoration and mMRC grade 3 of breathlessness for 3 weeks. He had no history of hemoptysis, fever, loss of weight, loss of appetite, chest pain, and wheezing. He was not a treated case for pulmonary tuberculosis or ATT intake. He is not a smoker and an alcoholic. On clinical examination, he had a 110/70 mm Hg of blood pressure, pulse rate of 98/min, and oxygen saturation of 87% in room air, maintaining 95 % with 5 liters of oxygen therapy. On chest auscultation, occasional fine inspiratory crepitations were heard in bilateral infrascapular and infra-axillary areas with bilateral normal vesicular breath sounds.

Chest X-ray showed multiple bilateral irregular nodular opacities with left lower zone patchy consolidation and elevated right hemidiaphragm (Figure 2). He was further evaluated by Computed tomography of the thorax which showed multifocal patchy air space opacities in the form of conglomerate nodules in which few nodules were cavitating throughout bilateral lung fields - suggestive of infective aetiology and eventration of right hemidiaphragm (Figure 2). No abnormality was detected in abdominal and pelvic CT.

Laboratory investigations on admission showed: white blood cells (WBC) 4.5×10^9 cells, DLC-(neutrophils 60%, lymphocytes 32%, monocytes 6%, eosinophils 2%, and basophils 0%), erythrocyte sedimentation rate (ESR) 20 mm·h-1, blood urea nitrogen (BUN) was 0.42g·mL-1 and Creatinine was 0.6 mg/dl. A restrictive defect was noted in the pulmonary function test. Arterial blood gas analysis showed PH-7.42, PCO2-34 mm Hg, PO2-55 mm Hg, and HCO3-24 mEq/L. Sputum pyogenic culture, fungal culture, and tubercular infection by gene expert (CBNAAT -cartridge-based nucleic amplification test) were done which was negative. Fibreoptic bronchoscopy guided bronchoscopic lavage (BAL) and transbronchial biopsy was done. BAL cytology and other cultures were normal. Transbronchial lung biopsy reported the presence of type II pneumocyte hyperplasia and chronic inflammatory cells along with foamy histiocytes. There is intra-alveolar and interstitial congestion with polypoidal plugs of loose connective tissue (Masson bodies) suggestive of cryptogenic organizing pneumonia (Figure 3). Because of organizing pneumonia, the patient was started on prednisolone at a dose of 1mg/kg/day for 4 weeks and tapered over 6 months. The patient has improved clinically and radiologically with steroids. Informed consent was obtained from both patients for reporting.

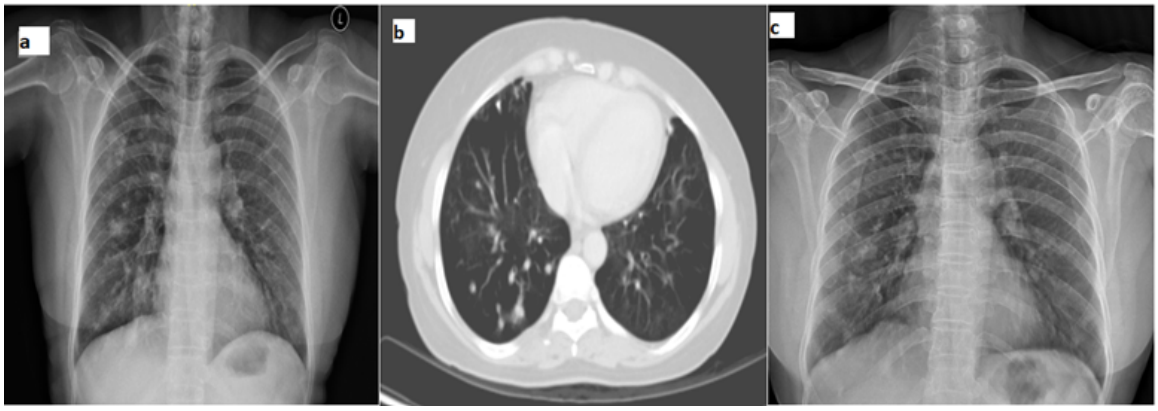

Fig. 1: Case 1 **a:** Chest X-ray showed ill-defined and irregular nodular opacities in right side lung mid zone, lower zones, and left lower zone; **b:** Contrast enhanced computed tomography of thorax which showed multiple nodules in bilateral lungs (Right>left); **c:** Post-treatment chest X-ray showing resolution.

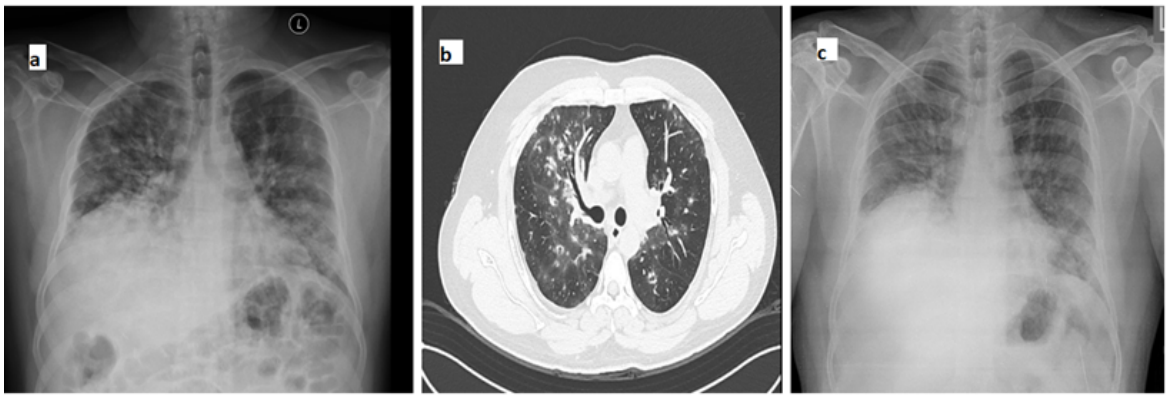

Fig. 2: Case 2 **a:** Chest X-ray showing multiple bilateral irregular nodular opacities with left lower zone patchy consolidation and elevated right hemidiaphragm; **b:** Computed tomography thorax showing multifocal patchy air space opacities in the form of conglomerate nodules in which few nodules were cavitating throughout bilateral lung fields; **c:** Post Treatment Chest X-Ray resolution.

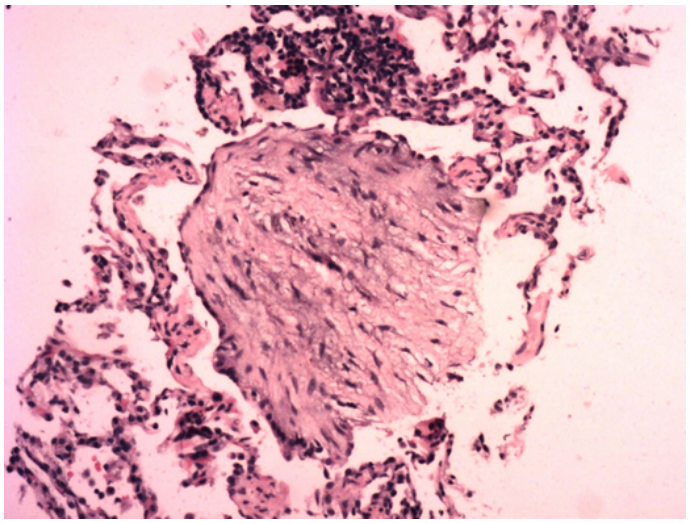

Fig. 3: HPE image showing Masson body with chronic inflammatory cells

3. Discussion

Here we reported two cases of OP with a varied clinical and radiological presentations. OP occurs due to the repair of pulmonary tissue that can be due to cryptogenic or secondary to lung injury (infection, inhalation of cocaine and toxic gases, drug toxicity, radiotherapy, organ transplant,). It can be rarely associated with vasculitis, lymphoma, primary lung cancer or metastasis, hypersensitivity pneumonitis, eosinophilic pneumonia, and other interstitial lung diseases. Most commonly seen in the fifth or sixth decade with equal distribution among both sexes but here the second case presented at a younger age.[2]

The presentation is usually subacute onset with the following manifestations like persistent dry cough (72 percent), difficulty in breathing (66 percent), fever (51 percent), malaise (48 percent), and weight loss (57 percent).[4] The above two cases was presented in different duration suggesting that organizing pneumonia may have both subacute and chronic duration. The absence of progressive worsening of the complaints,acute febrile symptoms, as well as repeatedly negative microbiological tests, make the possibility of an initial infectious process triggering the lung injury less likely. Also, on the extracted nodule the pathological examination did not reveal any necrosis or marked infiltration of polymorphonuclear lymphocytes, and the microbiological examination remained sterile.

Computed tomography is an important imaging diagnostic for the assessment of disease and is also useful for site assessment of biopsy. The appearance of OP on computed tomography is polymorphic which includes patchy radial bands of consolidation, ground-glass opacity, and nodules. The classical picture in HRCT includes an atoll sign or reverse halo sign and peripheral patchy consolidation with peribronchovascular predominant pattern. Atoll sign is not specific as it is seen in other conditions like granulomatosis with polyangiitis, sarcoidosis, Paracoccidioidomycosis, pneumocystis, tuberculosis, and lipoid pneumonia.[3] Niksarlioglu et al. found 76.6% of organizing pneumonia as consolidation.[5] Maimon et al. noted consolidation in 77%, ground-glass opacities in 86%, and nodules in 32% of organizing pneumonia.[6] In this report, Case one presented with multiple bilateral nodules in which few were cavitating whereas the second case presented as multifocal patchy air space opacities in the form of conglomerate nodules in which few nodules were cavitating throughout bilateral lung fields which is not specific to organizing pneumonia.

Cryptogenic organizing pneumonia manifesting as nodules are difficult to differentiate from primary or metastatic lung cancer and hence biopsy is necessary to get the final diagnosis. Because of the benign nature of organizing pneumonia and its, good response to steroid therapy, every attempt should be made to clinch the diagnosis.[7]

Microscopy typically shows extensive proliferation of granulation tissue, which comprises loose collagen-embedded myofibroblasts and fibroblasts, involving alveoli with or without intraluminal polyps. Other key histologic features are patchy and peribronchiolar distribution, preserved lung architecture, mild interstitial chronic inflammation, and the presence of foamy macrophages.[2]

To diagnose cryptogenic organizing pneumonia histopathological examination is necessary with the presence of the above-described findings along with an absence of features like fibrosis (honeycombing), granuloma, necrosis, abscess, vasculitis, and hyaline membranes. This will help in ruling out other causes like eosinophilic pneumonia, vasculitis, non-specific interstitial pneumonia, and hypersensitivity pneumonitis Henceforth, an effective search to find other causes of organizing pneumonia including stains to detect infectious agents is mandatory.[8]

Optimal management of organizing pneumonia depends on the severity of the symptoms. Patients who are asymptomatic/mild symptomatic can be monitored without therapy.[9] Reassessment to be done at 8-12 weeks. In symptomatic patients, it is recommended to start systemic glucocorticoid therapy. Usually, prednisolone is started at a dose of 0.75to 1mg/kg per day. In the case of rapidly progressing disease high dose glucocorticoid therapy is recommended (I.V methylprednisolone 500-1000mg for 3-5 days).[5] There was no consensus regarding the duration of treatment and it is based on the clinical and radiological assessment, however, there were reports which showed relapse during tapering or after stopping the steroids.[8]

Typical COP has an excellent prognosis following steroid treatment but determining the prognosis of organizing pneumonia due to secondary cause is more difficult because of the diversity of reported cases.[10]

4. Conclusions

Diagnosis of organizing pneumonia requires an integrated clinical, radiological and pathological approach. Although organizing pneumonia is not a rare lung condition, it should be kept in the differential diagnosis for nodules with or without cavitation in the CT thorax especially when the clinical onset is subacute and the initial microbiological workup is negative. We postulate that every case of multiple nodules with a cavity should undergo extensive diagnostic workup including most importantly the tissue diagnosis. Though a CT scan plays an important role in initial diagnosis, the role of a biopsy is vital.

5. Conflict of Interest

None.

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None.

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