Idiopathic aortitis presenting as pyrexia of unknown origin and delirium

Introduction

Delirium in the context of a febrile illness is commonly encountered in the older person and the underlying precipitant is usually easily identified by investigation. However, the pathological process accounting for the febrile illness may be more obscure, posing a diagnostic challenge.

This article describes a 76-year-old man who presented with a febrile illness and acute confusion. Despite extensive initial investigation a conclusive diagnosis remained elusive until an 18-fluorodeoxyglucose-positron emission tomography/computed tomography (18FDG-PET/CT) scan was performed, which demonstrated aortitis. He responded well to steroid treatment, with resolution of clinical and biochemical abnormalities. Isolated aortitis accounts for nearly three-quarters of cases of aortitis and usually involves the thoracic aorta. Owing to the often non-specific nature of presentation, a high index of suspicion is needed to establish an accurate and timely diagnosis.

Discussion

Delirium is a common syndrome of acute brain dysfunction affecting up to 30% of hospitalized older adults who have some degree of cognitive impairment or cerebrovascular disease (Young and Inouye, 2007).

An acute bodily stress and inflammatory response can trigger a rise in systemic inflammatory cytokine levels. The consequent release of cytokines in the brain results in a disturbance in the balance of neurotransmitters, subsequently manifesting as delirium, as in this patient. Cholinergic, dopaminergic, adrenergic, serotonergic and GABAergic neurotransmitters have been implicated (Banks et al, 2003; Maclullich et al, 2013). This patient's febrile illness lasted over 2 weeks before a definitive diagnosis was made and hence meets the criteria for pyrexia of unknown origin (Tal et al, 2007).

In the older person inflammatory conditions are the most frequent manifestation of pyrexia of unknown origin (Bleeker-Rovers et al, 2007). Rapid evaluation and prompt decision making are required to prevent functional deterioration.

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CASE REPORT

A 76-year-old man presented with a 2-day history of constitutional symptoms including malaise, high grade fevers and confusion, in the absence of any clear localizing infective symptoms.

His prior medical history included heart failure, atrial fibrillation, vascular cognitive impairment and benign prostatic hypertrophy with a long-term urinary catheter. He had a recent hospital attendance for complex re-catheterization following initial failed attempts, which was performed with antibiotic cover. His medications included perindopril, frusemide and rivaroxaban.

Initial observations showed temperature 38.9°C, blood pressure 156/86 mmHg, heart rate 76 bpm, respiratory rate 26/minute and oxygen saturation 97% on air. Comprehensive systemic examination, including cardiovascular, respiratory and abdominal examination, failed to show any signs of infection. Neurologically he was confused and disoriented, but there was no evidence of meningism clinically. Delirium was identified using the Confusion Assessment Method.

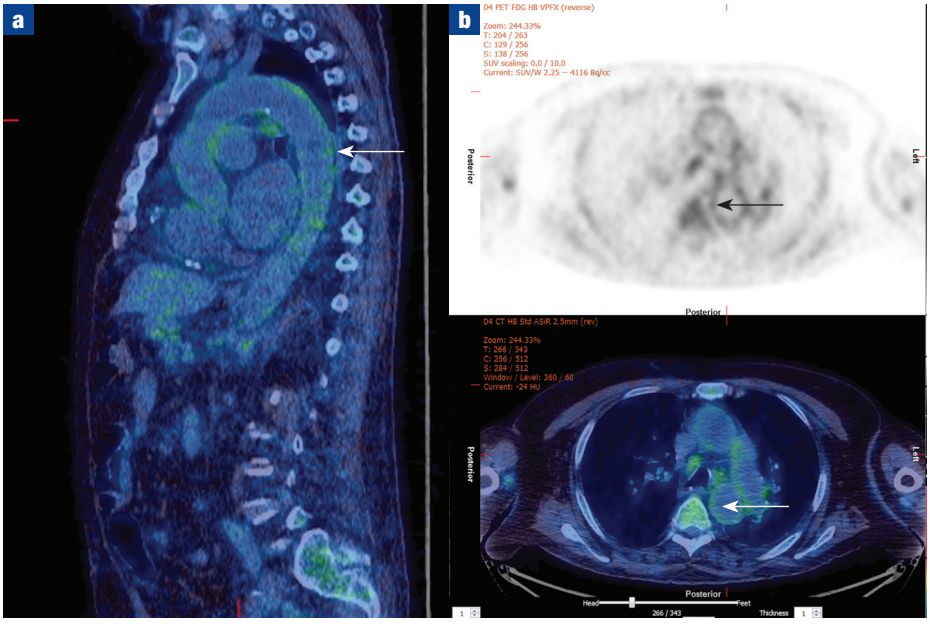
Laboratory tests showed raised inflammatory markers – white cell count 13.5 x10^9/litre, C-reactive protein 137 mg/litre and erythrocyte sedimentation rate 127 mm/hr. Renal function, coagulation, liver function, bone profile, thyroid function test, vitamin B_{12} and folate were all normal. Chest radiograph showed cardiomegaly. His catheter urine dip was positive for nitrites and leucocytes. His initial empirical treatment was directed towards presumed catheter-associated urinary tract infection. However, despite receiving three different antibiotics he continued to have swinging pyrexia, rising levels of inflammatory markers and worsening delirium.

Subsequent catheter specimen urine and blood culture results were negative. Computed tomography of the chest, abdomen and pelvis and ultrasound of the renal tract were non-contributory, with no source of sepsis or malignancy identified. Serology for HIV, syphilis and cytomegalovirus were negative. His serology was negative for anti-neutrophil cytoplasmic antibody, antinuclear antibody, anti-smooth muscle antibody, gastric parietal cell antibody, mitochondrial antibody, liver/kidney microsomal antibodies and Hep2 anti-nuclear antibody.

Owing to the ongoing pyrexia of unknown origin an 18-fluorodeoxyglucose-positron emission tomography/computed tomography (18FDG-PET/CT) scan was performed, which demonstrated prominent uptake in the thoracic aorta consistent with an aortitis. Sagittal (*Figure 1a*) and transverse (*Figure 1b*) 18FDG-PET/CT images demonstrated prominent uptake in the wall of the thoracic aorta (see arrow). Magnetic resonance imaging and magnetic resonance angiography of the brain did not show any evidence of cerebral vasculitis, but did demonstrate previously known age-related minor generalized cerebral atrophy and small vessel disease.

He was commenced on prednisolone 30 mg daily for idiopathic aortitis and made a dramatic improvement, both clinically and biochemically. When he started taking prednisolone his C-reactive protein level peaked at 294 mg/llitre and subsequently fell to 4 mg/litre within 9 days. He was later discharged with rheumatology outpatient clinic follow-up within 4 weeks and he has remained well on a tapering steroid dose.

Figure 1. **a.** Sagittal and **(b)** transverse views of 18-fluorodeoxyglucose-positron emission tomography/computed tomography demonstrate increased metabolic activity in the wall of the thoracic aorta (arrow) consistent with vasculitis.



As per a meta-analysis, the diagnostic yield of 18FDG-PET/CT in pyrexia of unknown origin is estimated at about 56% (Bharucha et al, 2017).

Aortitis is a general term denoting inflammation of the aorta, which can be broadly divided into inflammatory and infectious, along with isolated aortitis. Giant cell arteritis is the commonest inflammatory cause of aortitis in the older population. However, this patient met only two out of five of the American College of Rheumatology diagnostic criteria for giant cell arteritis (age and erythrocyte sedimentation rate). Old age is also a recognized risk factor for isolated aortitis. Isolated aortitis can be the sole manifestation of a large vessel vasculitis and is often diagnosed incidentally (Gornik and Creager, 2008; Pipitone and Salvarani, 2011). In this patient, there was a rapid improvement in clinical and biochemical parameters following treatment with low dose corticosteroids, suggesting an inflammatory aetiology.

For inflammatory aortitis a tapering regimen of corticosteroid is the first-line treatment. In order to avoid long-term steroid-related side effects, experts suggest adding an immunosuppressor such as methotrexate or, in refractory cases, anti-interleukin 6 (Unizony et al, 2013). **BJHM**

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LEARNING POINTS

- Delirium in older persons can be an occult manifestation of significant underlying pathology.
- Rapid evaluation and prompt decision making is required in cases of pyrexia of unknown origin to prevent functional deterioration.
- Modern imaging technology can be crucial for diagnostic accuracy when clinical clues are scant.
- Isolated aortitis may be the sole manifestation of large vessel vasculitis and, importantly, is a treatable condition.

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