CASE REPORT

Polyarteritis nodosa presenting as a pyrexia of unknown origin

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A case of an 18 year old woman is reported who presented with a pyrexia of unknown origin having returned from a trip to India. She initially had constitutional symptoms only, which rapidly progressed to a multisystem disorder. The difficulty in making the diagnosis of polyarteritis nodosa, especially with the possible differential diagnosis of infection after her recent travel, is discussed. The discussion reviews the condition of polyarteritis nodosa and analyses the diagnostic difficulties in this case.

An 18 year old college student was transferred to our hospital for further investigation of a pyrexia of unknown origin. She had been previously fit and well. Her only past medical history was of mastoiditis. Fifteen years earlier, when a family member had pulmonary tuberculosis, she had a positive Heaf test and so received antituberculous chemotherapy for nine months.

Her illness began in July 1997, when she returned from four weeks of travel in India, where she had visited only urban areas. She had had all her routine inoculations and a full course of antimalarial prophylaxis before travel and was well throughout her stay. Two days after her return to England she developed a sore throat and flu-like symptoms with polyarthralgia affecting her elbows, shoulders, and knees.

In August 1997 she was admitted to hospital with worsening symptoms of fever, rigors, a persistent dry cough, and one stone (6.5 kg) of weight loss over six weeks. At the time physical examination was unremarkable. She had a microcytic, hypochromic anaemia and a persistently raised C-reactive protein, but all other tests, including multiple bacteriological cultures, a chest radiograph, and ultrasound of the abdomen and pelvis were unremarkable. Despite empirical treatment for atypical pneumonia, her symptoms worsened.

During the next two months, she continued to have symptoms of a multisystem disorder, with fevers up to 39°C, drenching sweats, arthralgia, cough, and diarrhoea. She went on to develop bilateral ulnar nerve palsies and peripheral neuropathy. Investigations revealed a normochromic, normocytic anaemia with leucoerythroblastic features, a normal white cell count, differential count and platelet count, with normal urea and electrolytes and liver function tests. She had a normal serum angiotensin converting enzyme and antistreptolysin-O titre, a raised C-reactive protein and an increased IgG, with normal serum electrophoresis. Tests for autoantibodies, antineutrophil cytoplasmic antibody, rheumatoid factor, and double stranded DNA were negative. Tests for lymphoma or occult malignancy included a bone marrow aspirate and trephine, bone marrow cell surface markers and lymphocyte subpopulations, and were all normal. All bacteriological cultures and extensive serological tests for infectious agents (including hepatitis B, hepatitis C, and HIV) were negative. Radiographs of the chest and abdomen, computed tomogra-

Figure 1 Selective renal arteriogram obtained using a digital subtraction technique. Gross arteritic changes are seen, consisting of marked irregularity and truncation of many of the intrarenal arterial branches associated with numerous aneurysms. There is a "moth eaten" angiographic nephrogram due to intrarenal arterial branch occlusions.

phy of the thorax and abdomen, and ultrasound of the abdomen and pelvis were not diagnostic. Bowel investigations, endoscopy and colonoscopy, barium studies, and biopsies (liver, lymph nodes, and bowel) were also unhelpful. Abnormal results included a significantly reduced creatinine clearance, with proteinuria only on dipstick and no active sediment on urine microscopy. Serial echocardiograms showed development of a progressive dilated cardiomyopathy and faecal fats suggested malabsorption. In addition lung function tests showed severely reduced lung volumes, with gross diffusion impairment, and electromyography showed a severe distal axonal polyneuropathy in the lower limbs.

She showed no clinical response to antimalarial or antituberculosis treatment or to a trial course of 30 mg oral prednisolone (for possible vasculitis) or high dose aspirin (for possible adult onset Still's disease).

By November 1997 she was cachectic, spiking temperatures of 39°C, and having episodes of pulmonary oedema with evidence of severely impaired biventricular function on echocardiography. At this time the clinical picture and results had suggested a vasculitic disease process and so a visceral angiogram was requested; this showed classical changes of polyarteritis nodosa in both kidneys with numerous aneurysms of

small and medium sized arteries, marked vascular irregularity, and a "moth eaten" angiographic nephrogram due to numerous occluded intrarenal arterial branches (see fig 1). Extensive aneurysmal disease was also present within the pancreatic vessels. Disease was also present, but was less florid in the hepatic and superior mesenteric territories.

She was treated with 100 mg of intravenous hydrocortisone three times a day (a higher dose than conventional treatment in view of her recent liver enzyme induction with rifampicin, which would explain her lack of previous response to oral prednisolone) and 100 mg of cyclophosphamide once daily. Prophylactic isoniazid was given in view of her past medical history.

Her inpatient course was complicated by severe cardiac failure and recurrent arrhythmias, salmonella diarrhoea, and methicillin resistant *Staphylococcus aureus* sepsis.

After eight weeks of induction therapy with hydrocortisone and cyclophosphamide, she was successfully converted to maintenance treatment with prednisolone and azathioprine. Her renal function improved considerably (latest creatinine clearance is 31 ml/min) and repeat echocardiography has shown almost complete recovery of ventricular function.

DISCUSSION

Vasculitides are a heterogeneous group of disorders sharing the histological features of inflammation and usually necrosis and/or ischaemia of the blood vessels. The cause of these disorders is generally unknown. Polyarteritis nodosa is a focal segmental necrotising vasculitis affecting small and medium sized muscular arteries.¹

This case illustrates the potential difficulty in making the diagnosis of polyarteritis nodosa. The condition is rare with an estimated incidence and prevalence of 4.6 per 100 000 in England.² It is therefore important to exclude other commoner causes of pyrexia of unknown origin and multisystem involvement in patients at presentation before doing the necessary diagnostic test of intravenous angiography or biopsy to diagnose polyarteritis nodosa. (This is particularly important as bleeding from microaneurysms is not an uncommon complication of organ biopsy in polyarteritis nodosa.)

In addition to being uncommon, polyarteritis nodosa commonly presents with non-specific constitutional symptoms (for example fever, malaise, and weight loss).² The spectrum of the clinical presentation can range from an apparently limited disease to fulminant polyvisceral failure.² There is no single feature of the disease or common clinical presentation to suggest polyarteritis nodosa as a diagnosis.

Another difficulty was the fact that our patient had just returned from India and so considerable effort was made to exclude an infectious cause for the illness, especially as one of the most prominent early presenting features particularly was that of pyrexia of unknown origin. An estimated 20% of pyrexias of unknown origin are connective tissue diseases but polyarteritis nodosa is rare in the subgroup.³ Interestingly polyarteritis nodosa has been described in association with a variety of infectious agents, in particular hepatitis B virus, but also group A streptococcal infections, and numerous others including hepatitis C virus, human T cell leukaemia virus-1,

Learning points

- Polyarteritis nodosa can present as a pyrexia of unknown origin.
- Some infections are closely associated with polyarteritis nodosa especially hepatitis B.
- Early diagnosis and treatment significantly improves the prognosis.

cytomegalovirus, HIV, and human parvovirus B19.² However, in this case an extensive search for infectious agents (including hepatitis B and C, HIV, parvovirus B19, and streptococcus) were all negative.

It has long been thought that polyarteritis nodosa does not typically affect the lungs. Our patient had lung function tests suggestive of a restrictive lung pathology. In fact a postmortem study of 10 cases of the disease in Tokyo, Japan found arteritis affecting the bronchial arteries on seven out of the 10 cases and diffuse alveolar damage involving both lobes bilaterally in five out of the 10 cases, which was acute in two out of the five and organising in three out of the five cases.⁴ It is possible that lung involvement is commoner than previously thought and it should not exclude consideration of the diagnosis of polyarteritis nodosa.

One other difficulty in establishing the diagnosis in this case was the fact that the patient did not appear to respond to the trial of steroids early in the course of the illness. It is now felt that it is likely that her liver enzymes were induced by the course of rifampicin and this is an likely explanation for the lack of response to the low dose of prednisolone used.

In conclusion this case illustrates the potential difficulty in making the diagnosis of polyarteritis nodosa. Angiography should be considered in anyone with pyrexia of unknown origin and multisystem disorder even after return from foreign travel, irrespective of their age or racial group. Polyarteritis nodosa is a potentially fatal disease but with often favourable outcome with immunosuppressive treatment, especially if treated early. Our patient is now well, off all medication, and in her second year at university.

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