Multi-system IgG4-related disease: the value of positron emission tomography

Sreelakshmi Kotha, Philip Berry

DESCRIPTION
A patient in his 20s presented with a 6-month history of weight loss (25 kg over 6 weeks), lethargy and night sweats. Medical history includes idiopathic pancreatitis and latent tuberculosis (TB) treated 13 years ago. He had travelled to Southeast Asia 4 months prior to presentation, but the onset of symptoms preceded this trip. The patient denied unsafe sexual practices, use of recreational drugs, over-the-counter medication and insect or tick bites. Physical examination revealed cervical lymphadenopathy with no axillary or inguinal lymphadenopathy. Respiratory and abdominal examination was normal. Laboratory investigations revealed a mixed cholestatic and hepatitic liver function test profile (alanine aminotransferase 64 IU/L, alkaline phosphatase 275 IU/L). Full blood count, blood film and lactate dehydrogenase were normal. Extended bacterial, viral screen,
serology for auto-immune hepatitis and vasculitis was negative. Sputum microscopy for acid fast bacilli was negative. Serum immunoglobulin subclass-4 (IgG4) was elevated at 14.95 g/L (0.04-0.86 g/L) and the ACE was marginally elevated at 73 U/L (8–65 U/L). CT suggested diffuse infiltration of the liver with widespread lymphadenopathy, splenomegaly and diffuse swelling of the pancreas. A positron emission tomography (PET) scan was performed and demonstrated metabolically active lymph nodes above and below the diaphragm with multi-system inflammatory infiltrative involvement of pancreas, kidneys, spleen, prostate and intra-scrotal epididymis (figure 1). The patient’s presentation, clinical assessment and initial investigations led to a differential diagnosis of lymphoma, TB, sarcoidosis and IgG4-related disease (IgG4-RD). Fine needle aspirate of the lymph node showed reactive changes with a lymphoplasmocytic infiltrate, but no granulomas or IgG4-positive cells. Liver biopsy revealed a single discrete granuloma, lymphoplasmocytic infiltrates and several IgG4-positive cells (figure 2). However, the number of IgG4-positive cells was <10/high power field, which fails to fulfil the criteria for a definitive diagnosis of IgG4-RD.

As per 2019 American college of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria, this case fits the entry and inclusion criteria (score=31) for IgG4-RD, but there were two exclusion criteria (mild splenomegaly and single granulomata in liver biopsy). The case was discussed extensively in multi-disciplinary team meeting and based on significantly raised IgG4 levels, pancreatitis and multi-system involvement it was agreed to treat this as IgG4-RD, while maintaining a suspicion of sarcoidosis. Steroid therapy would be beneficial even if this was sarcoidosis. Excision lymph node biopsy was planned if there was no response to treatment. Six weeks after treatment with prednisolone 40 mg once a day, there was dramatic improvement in symptoms, normalisation of liver function tests and a fall in serum IgG4 level to 4.69 g/L. Repeat PET scan showed total resolution in multi-system inflammation (figure 3). The patient is currently well after completing the steroid course and is currently not on any treatment. A repeat PET scan 1-year post diagnosis did not show any activity.

Our case demonstrates the complexities involved in the diagnosis and management of multi-system inflammation and the importance of multidisciplinary approach. This case was particularly challenging due to history of latent tuberculosis, lymphadenopathy with night sweats and weight loss. These findings raised possibility of lymphoma and TB and the diagnosis had to be carefully teased out for the correct management. IgG4-RD is a rare entity with varied manifestations, presenting a diagnostic challenge. Diagnosis is based on a combination of clinical, biochemical, radiological and histological features. \(^2\) IgG4 levels lack sensitivity and specificity for diagnosis and monitoring this condition. Accurate diagnosis is important as IgG4-RD can mimic a malignant process. \(^3\) Steroids are the mainstay of treatment. Long-term immunosuppression is not recommended at diagnosis and should be considered if there is insufficient response to steroids or relapse following withdrawal of steroid treatment. Azathioprine, mycophenolate, mercaptopurine and rituximab have been used as steroid sparing agents. \(^4\)

**Patient’s perspective**

For 3 years prior to diagnosis—I was under immense pressure at work and was being bullied for a prolonged period. During this time, all lifestyle factors remained constant except work stress. Three months into my travel, I started to notice a few symptoms. At first, this was mainly tiredness, light cold and flu symptoms, which later led to feelings of nausea, particularly when I drank alcohol. For context, I would drink the equivalent of five pints—either every week or bi-monthly. As my travels continued, existing symptoms grew in severity and new symptoms like lower back pain, stomach pain, and issues passing urine, which I suspect were kidney pain as well as muscle stiffness and night sweats appeared. The night sweats were intense. Each night, I was waking up in what I can only describe as a soaking bed and was hot to the touch. All symptoms shifted from a mild/moderate state back in spring, to severe during summer. It got so bad that I lost all my appetite. For a period of around 6–8 weeks, I dropped from 75 kg to around 50 kg where the only food groups I could stomach could be a couple of pieces of fruit and some light proteins.

I saw a doctor who ran blood and a series of tests and concluded that I had rheumatoid arthritis and recommended I fly home as soon as possible. When I got home after my travels—the symptoms continued, and I admitted myself to emergency department at my local hospital. At first, they thought I had pancreatitis and gave a slightly patronising spiel in the emergency department that I was drinking too much. I appreciate the basic tests that were run; the results would point the medical professionals in that direction.

I challenged this and was referred to gastroenterology team and ran them through everything, step by step and in detail. They agreed that I needed more tests such as blood cultures, MRIs, PET, ultrasound, X-rays and biopsies—the works. It was then concluded that I had IGG-4. Without the patience to listen, the robustness of other types of tests and removing medical bias, I wouldn’t be here without those doctors. They’re a shining example of best practice within the trust and I hope anyone reading this takes inspiration from these wonderful doctors. They treated me with respect during such a turbulent time of my life and I’m eternally grateful.

**Learning points**

- IgG4 related disease is a rare and complex disease that can mimic malignancy and presents significant diagnostic challenges.
- Multidisciplinary approach is paramount to diagnosis and management.
- Steroids are the mainstay of treatment.

**Contributors** SK and PB were responsible for drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and algorithms and critical revision for important intellectual contact. SK and PB gave final approval of the manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Consent obtained directly from patient(s)

**Provenance and peer review** Not commissioned; externally peer reviewed.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.
REFERENCES


