Lessons of the month: ANCA-associated vasculitis – granulomatosis with polyangiitis: 'the great mimic'

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ABSTRACT

We describe the case of a 61-year-old woman who presented with progressive respiratory symptoms and imaging demonstrating multiple opacities in the right lung with hilar and mediastinal lymphadenopathy suggestive of multifocal adenocarcinoma. Subsequent biopsies were consistent with focal changes of organising pneumonia (OP) and no evidence of malignancy. She was treated with steroids for cryptogenic OP with limited response. There was clinical and radiological progression with new lung nodules, mediastinal and thoracic spinal canal infiltration. There was ongoing concern that clinical findings represented disseminated malignancy. Following further investigation and multidisciplinary respiratory and rheumatology review, a diagnosis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) – granulomatosis with polyangiitis (GPA) was confirmed. The case highlighted the multisystem nature of GPA with unusual dural and large vessel aortic and pulmonary trunk involvement.

KEYWORDS: granulomatosis with polyangiitis, vasculitis, anti-neutrophil cytoplasmic antibodies, pachymeningitis, aortitis

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Case presentation

A 61-year-old woman presented with 5 weeks of dry cough, dyspnoea and weight loss. There was no history of prior respiratory illness, with a background of stable Crohn's disease. She described a 2-year history of nasal congestion and crusting, but no bleeding or sinus pain. She was reviewed by otorhinolaryngology and investigations included non-specific changes on nasal biopsy and negative anti-neutrophil cytoplasmic antibody (ANCA) testing. Chest X-ray demonstrated a 6 cm right lung mass suggestive of lung malignancy. She was referred to the fast-track lung service where a computed tomography (CT) of the thorax, abdomen and pelvis revealed multifocal opacities in the right lung with multiple mediastinal and right hilar nodes concerning for multifocal adenocarcinoma (Fig 1a). Examination was otherwise non-contributory.

An endobronchial ultrasound guided – transbronchial needle aspiration (EBUS-TBNA) revealed lymphoid tissue but no evidence of malignancy, granulomas or plasma cell dyscrasia. Blood tests demonstrated a normal serum angiotensin converting enzyme (ACE) and negative ANCA. Because of the ongoing concern of intrathoracic malignancy, she underwent CT-guided lung biopsy, which showed basophilic necrosis with surrounding organising pneumonia. TB culture was negative with no acid-fast bacilli (AFB) seen on biopsy. The patient was treated for presumed cryptogenic organising pneumonia with steroids and empirical antibiotics but repeat chest X-ray failed to show a radiological response with progressive symptoms. Serial CT of the thorax showed progression of the right lung masses and a new nodule in the left lung alongside unchanged mediastinal lymphadenopathy. Bronchoalveolar lavage (BAL) showed low growth of *Staphylococcus aureus* and a minimal lymphocytosis with macrophage predominant cell type. The patient was treated with 2 weeks of doxycycline with no clinical response.

CT – positron emission tomography (PET) demonstrated multifocal areas of avidity in both lungs, thoracic spinal canal and along the mediastinal arterial vessel walls (aortic arch and pulmonary trunk) reported as possible malignant infiltrative process (Figs 1b and c). She re-presented with worsening thoracic back pain, progressive dyspnoea, dry cough and night sweats. Blood tests showed a significant acute phase response with microcytic anaemia, thrombocytosis, C-reactive protein of 165 mg/dL, and repeat serology was strongly positive for PR3 cANCA (levels 60–90). Renal function was stable with no active urinary sediment including no proteinuria. Contrast-enhanced magnetic resonance imaging of the whole spine demonstrated circumferential thoracic epidural thickening that correlated with PET avidity. She was reviewed by the rheumatology vasculitis team and diagnosed with granulomatosis with polyangiitis (GPA) with lung, dural, aortic arch and pulmonary trunk inflammation. She was commenced on steroid wean, induction intravenous cyclophosphamide and then subsequent induction maintenance regimen with B cell therapy rituximab. This resulted in clinical, serological (normalisation of acute phase markers and negative ANCA) and radiological remission.

Discussion

GPA is an ANCA-associated vasculitis, typically associated with small vessel inflammation and granulomatous infiltration of tissues.

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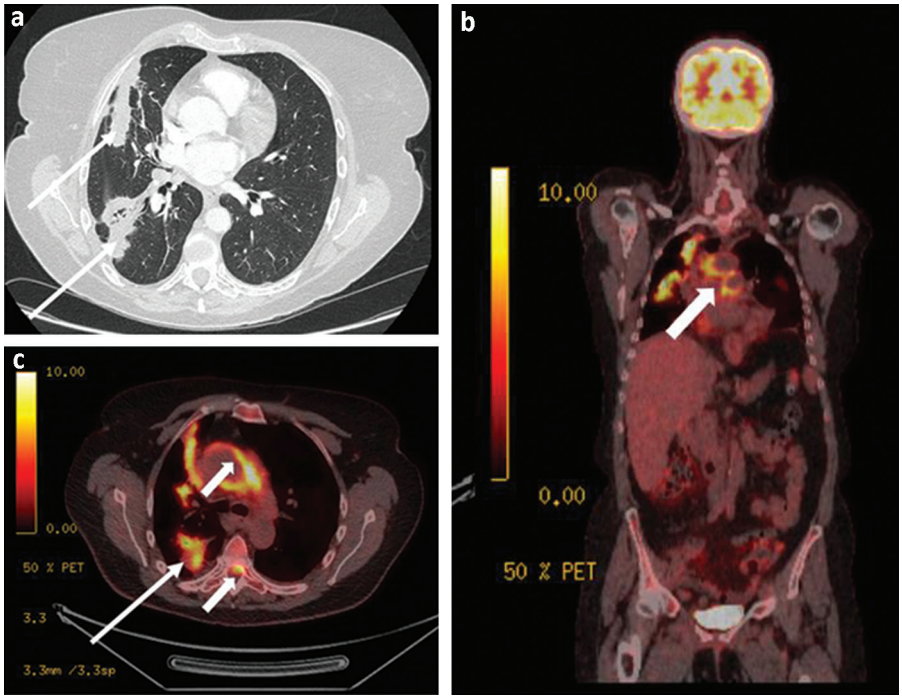

Fig 1. a) Axial computed tomography of the chest showing multifocal right lung lesions (longer arrows). b) and c) Computed tomography – positron emission tomography showing avid right lung lesion (longer arrows) and avid fluorodeoxyglucose uptake in the aortic arch, pulmonary trunk and thoracic dura (shorter arrows).

Typical organs affected include the sinuses, lungs and kidneys. GPA can present with a myriad of symptoms, involve other organs and masquerade or mimic as cancer or infection. Recognition can be difficult, which can lead to delays in diagnosis that can affect prognosis. Clinicians should be aware of the potential for AAV including GPA to present with variable and sometimes unusual manifestations (such as those highlighted in this case), where the patient had dural and large artery involvement as well as lung infiltration and associated lymphadenopathy.

Patients often face delays in diagnosis with a mean of 6 months in non-head and neck manifestations of GPA, and 9 months if presenting with solely head and neck symptoms.[1] This could partly be due to a lack of awareness of the condition but also how closely it mimics other diseases. GPA can present similarly to diseases (including intrathoracic malignancy and cryptogenic organising pneumonia) for several months, as in this patient. Furthermore, although GPA cannot be excluded by a negative ANCA, serial negative ANCA results at initial presentation, additional imaging findings that were felt to represent dural and mediastinal large artery malignant invasion and a partial response to steroids made the diagnosis more challenging.

Neurological manifestations of GPA are common, affecting 33% of patients, however, this is typically either mononeuritis multiplex or peripheral polyneuropathies.[2] In previous reported cases of pachymeningeal disease with GPA, the most common symptom was a chronic headache.[3] It is important to recognise pachymeningeal disease due to its associated serious consequences (including stroke, subdural haematoma and cranial nerve palsies).[4–6] Our patient presented with thoracic back pain several months after initial respiratory manifestations and this coincided with ANCA seropositivity with progressive elevation in PR3 cANCA levels and rise in acute phase markers heralding further systemic involvement. Recognition of GPA dural infiltration and pseudotumour mass like lesions can lead to spinal cord compression, so early recognition of this rare manifestation is important.[7] As GPA is typically a disease that affects small vessels (arterioles and capillaries), our case is also unusual with the additional finding of aortic arch and pulmonary trunk inflammation. Aortitis is also a rare manifestation of GPA but can have profound consequences including aortic dissection and aneurysm formation.[8,9] The combination of pachymeningitis with aortitis in GPA has only been described in one previous case and this was associated with pANCA myeloperoxidase (MPO) antibodies, unlike our case who was PR3 cANCA positive.[10] Once the diagnosis was established, the patient responded well to immunomodulatory therapy with clinical and radiological resolution.

In summary, we present a case that highlights that GPA can be a great masquerade in general medicine because the protean symptoms and myriad of clinical manifestations to any clinical specialty. This can lead to delay in recognition and potential irreversible tissue and organ damage. Once diagnosis is made, patients generally respond well to combination immunomodulatory therapy and can achieve clinical remission.

Key points

- AAV and GPA can mimic lung cancer or thoracic lymphoproliferative disease and should be considered in the differential diagnosis of patients with unexplained chest X-ray masses.
- AAV and GPA should also be considered in unexplained organising pneumonia resistant to conventional first-line treatment.
- Pachymeningitis secondary to GPA is an important differential when presenting with back pain or chronic headaches.

> Mediastinal large artery involvement (aorta and pulmonary trunk) is an unusual disease manifestation in classical small vessel vasculitis. ■

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