CASE REPORT

Histoplasmosis mimicking primary lung neoplasm

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SUMMARY

A 70-year-old man, ex-smoker with a 3-pack-year smoking history, presented with a 5-week history of persistent cough. There were no positive findings on clinical examination. The patient's chest X-ray showed a nodular density in the right lung, initially thought to be malignant. After an extensive workup which included CT-guided lung biopsies, bronchoscopies, positron emission tomography scanning, among many other investigations, discussion at the respiratory multidisciplinary team meeting, and a right upper lobe lung resection, a diagnosis of histoplasmosis was performed.

BACKGROUND

Histoplasmosis is a systemic mycosis most prevalent in North and South America, parts of Asia and Africa. Outside these areas, histoplasmosis is rarely seen.¹ Presentation can range from an asymptomatic patient, with an incidental finding of hilar adenopathy on chest X-ray (CXR), to rapidly progressive pulmonary disease and respiratory failure.² While cases are unusual in non-endemic areas, the prevalence is increasing.²

CASE PRESENTATION

A 70-year-old man presented with a 5-week history of persistent, dry cough despite antibiotics. Examination was unremarkable. He was an ex-smoker of 3 pack-years and had a medical history consisting of peptic ulcer disease, previous deep vein thrombosis and pulmonary embolism post-total knee replacement and prostate cancer treated with radiotherapy and hormonal therapy.

INVESTIGATIONS

CXR was performed showing a rounded opacity in the right lower zone, close to the right heart border. CT thorax confirmed a 2.1×1.5 cm right upper lobe spiculated lesion (figure 1). Two pulmonary nodules in the right upper lobe, and prominent mediastinal and hilar lymph nodes were also noted. Completion CT staging revealed enlarged lymph nodes in the abdomen.

Bronchoscopy showed no endobronchial lesion. Bronchoalveolar lavage of the right upper lobe showed no growth or malignant cells. He underwent positron emission tomography (PET) CT scan which showed intense tracer uptake in the sigmoid colon and a fluorodeoxyglucose-avid nodule in the right lower lobe, consistent with a nodule previously identified on CT. A CT-guided lung biopsy was non-diagnostic, showing atypical epithelial cells.

After discussion at the lung cancer multidisciplinary team meeting, colonoscopy was arranged.

Polyps were seen and removed, and reported as tubulovillous adenomas with low-grade dysplasia. At this point, he was discussed at the gastroenterology multidisciplinary team meeting and a decision was made to conduct a biopsy on a PET-positive abdominal node. He then underwent laparoscopy at which the left hepatoduodenal node was removed. Histology showed a non-necrotising granuloma. There was no evidence of malignancy and no micro-organisms. A further endobronchial ultrasound and CT-guided lung biopsy were again non-diagnostic.

The patient was then referred to the cardiothoracic team who performed a wedge resection of the right upper lobe. The resulting histology revealed necrotising and xanthogranulomatous inflammation with foamy macrophages containing multiple intracytoplasmic cysts (H&E staining; figure 2). These intracytoplasmic cysts stained positive for Grocott's methenamine silver stain (figure 3). This was found to be consistent with histoplasmosis after consultation with Infectious Diseases, King's College Hospital, London.

DIFFERENTIAL DIAGNOSIS

Given the smoking history and chronic cough, the initial CXR and CT were highly concerning for a primary lung tumour. Following PET-CT, a colorectal primary with lung metastases was also a strong consideration. Following hepatoduodenal node biopsy, which showed non-necrotising granuloma, it was thought that sarcoidosis was likely. However, due to difficulties in obtaining a histological diagnosis, malignancy remained a likely diagnosis until after the wedge resection.

TREATMENT

Following confirmation of diagnosis after wedge resection, the patient was given a full course of

Figure 1 CT taken on 14 June 2011, spiculated right upper lobe lesion.

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Figure 2 H&E stain of section from 18 mm lung nodule showing xanthogranulomatous inflammation with foamy macrophages containing multiple intracytoplasmic cysts.

itraconazole treatment, following discussion with infectious diseases team.

OUTCOME AND FOLLOW-UP

The patient had a difficult postoperative course, with the development of haemothorax and a prolonged intensive care unit admission. However, he made an excellent recovery. The initial lesion was fully excised in the operation theatre and the second lesion resolved completely following itraconazole therapy. There is a relapse rate of 10–20% associated with histoplasmosis after treatment, and it is recommended that patients are reviewed for up to 2 years post-treatment.³ This patient has been well following treatment. Follow-up CT of the thorax at 1 year showed no nodules or lymphadenopathy.

DISCUSSION

This case demonstrates a number of difficulties in making the diagnosis of histoplasmosis. These difficulties include Ireland being a low-prevalence area, the patient having no clear exposure or immunodeficiency, the similarity on multiple imaging modalities to a lung neoplasm, and the difficulty in getting a definitive histological diagnosis.

Histoplasmosis is a fungus, acquired by inhalation of mycelium spores.³ This is particularly likely to occur in areas of soil with high rates of bird droppings or in areas inhabited by bats.

Figure 3 These intracytoplasmic cysts stain positive for Grocott's methenamine silver stain. The morphology is consistent with histoplasmosis.

This inhalation may cause a localised inflammatory response, where macrophages phagocytose the fungus. However, often it is not completely destroyed, allowing it to spread and remain within the body where it can reactivate at a later stage, not unlike tuberculosis.³ It is more common for reactivation to occur when a patient has become immunosuppressed, most commonly secondary to human immunodeficiency virus, however, this patient had no history of this. It has been reported that histoplasmosis can present as an asymptomatic solitary pulmonary nodule, often calcified and with a fibrous capsule.⁴ However, as demonstrated above, this patient had a large spiculated lesion, which is highly suspicious for lung cancer. Histoplasmosis also more often presents as a peripheral nodule.

In chronic diseases, the diagnosis is usually performed by isolation of fungus from a respiratory sample, with sensitivity rates of 50–85%.⁵ Antigens may also be found in blood, or urine but these are typically less sensitive in chronic cases.

This case has particular relevance with the current ongoing investigation of CT as a possible population screening tool for lung cancer. In areas of high prevalence of histoplasmosis, it is thought that CT may be a less useful tool, due to a likely higher number of pulmonary nodules secondary to histoplasmosis. There is also a concern that this could lead to more invasive tests being required to definitely rule out a lung neoplasm. Starnes *et al*,⁶ based in Cincinnati, Ohio (an area of particularly high prevalence), recently evaluated this, and found that the rates of positive findings on first CT were 61%, close to triple the rate typically found. Similarly, McMahon *et al*,⁷ in the Mayo clinic, found rates of 51%. However, Starnes *et al* went on to evaluate the numbers of cancers found, biopsies performed and found that no patient underwent an invasive lung biopsy for a lesion that was in fact benign.

Learning points

- ▶ Spiculated lesions on CT of the thorax are often thought to be malignant, but as demonstrated above, a wide differential must be considered.
- ▶ It is hugely important to have a respiratory multidisciplinary discussion about such complex patients, particularly where there is a difficulty in reaching a diagnosis. In our hospital, the multidisciplinary team includes respiratory physicians, medical oncologists, cardiothoracic surgeons, radiologists and histopathologists.
- ▶ It is preferable to have a definitive diagnosis before a patient undergoes such an invasive procedure as a wedge resection. However, sometimes it is not possible to do so, nor is it in the patient's best interests, if it delays treatment unnecessarily.

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Competing interests None.

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