Case Report

A case of Cryptogenic Organizing Pneumonia (COP): Atypical presentation

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ABSTRACT

We report a case of cryptogenic organizing pneumonia (COP) with rare radiological presentation. A 29-year-old female presented to us with symptoms of progressive breathlessness and dry cough for 3 weeks. Chest X-ray showed bilateral all zones non-homogenous opacities. She was treated in an outside hospital with antibiotics and was referred to us as the symptoms progressed. High-resolution computed tomography of the chest revealed bilateral diffuse ground glass opacities in a centrilobular pattern involving all the lobes. Fiber-optic bronchoscopy with transbronchial lung biopsy was done. Histopathological examination (HPE) was consistent with organizing pneumonia. Additional investigations could not delineate a specific cause. Hence, the patient was diagnosed with COP. She was treated with immunosuppressants. The patient improved clinically, and subsequent Chest X-rays showed radiological improvement. COP is a rare disease and is suspected when there is no response to routine management along with the typical radiological picture. Our patient presented with atypical radiological presentation. Tissue biopsy and HPE helped us to arrive at a diagnosis. Prompt treatment aided in an uneventful outcome.

Key words: Cryptogenic organizing pneumonia, Fiber-optic bronchoscopy, Transbronchial lung biopsy

Cryptogenic organizing pneumonia (COP), known formerly as bronchiolitis obliterans organizing pneumonia, is a form of idiopathic interstitial pneumonitis. COP is a consequence of alveolar injury due to an unknown insult and is characterized by the formation of organized buds of granulation tissue obstructing the alveolar lumen and bronchioles without disruption in the lung architecture [1]. The diagnosis of COP is usually delayed because of non-specific clinical presentation. Patients usually present with cough, breathlessness, and fever, which mimics infective pneumonia, leading to treatment with antibiotics. An alternative diagnosis is sought when there is no clinical response, and the pneumonia is non-resolving. A definitive diagnosis is achieved by invasively acquiring tissue for histopathological demonstration of diagnostic features. The exact incidence and prevalence in India is not known due to the complexity involved in diagnosis. However, incidence is estimated to be around 1–3/1,00,000 hospital admissions [2]. Typical radiological presentation of bilateral asymmetrical peripheral consolidation or ground glass opacities (GGOs) in high-resolution computed tomography (HRCT) usually hints at the diagnosis of COP [3]. However, atypical radiological presentations have also been reported in the literature [4,5].

In this article, we report a case of COP with atypical radiological presentation, intending to share our unusual clinical observation and our approach to the management of this case.

CASE REPORT

A 29-year-old female with no known comorbidities, never a smoker, and mother of two children presented to our outpatient department with 3 weeks of progressive exertional dyspnea and dry cough. She had no complaints of hemoptysis, chest pain, loss of appetite, loss of weight, myalgia, joint pain, or rashes. She had no history of tuberculosis or antitubercular therapy in the past. There was no significant exposure history. Initially, the patient was treated with antibiotics and was referred to our center as symptoms worsened.

Her general examination was unremarkable (body mass index - 23 kg/m^2), except that her oxygen saturation was 94% in

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room air. Respiratory system examination revealed bilateral fine inspiratory crepitations over all areas.

A chest X-ray was performed, which showed bilateral all zones of ill-defined non-homogenous opacities with cardiomegaly (Fig. 1a). We proceeded to perform an HRCT of the chest, which showed bilateral diffuse GGOs in a centrilobular pattern involving all the lobes with no specific gradient of distribution. The pulmonary artery trunk appeared dilated with few subcentimetric paratracheal and subcarinal nodes (Fig. 2a-c).

The 2D echocardiography showed normal ejection fraction, dilated right atrium and right ventricle, and tricuspid regurgitation with severe pulmonary hypertension (PHT) (mean pulmonary arterial pressure [mPAP]=68 mmHg). Blood investigations were done: Complete blood counts and liver and renal function tests were within normal range. Erythrocyte sedimentation rate and C-reactive protein were elevated. Other investigations, such as the rheumatoid arthritis factor, anti-cyclic citrullinated peptide, antinuclear antibody profile, anti-neutrophil cytoplasmic antibody profile, and angiotensin-converting enzyme, were negative. Pulmonary function tests – spirometry showed moderate restriction with severely impaired carbon monoxide (CO) transfer (21% of predicted). Fiber-optic bronchoscopy (FOB) with transbronchial lung biopsy (TBLB) was done. Broncho-alveolar lavage (BAL) cultures and gene X-pert were negative.

The histopathological examination (HPE) of the biopsy unveiled type 2 pneumocyte hyperplasia of the alveolar walls, focal lymphoid aggregates in the interstitium with occasional foci of secondary atelectasis showing prominent hyalinization and collagenization with prominent fibroblast, fibro-collagenous plugs and organized desquamated cells (Fig. 3). Hence after thorough history taking, examination, and investigations a diagnosis of COP with PHT was made.

Immunosuppressant therapy with the steroid prednisolone 1 mg/kg (60 mg) was started. A cardiology opinion was obtained, and the patient was started on diuretics and sildenafil. With the initiation of treatment, the patient started experiencing gradual improvement in symptoms. The steroid dose was tapered over a period of 6 months, and mycophenolate mofetil (MMF) was introduced during the course of tapering steroids as the patient had a reversion of symptoms while tapering. Serial chest X-ray showed radiological improvement (Fig. 1b). The patient improved clinically and mPAP has reduced to 25 mmHg. The patient is on our regular follow-up.

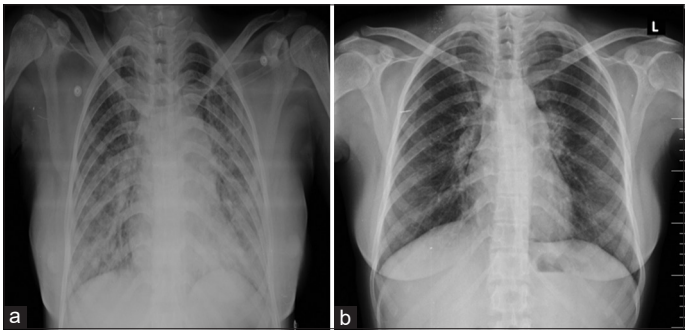

Figure 1: (a) Chest X-ray shows bilateral all zones ill-defined non-homogenous opacities with cardiomegaly; (b) Follow-up chest X-ray shows resolution of opacities

DISCUSSION

Organizing pneumonia is a pattern of healing of lung tissue after an injury. It can be either cryptogenic or secondary to a specific injury. In COP, usually, there is no specific cause identified. Secondary organizing pneumonia occurs due to a specific injury such as viral infection, drug toxicity, inhalation injury, radiation therapy, or due to underlying conditions such as connective tissue disorders [6]. The mean age of presentation is 50–60 years, whereas it is uncommon in younger age groups [7].

Patients usually present with non-specific symptoms such as non-productive cough, fever, malaise, fatigue, and a few complaints of dyspnea with or without respiratory failure [8]. General and respiratory system examination may be unremarkable or may reveal crepitations in a few cases. Pulmonary function tests may show a restrictive defect in spirometry with impaired diffusion of CO [9]. A chest X-ray may reveal bilateral non-homogenous opacities. The characteristic finding in the HRCT chest includes bilateral asymmetric peripheral consolidation or GGOs. Less common findings include reverse Halo sign (Atoll's sign) (20%), nodular opacities, pleural effusion (10–30%), and mediastinal lymphadenopathy (20–40%) [3]. Based on the symptoms and presentation, patients are misdiagnosed to have pneumonia. A diagnosis of organizing pneumonia is suspected only when there is no response to antibiotic therapy, and a radiological picture consistent with organizing pneumonia is encountered. A definitive diagnosis requires obtaining lung tissue for HPE. A surgical lung biopsy (SLB) will provide adequate tissue for HPE. However, it is associated with the risk of several complications. The diagnostic accuracy of computed

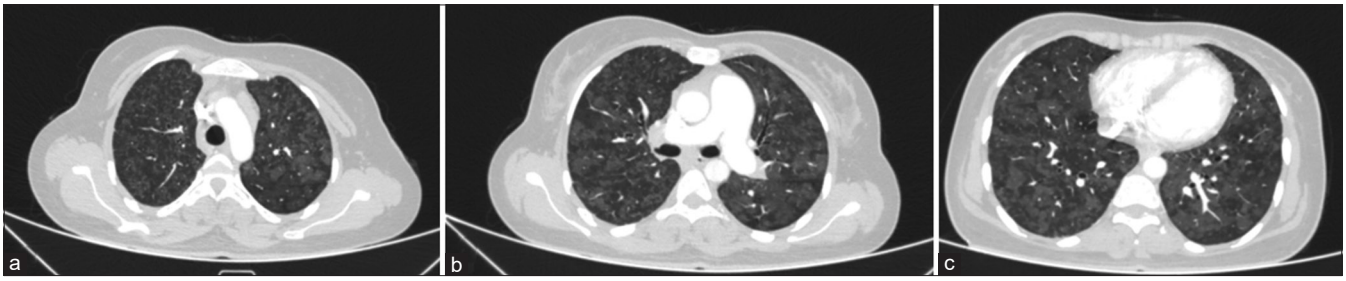

Figure 2: (a-c) High-resolution computed tomography of the chest, which shows diffuse ground glass opacities in a centrilobular pattern involving all the lobes with no specific gradient

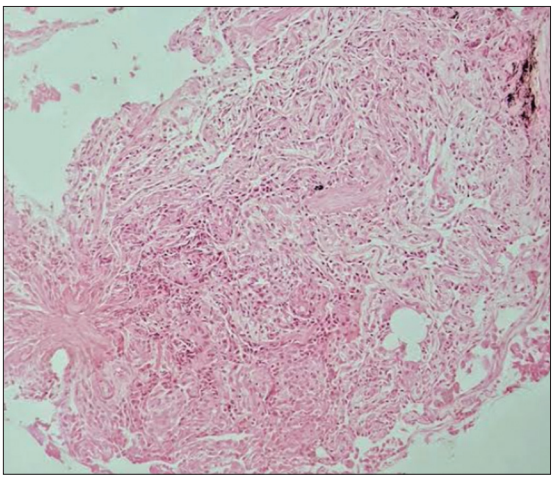

Figure 3: Histopathological examination of the biopsy shows type 2 pneumocyte hyperplasia of the alveolar walls, focal lymphoid aggregates in the interstitium with occasional foci of secondary atelectasis showing prominent hyalinization and collagenization with prominent fibroblast, fibro-collagenous plugs, and organized desquamated cells

tomography-guided lung biopsy has been shown to be comparable to that of SLB [10]. FOB with BAL and TBLB is an alternative to rule out infectious etiology and establish the diagnosis of organizing pneumonia. Transbronchial lung cryo-biopsy should be utilized where equipment and expertise are available. On HPE on the obtained tissue, the presence of buds of granulation tissue made up of fibroblasts and myofibroblasts implanted in connective tissue points toward organized pneumonia. The proliferation of these granulation tissue buds (Masson bodies), which are found predominantly within airspaces (alveoli, alveolar ducts, and terminal bronchioles), represents the hallmark feature of organizing pneumonia [11]. Additional investigations should be performed to identify the cause of secondary organizing pneumonia. COP is diagnosed when a definite cause cannot be identified.

Our case presented with the atypical radiological presentation of bilateral diffuse centrilobular GGOs. Viral pneumonia, including COVID-19, non-specific interstitial pneumonia, acute pulmonary edema, pneumocystis carinii pneumonia, drug-induced lung injury, diffuse alveolar damage, and pulmonary alveolar proteinosis are the speculated differential diagnoses for the radiological picture of bilateral GGOs in HRCT [12]. Diagnosing COP in the absence of characteristic presentation was a challenge, as the disease presented with non-specific symptoms and atypical radiology. However, lung biopsy and HPE played a significant role in diagnosis. On certain occasions where uncommon etiologies are presumed, a multidisciplinary team discussion, including the treating pulmonologist, radiologist, pathologist, and rheumatologist may aid in arriving at a definitive diagnosis [13].

Studies have shown that early diagnosis and prompt treatment with immunosuppressants are associated with excellent outcomes in COP [14,15]. Steroids are the first choice of immunosuppressants in the treatment of COP and it is associated with rapid and complete resolution of symptoms and radiological abnormalities [9]. However, till date, there are no protocols or supportive literature on the choice of steroid, route of administration, dose, or duration [16]. Steroid therapy has to be tailored according to the patient's disease severity and other factors such as response to therapy, relapse, tolerance, and comorbidities [17]. Significant relapses of up to 66% with steroid therapy have been reported [18]. An additional immunosuppressant alongside steroid therapy is added in such cases as azathioprine, cyclophosphamide, or MMF [19]. According to various studies and reports, COP has a favorable prognosis when treated, and fatalities are rare [1].

CONCLUSION

Diagnosis of COP requires a multi-disciplinary approach. Since clinical and radiological features are non-specific, pathological confirmation is essential. Physicians should keep an eye out for unusual presentations of COP, especially when there is no response to routine management, as early diagnosis and appropriate management are associated with improved patient outcomes.

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