Novel Insights from Clinical Practice

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Organizing Pneumonia due to Actinomycosis: An Undescribed Association

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Established Facts

- Organizing pneumonia is a pulmonary histological pattern that can be either cryptogenic or a response to various insults.

Novel Insights

- Actinomycosis, a rare infectious disease, can present itself with this pattern and should therefore be part of the differential diagnosis of organizing pneumonia.

Key Words
Actinomycosis · Interstitial lung diseases · Organizing pneumonia · Pulmonary inflammation

Abstract
Organizing pneumonia is a pathologic entity characterized by intra-alveolar buds of granulation tissue that can extend to the bronchiolar lumen. It is a non-specific finding reflecting a pattern of pulmonary response to aggression that can be cryptogenic or associated with several causes. Pulmonary actinomycosis is a rare infectious disease, of bacterial aetiology, and of difficult diagnosis. This disease usually causes non-specific respiratory symptoms and radiological findings, and the treatment is based on the use of antibiotics. The authors describe a clinical case of a 53-year-old male smoker (50 pack years), initially seen for complaints of right-sided chest pain and sub-febrile temperature. Imaging studies revealed a mass in the inferior right lobe and enlarged mediastinal lymph nodes. Empirical treatment with antibiotics caused partial and temporary improvement. Transthoracic biopsy revealed a pattern of organizing pneumonia with giant multinucleated cell granulomas. Repeat imaging studies revealed an enlargement of the pulmonary mass and therefore a right inferior lobectomy was performed. The pathologic study revealed a histological pattern of organizing pneumonia surrounding inflammatory bronchiectasis with a large number of *Actinomyces* colonies. To our knowledge there is presently no report in the literature of organizing pneumonia associated with *Actinomyces* infection.

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Introduction

Organizing pneumonia (OP) describes a histopathologic pattern characterized by the development of anastomosing plugs (buds) of granulation tissue, consisting of proliferating fibroblasts and myofibroblasts embedded in connective tissue, filling the distal pulmonary airspaces (alveoli and alveolar ducts) [1]. Mild interstitial inflammation and foamy macrophages in the non-filled alveoli are also typical [2]. The buds can also involve bronchiolar lumina (bronchiolitis obliterans), and in the past this entity was also called 'bronchiolitis obliterans organizing pneumonia'. However, currently the preferred designation is OP, to prevent confusion with other histological patterns [3] as, from a histological point of view, the pathology mainly concerns alveoli rather than bronchioles and the pulmonary function test findings reveal a restrictive rather than obstructive pattern.

This finding is a form of pulmonary response to a variety of insults and is not specific to a determinate disease. It can be related to infectious disease, drug induced injury [4], connective tissue disease [5], transplants, malignancy, post-radiotherapy (outside the radiation ports), inhalational injury, and vaccination. When extensive investigation fails to determine a cause in a patient with this pulmonary lesion, the diagnosis is then cryptogenic organizing pneumonia, a disease with variable clinical and radiological manifestations that usually responds in a favourable way to steroids [6–10].

Actinomycosis is a rare infectious disease caused by bacteria from the genus *Actinomyces*. These are Gram-positive, facultative anaerobic, filamentous organisms, and can be found in the normal flora of the oral cavity, bronchial secretions and gastro-intestinal tract. The disease is usually caused by *Actinomyces israelii*, although other species may be involved [11]. The cervicofacial area is the most frequent site of involvement, but almost any organ can be affected. Pulmonary involvement occurs in about 15% of the cases and is therefore a very rare finding [12].

The disease occurs in all ages, and is more frequent in men. Alcoholism, underlying respiratory disease (chronic bronchitis, emphysema and bronchiectasis) and poor dental hygiene and dental disease are the known risk factors. Clinical features have changed in the last decades, presumably due to better overall hygiene and widespread availability of antibiotics. Presently, the usual presentation is of a slowly progressing pneumonia, with fever, weight loss, productive cough, and chest pain. Radiographic manifestations are also non-specific, unless there is direct involvement of the chest wall, with pleural involvement and bone destruction [13, 14]. Confusion with tuberculosis and malignancy is common, but the infection may also be associated with neoplastic lesions, which should therefore be excluded [15].

The diagnosis of actinomycosis is usually a difficult one, with most patients being investigated for other diseases, before the diagnosis is made. Definitive diagnosis is made by culture of the bacteria in anaerobiosis, but often a presumptive diagnosis is made by histological observation of the characteristic sulphur granules [16]. The clinical material can be obtained by transthoracic or transbronchial biopsy though surgical biopsy is also frequently performed, mostly due to the suspicion of cancer.

Without treatment, actinomycosis can be fatal, but correct diagnosis provides the opportunity to institute treatment with long-term antibiotherapy, usually penicillin or its derivatives [17, 18].

Case Report

A 53-year-old male was seen in the outpatient clinic for complaints of right-side chest pain and mild fever of 2 weeks duration. He also complained of chronic cough and sputum, mostly in the morning, without any recent changes. He denied shortness of breath, headache, excessive sudoresis or other complaints. His pain was not related to movement or exercise.

Past medical history and habits included smoking (50 pack years) and a kidney stone several years ago.

He was self-medicating with paracetamol for the pain and fever with good results.

Examination showed a middle-aged man in good general condition, and no respiratory distress. His vital signs were normal. Oropharingeal examination revealed a dental prosthesis and several dental caries. Cardiac auscultation did not reveal any abnormalities, and on pulmonary auscultation scattered ronchi and crackles were present on the lower right pulmonary field. There was no peripheral oedema.

He was medicated with antibiotics for presumed low respiratory tract infection and discharged with an order for a chest X-ray.

Six weeks later, on a follow up visit he mentioned only temporary and partial improvement with the treatment and was now also complaining of cough and bloody sputum. Examination was unchanged. The chest X-ray, revealed an obliteration of the right cardio-phrenic angle, and was followed by chest CT, which showed a mass in the posterior right lower lobe of 6.6 × 3.3 cm, soft-tissue density and also right para-tracheal and subcarinal enlarged lymph nodes.

A transthoracic biopsy was performed to exclude cancer and histological study revealed a pattern of organizing pneumonia with giant multinucleated cell granulomas (fig. 1).

The patient was then referred for bronchoscopy which revealed no abnormal findings and microbiological (direct exam and culture) and cytological studies were negative.

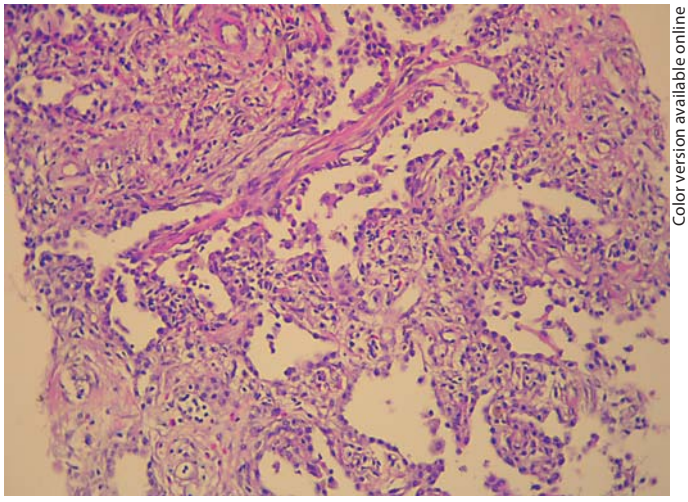

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Fig. 1. Pulmonary trans-thoracic biopsy showing predominant myofibroblastic polyps occupying bronchiolar and alveolar spaces, interstitial uniform inflammation and fibroblast proliferation, associated with various multinucleated giant cell granulomas. HE, ×200.

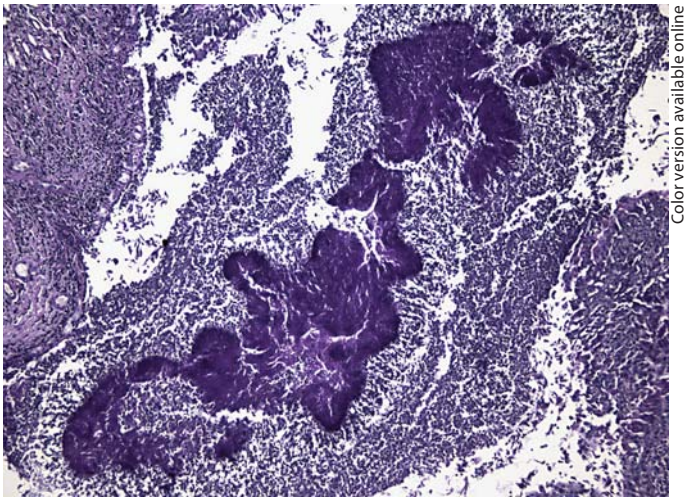

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Fig. 3. Lower lobe resection: extensive areas of organizing pneumonia surrounding an inflammatory bronchiectasis occupied by large actinomyces colonies. PAS, ×200.

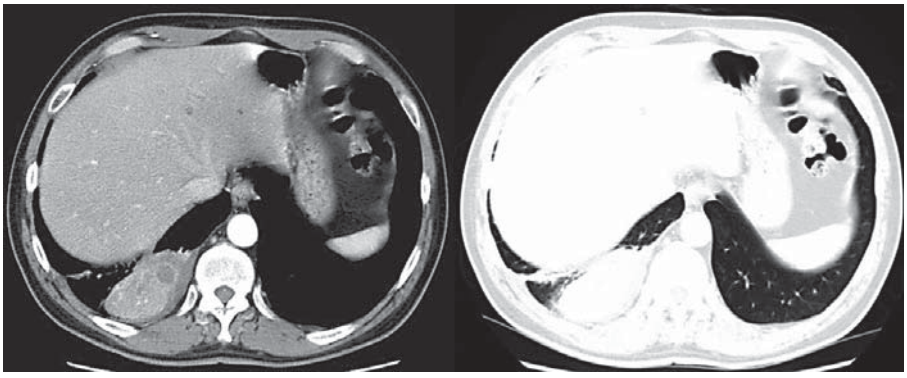

Fig. 2. Second chest CT showing a parenchymal heterogeneous opacity in the right lower lobe and a small associated pleural effusion.

Electrocardiography showed sinus rhythm, and no signs of ischemic heart disease.

Lung function tests were remarkable for moderate obstruction with lung hyperinflation and a positive response to bronchodilators: FVC 2.83 l (73.6% predicted), FEV_1 2.00 l (64.2% predicted), FEV_1/FVC 70.64, TLC 7.13 l (115.3% predicted), RV 3.49 l (165.5% predicted).

Due to the still high clinical suspicion of cancer or pulmonary tuberculosis, the patient was kept under close observation, but the complaints got progressively worse.

A repeat chest CT after 8 weeks revealed mass growth, now with 7 × 6.8 cm, the same enlarged lymph nodes and a small pleural effusion on the right side (fig. 2).

The decision was made to undertake a surgical approach. During surgery an inflammatory mass of 7-cm diameter and with pleural adhesion was found and the surgeon decided to perform right inferior lobectomy with curative intent (no intra-operative pathology analysis was made).

Histological analysis revealed extensive areas of organizing pneumonia, surrounding an inflammatory bronchiectasis with a large number of *Actinomyces* colonies (fig. 3). Due to the initial high suspicion of cancer, no microbiological analysis was made. After surgery the patient became asymptomatic.

Discussion

Pulmonary actinomycosis is rarely included in the differential diagnosis of a patient with a pulmonary infiltrate. The diagnosis is usually obtained by microbiological analysis of sterile fluid or by histological observation. The typical histological appearance includes a variable number of abscesses composed of actinomycotic granules (sulphur granules), surrounded by fibrosing granula-

tion tissue. Giant cells may also be seen, and seem to be associated with aspiration [19]. The observed bronchiectasis in this patient's surgical biopsy argues in favour of this possibility.

Organizing pneumonia has been previously described in association with various bacterial infections, but not with actinomycosis. Although the clinical and imaging features of secondary organizing pneumonia are similar to cryptogenic organizing pneumonia, haemoptysis is uncommon in organizing pneumonia [1] and could be attributed in this case to the co-existant pulmonary actinomycosis [12]. The obstructive pattern found on the lung function tests is probably due to the patient's smoking history [6, 20]. Histological exam alone is not enough to distinguish between cryptogenic and secondary OP [6, 21], although secondary OP may be associated with more interstitial inflammation or fibrosis and diffuse alveolar damage [1]. In the present case, the nature of the disease (unifocal infiltrate in a smoker with haemoptysis) led to a more invasive management option, with surgical excision, which is frequent in patients with focal OP [8]. This led to the diagnosis of an infection as the probable cause of the OP revealed by the trans-thoracic biopsy.

In conclusion, this case is remarkable not only for the development of pulmonary actinomycosis in an immunocompetent patient, but mostly for the associated histological appearance of organizing pneumonia, which was most likely caused by this infection. As far as the authors are aware this is the first report of organizing pneumonia in a patient with pulmonary actinomycosis. The differential diagnosis of this entity should therefore include this infection from now on.

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