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Lesson of the week

Pulmonary Wegener's granulomatosis misdiagnosed as malignancy

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Cytoplasmic antineutrophil cytoplasmic antibody tests can prevent misdiagnosis of Wegener's granulomatosis as malignancy

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Wegener's granulomatosis is a systemic vasculitis that primarily involves the upper and lower respiratory tracts and kidneys. Pulmonary Wegener's granulomatosis can present with multifocal lung involvement or solitary lung lesions with no evidence of extrapulmonary disease.[1] Diagnosing Wegener's granulomatosis on the basis of cytological material obtained from fine needle aspiration or sputum may present a challenging problem to the pathologist. A wrong diagnosis may lead to inappropriate treatment for the patient. We describe two patients with Wegener's granulomatosis originally diagnosed as malignancy.

Case reports

Case 1

A 70 year old woman presented with an 18 month history of intermittent productive cough and pain of the left lower chest. Clinical examination of the chest gave normal results. A chest *x* ray film showed a hazy left base with loss of radiological markings of the left hemidiaphragm and left heart border. A computed tomogram showed three nodules within the lungs: one at the right apex, one in the apical segment of the left lower lobe, and one in the posterobasal segment of the right lower lobe. The nodules were non-enhancing and had irregular margins. Fibreoptic bronchoscopy gave normal results. Bronchial washings showed no acid fast bacilli or malignant cells. Fine needle aspiration of the lesion in the right lower lobe guided by computed tomography showed foamy and epithelioid histiocytes together with a few groups of cells with an increased nuclear to cytoplasmic ratio. Prominent nucleoli were identified, which were suggestive but not diagnostic of adenocarcinoma. Positron emission tomography was performed, which showed multiple, bilateral lung nodules with no evidence of extrapulmonary lesions. A metastatic pulmonary adenocarcinoma from an unknown primary was diagnosed. A conservative " wait and watch" policy was adopted.

Twelve weeks later the patient presented to the department of otorhinolaryngology with nasal congestion which had failed to respond to nasal steroids and antibiotics. Examination showed a saddle nose deformity with bilateral rhinosinusitis. The cytoplasmic antineutrophil cytoplasmic antibody titre suggested Wegener's granulomatosis. A biopsy sample of the nasal mucosa showed features consistent with the condition. The patient responded well to treatment with cyclophosphamide and high dose prednisolone.

Case 2

A 52 year old man presented with a seven week history of cough, dull chest pain, increasing shortness of breath on exertion, loss of weight, fever, and night sweats. There was no haemoptysis or nasal symptoms. A chest *x* ray film showed irregular lesions of the left apical and upper lobe. No hilar lymphadenopathy was evident. Sinus *x* ray films showed thickening of the mucosa. Sputum cytology showed atypical cells suspicious of bronchogenic carcinoma. Bronchoscopy was performed with an intention to proceed to left upper lobectomy or pneumonectomy if required. During the preanaesthetic check the patient was found to have raised blood pressure, splinter haemorrhages under the fingernails, a vasculitic skin rash on his legs, and ulcerated left nasal mucosa. Subsequent investigations showed proteinuria and increased blood urea and serum creatinine concentrations. A renal biopsy sample showed segmental or complete necrosis of glomeruli with fibrocellular crescent formation. Nothing was seen on immunoflorescence. The cytoplasmic antineutrophil cytoplasmic antibody titre gave a strongly positive result, and Wegener's granulomatosis was diagnosed. The patient was treated with cyclophosphamide and prednisolone. Over the following four months the lesion in the left apical chest resolved completely, and the patient improved.

Discussion

Wegener's granulomatosis is a systemic necrotising granulomatous inflammatory condition that may be accompanied by vasculitis, classically involving the upper respiratory tract, lungs, and kidneys. The disease affects a wide age range, with a peak incidence in middle age, with a male to female ratio of 3:2. If left untreated the disease can be fatal.[2] Early diagnosis and treatment can prevent renal failure, which is the most common cause of death.[3] Prompt institution of immunosuppressive drug therapy, including steroids and cyclophosphamide, results in remission of the disease in more than 90% of patients.[4]

Pulmonary and upper respiratory tract involvement often occurs early in the disease. Involvement of lungs has been reported in up to 94% of patients.[4] A limited form of Wegener's granulomatosis confined to the lungs has been described.[5] Patients may present to the clinician with pulmonary symptoms only, and chest radiographs may show ill defined nodules, often bilateral, resulting in the differential diagnosis of malignancy.[2]

Sputum cytology, transbronchial biopsy, or fine needle aspiration cytology can aid diagnosis. Open lung biopsy is, however, usually necessary for the definitive diagnosis of pulmonary Wegener's granulomatosis.[6 7] The pathologist must be aware of the histopathological variability in fine needle aspirates and of the potential pitfalls of mistakenly equating reactive epithelial cells and histiocytes with carcinoma.[2] Positive results for the serum marker cytoplasmic antineutrophil cytoplasmic antibody have been obtained for patients with Wegener's granulomatosis, with an overall sensitivity of 85-90% and specificity of 90% for active disease.[8] These may suggest Wegener's granulomatosis in patients with atypical presentations.[9]

Bronchial epithelial cells that are atypical are often present in patients with Wegener's granulomatosis. The cells may have enlarged eccentric and slightly hyperchromatic nuclei with prominent nucleoli, resembling a well differentiated adenocarcinoma.[10] Reactive alveolar cells seen on fine needle aspirates of the lung may lead to a false positive result or false suspicion of adenocarcinoma.[11] In the cases described, the cytological features were suggestive but not diagnostic of adenocarcinoma. Because the patients had only pulmonary disease in the initial stages and the radiology was also suggestive of metastatic lung lesions, Wegener's granulomatosis was not considered. This was compounded by the fact that the cytoplasmic antineutrophil cytoplasmic antibody titres, which have a high sensitivity and specificity in cases of active Wegener's granulomatosis, were not performed. This led to a major delay in diagnosis.

These cases emphasise that Wegener's granulomatosis must be considered when assessing multiple pulmonary lesions in the absence of other clinical signs. Antineutrophil cytoplasmic antibody titre should be tested. Close communication between the cytopathologist and the clinician is essential to avoid an erroneous diagnosis in the presence of equivocal cytological test results. This is necessary to ensure that Wegener's granulomatosis is diagnosed early so that lifesaving treatment can be started promptly.

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Corrections and clarifications

Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study
Two errors in table 3 of this paper by Amanda I Adler and colleagues (12 August, pp 412-9) persisted to final publication. In the fifth column (Updated mean SBP, Decrease in risk) the values for microvascular disease should read 13 (9 to 16) [not 13 (9 to 26)] and those for heart failure should read 12 (4 to 19) [not 15 (4 to 19)].

Efficacy and safety of galantamine in patients with mild to moderate Alzheimer's disease: multicentre randomised controlled trial
Readers may have been confused by an error in this paper by Gordon K Wilcock and colleagues (9 December, pp 1445-9). In table 1, the fourth characteristic should have read "No (%) of non-smokers" [not "No (%) of smokers"].

Suicides rise after Diana's death
In this news article by Raj Persaud (18 November, p 1243) Diana, Princess of Wales was wrongly reported as dying at age 37; she in fact died when she was 36.

Atypical antipsychotics
We made a late change to the subtitle of this editorial by Shitij Kapur and Gary Remington (2 December, pp 1360-1) but failed to notice that in revising it we had spelt extrapyramidal with too many i's.

Representing infant feeding: content analysis of British media portrayals of bottle feeding and breast feeding
In reference 2 in this paper by Lesley Henderson and colleagues (11 November, pp 1196-8) the year, volume, and page numbers were wrong. The reference should read "Begg N, Ramsay M, White J, Bozoky Z. Media dents confidence in MMR vaccine. *BMJ* 1998;316:561."

BMA approves acupuncture
In the letter "Is approval letter of acupuncture for back pain really evidence based?" by Francisco M Kovacs and María Teresa Gil del Real (11 November, p 1221), we slipped up on the email address, wrongly using two k's. The correct address is mtgildelreal@kovacs.org. Additionally, we struggled with María Teresa Gil del Real's name on the contents page, wrongly assuming her surname to be del Real; it is in fact Gil del Real.