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ENDGAMES

CASE REPORT

A persisting puzzling pneumonia in a young man

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A 23 year old immunocompetent man with a history of childhood asthma was referred to the respiratory physicians with a four week history of productive cough, painful throat, fever, rigors, generalised myalgia, and vague discomfort in his left chest. He also had slight abdominal tenderness in the left upper quadrant.

He was a non-smoker, with no history of recent foreign travel, seizures, or misuse of alcohol or drugs. There was no family history of note.

A chest radiograph organised by his general practitioner showed multiple cavities and consolidation in the left lower lobe. A radiological diagnosis of cavitating pneumonia in the left lower lobe was made.

On examination he had a fever (39°C), looked unwell, and had a respiratory rate of 16 breaths/min, resting oxygen saturation of 96% on air, and blood pressure of 130/72 mm Hg. He was tachycardic (112 beats/min), with reduced chest expansion, dullness on percussion, and reduced breath sounds over his left lower lobe.

Blood tests confirmed an acute phase response, with a raised C reactive protein of 187 mg/L (normal range 0-4), white cell count 17.2×10^9/L (4.0-10) (with neutrophilia 15.3×10^9/L), urea 4.7 mmol/L (3.4-7), and albumin 35 g/L (37-49). The results of urinalysis and electrocardiography were normal. Blood and sputum cultures were consistently negative.

Despite antibiotics (oral amoxicillin) given as per regional guidelines, his fever continued over the next four days and he underwent computed tomography of the chest. This confirmed left lower lobe basal segment consolidation, with multiple air and fluid filled cavities, and associated left hilar and subcarinal lymphadenopathy. In addition, an 18 mm lesion was seen in his left lower lobe bronchus. Bronchoscopy was performed and the lesion biopsied.

The bronchoscopic biopsy samples confirmed a diagnosis of pulmonary carcinoid tumour.

Questions

1 What are the causes of a non-resolving pneumonia?

2 How do pulmonary carcinoid tumours most commonly present?

3 How should pulmonary carcinoid tumours be managed?

4 What other conditions are associated with carcinoid tumours?

Answers

1 What are the causes of a non-resolving pneumonia?

Short answer

The differential diagnoses for non-resolving pneumonia include atypical, viral, or mycobacterial pneumonia; foreign body aspiration; vasculitis; and carcinoma of the bronchus.

Long answer

The clinical findings in this patient were the result of bronchial obstruction secondary to an occluding mass (fig 1). The patient's age, together with the subacute presentation and the characteristic findings on bronchoscopic examination, suggested the diagnosis of pulmonary carcinoid tumour.

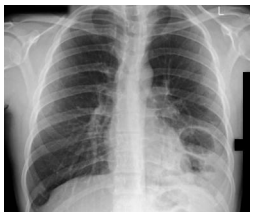

Fig 1 Chest radiograph

However, several other conditions should be considered in patients who present with symptoms of pneumonia that are refractory to conventional treatment. These possibilities should be investigated via a thorough clinical history, relevant routine and specific blood tests, radiological examination, and bronchoscopy with appropriate sampling. Most of these conditions are rare.

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Infection: The lack of symptom resolution after conventional treatment raises the possibility of pneumonia caused by an organism that is resistant to amoxicillin, such as mycoplasma, coxiella, legionella, mycobacteria, viruses, and fungi. Infection with *Aspergillus fumigatus* was unlikely given that our patient was immunocompetent. He had no travel history to suggest histoplasmosis, coccidiomycosis, or cryptococcal infection. Risk factors for these infections are a history of exposure through foreign travel, occupational exposure, and increased susceptibility (immunosuppresion). The number of cases of mycobacterial tuberculosis in the United Kingdom has been steadily rising over the past 20 years, with 9040 cases being reported in 2009 (www.hpa.org.uk). Pulmonary abscess should also be considered in patients who present with symptoms of pneumonia that are initially resistant to treatment. Sputum microbiology is therefore an essential test in all cases of suspected pneumonia.

Inflammation: Pulmonary vasculitis can be secondary to other conditions or a primary idiopathic disorder. Thoracic involvement is most common with primary idiopathic large vessel vasculitides (Takayasu's arteritis, giant cell arteritis, Behçet's disease) and primary small vessel antineutrophil cytoplasmic autoantibody (ANCA) associated vasculitides (Wegener's granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome). These conditions are rare; the annual incidence of Wegener's granulomatosis in the United Kingdom is 8.4/million.[1] Inflammatory lung disorders, such as pulmonary eosinophilia or bronchiolitis obliterans organising pneumonia, can also mimic pneumonia.

Cancer: All pulmonary cancers are rare under the age of 40 years. Given that carcinoid tumours most commonly present with symptoms secondary to an obstructing mass, these tumours and other neoplastic masses (primary or secondary)—including sarcoma, which can cause a cavitating mass—should be considered. The differential diagnosis should also include haematological cancers such as lymphoma, which is an important consideration in this age group and might be suggested on initial full blood count and film.

Aspiration: Foreign body aspirations typically, but not exclusively, localise to the right lung because of the anatomical configuration of the right and left main bronchi. Pneumonia secondary to an endobronchial foreign body does not respond to antibacterial treatment.

2 How do pulmonary carcinoid tumours most commonly present?

Short answer

Patients with pulmonary carcinoid tumours typically present with persistent atelectasis or collapse of the lung, recurrent or unresponsive pneumonia, and pulmonary abscess.

Long answer

Most carcinoid tumours arise within the gastrointestinal system, with only about 10% being bronchopulmonary in origin.[2] The typical features of carcinoid syndrome (flushing, diarrhoea, nausea, vomiting, and bronchoconstriction) are more common in carcinoid tumours of the gastrointestinal system, usually when hepatic metastases are present. In cases of pulmonary carcinoid tumour these symptoms are more indicative of metastatic disease.

Carcinoid tumours characteristically occur at a younger age than other lung cancers. They typically present in the fourth and fifth decades, although they can occur in all age groups. The use of tobacco is not clearly correlated with the incidence of pulmonary carcinoid tumours.[3]

About 25% of patients with pulmonary carcinoid tumours are asymptomatic at the time of diagnosis.[2] Most symptomatic patients have symptoms and signs that directly reflect obstruction of the bronchopulmonary tree, including persistent atelectasis, recurrent pneumonia, pulmonary abscess, and bronchiectasis. In addition, the highly vascular nature of carcinoid masses makes them prone to bleeding, so haemoptysis is a common presenting feature.

Carcinoid tumours are classified according to their microscopic appearance as typical or atypical. The more common typical carcinoid tumours are well differentiated, less likely to metastasise, and usually identified at an earlier stage of disease than atypical tumours (fig 2). Staging of these tumours follows the same criteria (TNM classification) as other lung cancers.[4]

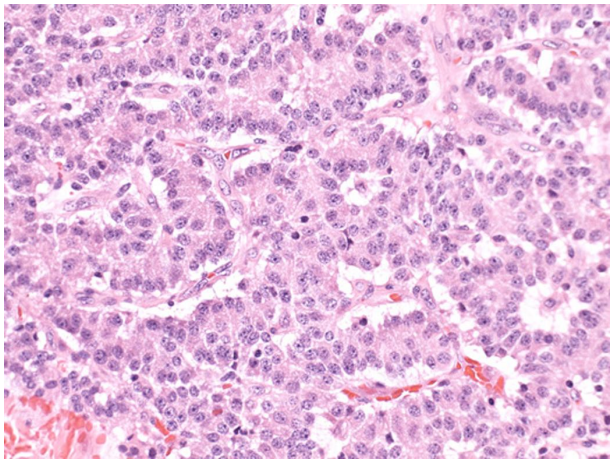

Fig 2 Pathology slide showing typical carcinoid tumour morphology—a trabecular arrangement of uniform polygonal cells, with abundant eosinophilic cytoplasm; the nuclei are round to oval and have a granular chromatin pattern; the surrounding stroma is highly vascularised

Only 50% of atypical tumours are diagnosed at stage I, whereas 80-90% of typical pulmonary carcinoid tumours present at this early stage. This is because typical masses have an indolent course and rarely metastasise, unlike atypical tumours, which are more likely to grow and spread.

Survival rates for typical carcinoid tumours are good, with reported five year survival rates of 87% to 100% and 10 year survival rates of 87% to 93%. Survival rates from atypical tumours are not as good but are still impressive: 40-59% at five years and 31-59% at 10 years. Metastatic disease is inevitably associated with a worse prognosis.[2]

In all cases survival rates depend on the feasibility of complete surgical resection.

3 How should pulmonary carcinoid tumours be managed?

Short answer

If no contraindications are evident, all carcinoid tumours without evidence of metastatic disease should be treated by complete surgical resection

Long answer

Typical carcinoid tumours are the most well differentiated and least biologically aggressive type of pulmonary neuroendocrine

tumour. They usually grow slowly and metastasise rarely.[3] They may bleed profusely at biopsy.

Nonetheless, all carcinoid tumours should be treated as malignancies. Treat all carcinoid tumours without evidence of metastatic disease or contraindications by segmentectomy, lobectomy, or pneumonectomy.[2] Despite the relatively indolent course of carcinoid tumours, aggressive surgical intervention is justified in patients who are fit enough for thoracotomy and resection. Cure rates are high, and no other form of treatment has been shown to approach this level of effectiveness.

More recent advances in chemotherapy have led to renewed interest in this field. The development of agents that target vascular endothelial growth factor and platelet derived growth factor, both of which promote angiogenesis, has led to ongoing research into the use of chemotherapy to treat carcinoid tumours. Although results are promising, surgical resection remains the optimal treatment modality, with a strong evidence base as a curative procedure.[4]

Radiotherapy has a limited role in the treatment of these tumours and is mostly indicated for non-resectable and palliative cases only.

Targeted lymph node dissection should also be included to assess the presence of metastatic spread.

4 What other conditions are associated with carcinoid tumours?

Short answer

Several endocrinopathies including carcinoid syndrome, hypercortisolism, and inappropriate secretion of antidiuretic hormone are associated with pulmonary carcinoid tumours.

Long answer

Although uncommon, various endocrine or neuroendocrine syndromes can be initial clinical manifestations of typical or atypical pulmonary carcinoid tumours. Carcinoid syndrome, hypercortisolism, Cushing's syndrome, inappropriate secretion of antidiuretic hormone, increased pigmentation secondary to excess melanocyte stimulating hormone, and ectopic insulin production resulting in hypoglycaemia can be caused by a pulmonary carcinoid tumour in a patient who is otherwise asymptomatic.[5]

The typical features of carcinoid syndrome are caused by excess serotonin secretion. In cases where this may be a possible diagnosis, measurement of 24 hour urine concentrations of 5-hydroxyindoleacetic acid, the end product of serotonin metabolism, is the most useful initial test. Octreotide, a somatostatin analogue, neutralises the effects of serotonin and can be used to reduce the symptoms of carcinoid syndrome and minimise the concentrations of urinary 5-hydroxyindoleacetic acid.[3]

Patient outcome

Our patient was diagnosed with a typical carcinoid tumour using samples taken during bronchoscopy. Computed tomography showed this to be an isolated mass with no metastatic lesions (fig 3). A left lower lobectomy was performed by the cardiothoracic surgeons (fig 4). His recovery was uneventful and he continues to be well at follow-up outpatient appointments.

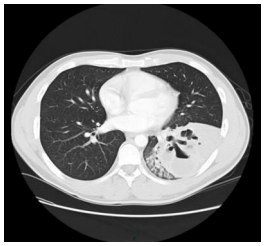

Fig 3 Computed tomogram of the chest

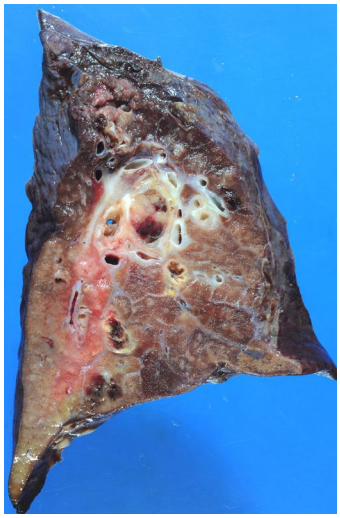

Fig 4 Postoperative specimen. Section of lung showing a cream coloured, polypoid, intrabronchiolar mass. The lung parenchyma distal to the obstructing tumour shows pneumonia with abscess formation

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Patient consent obtained.

1 Watts RA, Al-Taiar A, Scott DG, Macgregor AJ. Prevalence and incidence of Wegener's granulomatosis in the UK general practice. *Arthritis Rheum* 2009;61:1412-6.
2 Bertino E, Confer P, Colonna JE, Ross P, Otterson GA. Pulmonary neuroendocrine/carcinoid tumours. *Cancer* 2009;115:4434-41.
3 Hage R, de la Rivière AB, Seldenrijk CA, van den Bosch JM. Update in pulmonary carcinoid tumors: a review article. *Ann Surg Oncol* 2003;10:697-704.
4 De Dosso S, Bajetta E, Procopio G, Cortinovis D, Buzzoni R, Catena L, et al. Pulmonary carcinoid tumours: indolent but not benign. *Oncology* 2007;73:162-8.
5 Coe SG, Tan WW, Fox TP. Cushing's syndrome due to ectopic adrenocorticotropic hormone production secondary to hepatic carcinoid: diagnosis, treatment, and improved quality of life. *J Gen Intern Med* 2008;23:875-8.

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