53. AN UNCOMMON CAUSE OF PYREXIA OF UNKNOWN ORIGIN

Noora Soobraty¹, and Michael Green²
¹Department of Rheumatology, Midyorks NHS Trust, Wakefield, United Kingdom, and ²Rheumatology, York Teaching Hospital NHS Foundation Trust, York, United Kingdom

Introduction: We report the case of a 58-year-old lady with pre-existing primary pulmonary hypertension presenting with a pyrexia of unknown origin (PUO). On review of her previous CT imaging, it was noted that the aortic wall was thickened which prompted further investigations in the form of a PET CT and IgG subclasses that led to the final diagnosis of large vessel vasculitis (LVV) and IgG4-related disease. She was successfully treated with prednisolone and mycophenolate mofetil (MMF). Interestingly she subsequently developed neurological symptoms and diagnosed with Miller-Fisher syndrome and further down the line she was diagnosed with adrenal insufficiency (AI).

Case description: A 58-year-old lady was admitted under the cardiology team in April 2014 for investigation of a PUO. The patient also complained of worsening breathless on exertion, malaise and myalgia. Past medical history revealed pulmonary arterial hypertension (diagnosed 2000) with secondary right sided heart failure, an incidental secundum ASD defect and recurrent anterior uveitis. She was on sildenafil and warfarin long term. Clinical examination did not reveal any abnormal findings. Initial investigations to rule out a bacterial cause for her symptoms were...
performed and were unremarkable. She had a mild anaemia and persistently raised CRP. Her initial autoimmune screen showed no abnormality. An outpatient CT chest, abdomen and pelvis showed a small pericardial effusion and no evidence of malignancy.

In July 2014 she was reviewed in the rheumatology clinic and in view of her symptom profile and persistently raised inflammatory markers in the absence of infection, this raised the possibility of a systemic inflammatory problem related to a vasculitis. The recent CT imaging was reviewed at the rheumatology/radiology MDT and the radiologists felt that there was some probable inflammatory change in the aorta and some wall thickening. Further investigations with PET CT confirmed inflammatory changes in the large vessels and IgG subclasses were elevated at 2.06g/L. She was started on treatment for LVV and possible IgG4 disease, initially with 40mg prednisolone and MMF was later introduced. A repeat PET in May 2015 was normal.

In January 2016 she developed sudden ataxia, hyporeflexia and weakness. She was found to have positive anti–gq1 antibodies and diagnosed with Miller–Fisher syndrome. Her symptoms resolved with an increase in the prednisolone dose.

She had 3 further hospital admissions, each with similar symptoms of collapse and loss of consciousness, which was subsequently felt to be due to AI.

Discussion: In this patient presenting with fevers and raised inflammatory markers, the initial investigations were rightly aimed at trying to identify a source of infection as this is the main concern in a patient with an ongoing pyrexia. Reviewing the images in clinic and at our MDT meeting identified the thickened aortic wall. This was key in providing further information as to what might be the cause of the patient’s presentation and led us to order the appropriate and more detailed investigations in the form of PET CT and IgG subclasses. It was not possible in this case to get a histological diagnosis and therefore, based on the elevated IgG subclasses and PET findings, a presumptive diagnosis of IgG4 related disease and LVV was made. The initial treatment choice of prednisolone 40mg is based on current practice for treating LVV. In view of the IgG4 disease and after discussion with the Immunologists, it was decided that MMF would be the most appropriate steroid-sparing agent. This case highlights the fact that making a diagnosis of large vessel vasculitis is somewhat difficult due to the non-specific clinical presentations and laboratory findings.

Once the diagnosis was made, this raised the question as to whether the pulmonary hypertension was in any way connected to the LVV or coincidental. This case also highlights the fact that patients with several immune-related diseases can develop further autoimmune conditions. In this case she was initially diagnosed with a LVV and IgG4-related disease then Miller–Fisher syndrome and following that adrenal insufficiency. Is this phenomenon becoming more common in clinical practice?

One other point for discussion is the choice of steroid-sparing agent, in this case we opted for MMF. Is there a case for rituximab in this patient?

Key learning points: This case illustrates the fact that looking at previous imaging was crucial at providing further information and decide on further imaging that would aid in the diagnosis. The CT images were reviewed with the relevant laboratory findings, clinical picture and asking the right questions to the radiologists. In this case, we asked them to have a look at the large vessels in more detail as this can sometimes be missed and not properly looked at if the radiologists are not asked to specifically look at the large vessels.

The differential diagnosis for these patients are broad and include infection, malignancy and inflammatory conditions such as a vasculitis or autoinflammatory disorder. Therefore keeping an open mind where these patients are concerned is important, especially in exploring the rarer causes of such a presentation.

There is no single diagnosis to explain all the symptoms experienced by the patient. The presence of one autoimmune disease should alert one to watch for another one in these patients.

A multi-disciplinary team approach to the management of these complex patients with several autoimmune disorders, is essential. Reviewing the images with the radiologists helped identify thickening of the aortic wall. The regional immunology team was also involved in discussions about long-term management. The Neurology team was also involved and diagnosed Miller–Fisher syndrome.

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