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An unusual presentation of a more common disease entity

Case report

A 66-year-old, male patient with a 10-pack-year history of smoking was referred to the internal medicine consultation because of a 4-week history of fatigue, weakness, intermittent low-grade fever, appetite and weight loss, and a mild dry cough. His previous history was unremarkable and his physical examination was normal. Routine laboratory screening revealed leukocytosis (11.08×10^9 leukocytes per L), elevated C-reactive protein (72.1 mg·L^{-1}) and erythrocyte sedimentation rate 57 mm·h^{-1}. Analyses for rheumatoid factor, antinuclear antibodies, and cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies were all negative. Pulmonary function tests (static and dynamic volumes, flow–volume curve, and lung diffusion capacity) were within the predictive values. Chest radiography demonstrated bilateral hilar enlargement. The patient subsequently underwent a computed tomography (CT) scan of the chest (figure 1).

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Task 1
Describe the imaging findings noted on the CT scan of the chest.

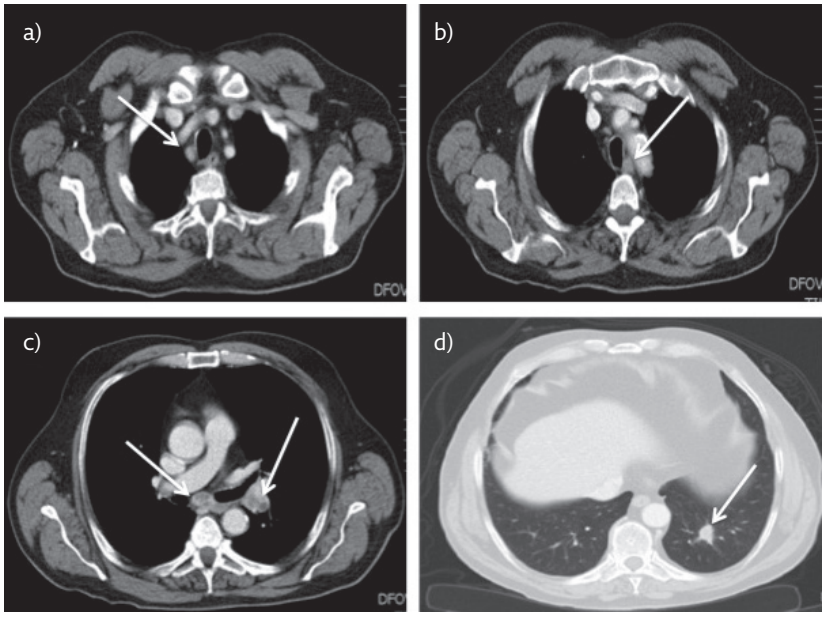

Figure 1 *Chest CT.*

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Answer 1
The images demonstrate a new spiculated lung nodule 2 cm in diameter in the left lower lobe (figure 1d). Hilar and mediastinal lymphadenopathies in positions 2R (figure 1a), 4L (figure 1b), 7 and 10L (figure 1c) are present.

Positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) was performed, showing hypermetabolic activity of the focal lung lesion (figure 2d), and moderate-to-strong FDG-positive left and right paratracheal, subcarinal and hilar mediastinal lymph nodes (figure 2).

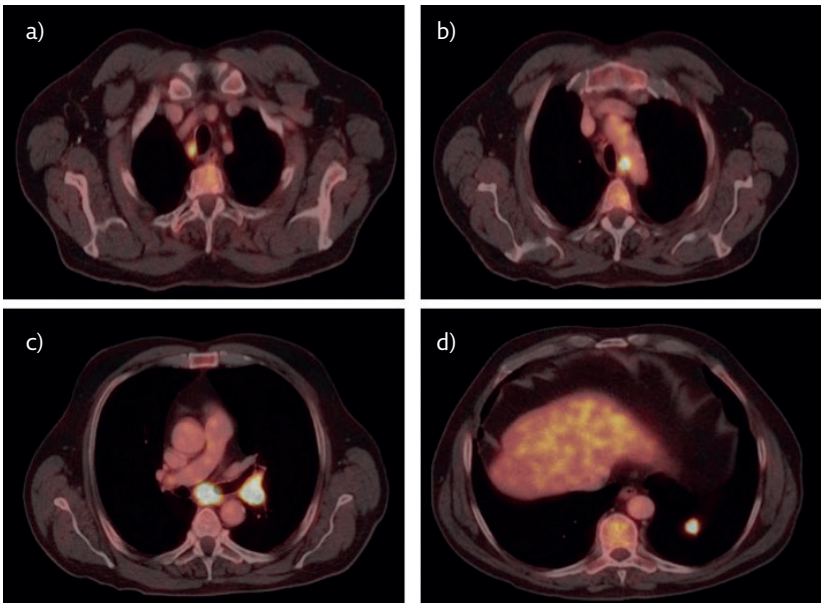

Figure 2 *Fusion PET-CT.*

Task 2
What is your differential diagnosis and what is the most appropriate diagnostic step?

Answer 2

Lymph nodes may be enlarged for a variety of inflammatory, infectious or malignant reasons. Here, the differential diagnosis would be lung carcinoma, lymphoma, tuberculosis, sarcoidosis and organising pneumonia (OP). His smoking history and the PET pattern prioritised malignancy as a key differential diagnosis.

The next step should be an attempt to obtain lung tissue for histopathological diagnosis. Because the lung lesion was not easily accessible, the decision was made to proceed to endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of the enlarged lymph nodes.

Bronchoscopy with EBUS-TBNA of the lymph nodes in stations 4R, 4L and 7 was performed. The bronchoscopy findings were normal. Results of Gram and Ziehl–Neelsen stains on bronchoalveolar lavage fluid were negative. Cytological analysis of the lymph nodes revealed a neutrophilic cell infiltrate without malignant cells. Following multidisciplinary team discussion, a CT-guided, percutaneous, transthoracic needle biopsy of the left lower lobe mass was performed in order to rule out malignancy. Histological examination revealed thickening of the alveolar septa because of interstitial mononuclear inflammation, hyperplasia of type 2 cells and young, fibrotic, intra-alveolar plugs (figure 3).

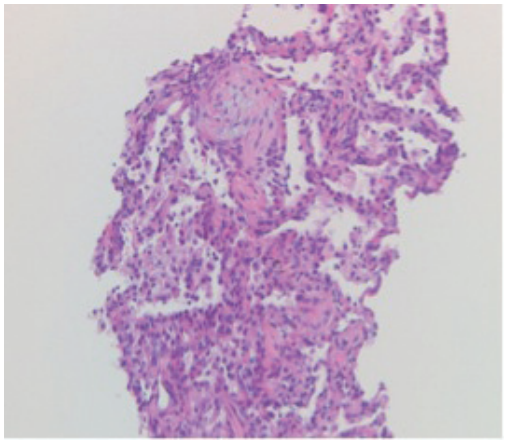

Figure 3 *Histological examination of the transthoracic needle biopsy specimen (haematoxylin and eosin staining, 200×).*

Task 3

What is the final diagnosis and how would you manage this patient?

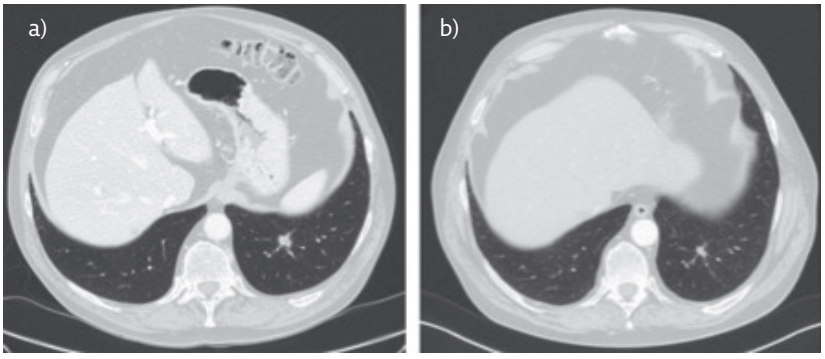

Figure 4 *Follow-up CT after a) 2 and b) 4 months showed marked improvement, with only a small, residual millimetric nodular lesion being present.*

Answer 3

The histological pattern of this lesion resembled that of OP. Because no underlying aetiology or associated disorder was found, cryptogenic organising pneumonia (COP) is the most likely diagnosis.

The management of COP has not been studied in prospective randomised trials, so treatment decisions are based on general clinical considerations including the severity of symptoms and the rapidity of disease progression. Corticosteroids are the current standard treatment, although the optimum dose and duration are less certain [1].

The patient was started on methylprednisolone 32 mg·day^{-1}, which was gradually tapered, and stopped after 3 months. We observed a rapid clinical improvement and a gradual resolution of the abnormal CT findings on follow-up scans (figure 4).

Discussion

COP, the idiopathic form of OP, formerly called "bronchiolitis obliterans organising pneumonia", is a well described entity with characteristic clinicoradiological features and pathological diagnostic criteria [2]. COP can present with a wide variety of radiological manifestations. Three main imaging patterns may be distinguished:

- multiple patchy alveolar opacities (typical pattern)
- a solitary focal lesion (focal pattern like in our case)
- diffuse bilateral infiltration

Definitive diagnosis of COP relies on finding of typical pathological and clinical–radiologic features, and the exclusion of possible causes or associated disorders [3, 4].

Focal organising pneumonia (FOP) is a rare form of OP and presents as an isolated focal lesion on chest imaging, which may mimic lung cancer [5]. Only sporadic FOP cases or small case series have been reported in the literature. FOP accounts for approximately 10–15% of all cases of OP and the majority of cases are cryptogenic [6, 7]. Patients are usually asymptomatic or mildly symptomatic and it is more frequent in middle-aged male smokers [6–8]. Reported CT features of FOP show a wide range of variations, including solitary or multiple nodules or masses with irregular margins and a round or oval shape [9]. FOP lesions are predominantly located in the periphery of the lungs. Mediastinal lymphadenopathy involvement is an uncommon feature in OP. A retrospective study by Niimi *et al.* [10] showed that enlarged mediastinal nodes were present in 36% (eight out of 22) of the patients with COP. Usually, only one or two nodal stations are enlarged. Althoff Souza *et al.* [11] reported detectable enlargement in 38% (six out of 16) patients with COP. The presence of enlarged nodes was less common in COP than in the other idiopathic interstitial pneumonias (p=0.04). In the series of Zhao *et al.* [12], mild mediastinal lymph node enlargement was present in ~20% of the patients. To our knowledge, three previous cases of OP presenting with extensive lymphadenopathy have been reported in literature [13–15].

OP is one of the benign thoracic conditions that may cause false positive results on PET-CT. Data on increased FDG uptake in OP are limited. In the series of Baha *et al.* [16], hypermetabolic activity of the focal lung lesion was demonstrated in all 14 FOP cases with a median maximal standardised uptake value (SUV_{max}) of 3.5±2.7 (range 2.1–13.1). Erdoğan *et al.* [17] demonstrated hypermetabolism on FDG-PET in all radiological subtypes of OP, with a mean SUV_{max} of the lesions calculated as 6.5.

The diagnosis of FOP requires histopathological identification of a predominant pattern of OP, characterised by polypoid intraluminal plugs of proliferating fibroblasts and myofibroblasts within alveolar ducts and airspaces, with varying degrees of bronchiolar involvement [2–4]. Reports suggest that most patients underwent surgical resection of their lung lesion because of suspicion of lung cancer [7, 8, 12]. Although curative, pulmonary resection of FOP should be avoided, as it is unnecessary considering the benign nature of the disease and the efficacy of steroid therapy. CT-guided biopsy may be a valid alternative to more invasive procedures as shown in our case and in the series of Poulou *et al.* [18], where in all 14 patients, a single procedure yielded a diagnostic specimen.

Rapid clinical and imaging improvement is usually obtained with corticosteroid therapy. The efficacy of steroids has been widely documented, and steroids continue to be recommended as the first choice of therapy for patients with symptomatic and progressive COP [1, 4]. The majority of patients recover completely with oral corticosteroids but relapse is common.

Conclusion

The combination of a FDG-PET-positive solitary lung nodule with significantly enlarged bilateral hilar and mediastinal lymph nodes, as observed in the present case, initially strongly suggested the diagnosis of locally advanced lung cancer. FDG-PET cannot differentiate FOP from a malignant tumour but it can help guide invasive procedures that should be performed when there is suspicion of malignancy. The presence of mediastinal lymphadenopathy has been very rarely reported in patients with COP. Finally, this case highlights the importance of obtaining histological confirmation of a suspicious pulmonary lesion, not only for establishing a definitive diagnosis but also for the planning of invasive surgical treatment or not.

Conflict of interest

None declared.

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