Vasculitic appendicitis

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The surgical diagnosis of appendicitis is clinical, relying on accurate history-taking and examination, but histopathology of the specimen influences subsequent management.

CASE HISTORY

A man of 41 reported two days of lower abdominal pain and nausea. Six months earlier, after a deep vein thrombosis, he had been found to have antiphospholipid syndrome—evidenced by a prolonged activated partial thromboplastin time, lupus anticoagulant and raised IgG anticardiolipin antibody. Abdominal ultrasound and CT at that time were normal. Since then he had been taking warfarin.

When examined on the present admission he was flushed, tachycardic and pyrexial (temperature 38.4°C) but normotensive. His abdomen was tense, with rebound and guarding worse on the right side. The white cell count was $3.4 \times 10^9/L$. The clinical diagnosis was acute perforated appendicitis with pelvic sepsis, and in preparation for operation he received 4 mg vitamin K and four units of fresh frozen plasma to normalize clotting. At operation, the appendix was inflamed with patchy areas of gangrene. There was pus in the lower abdomen and pelvis. After appendicectomy the pelvis was washed out with normal saline. Antibiotics were given at operation and continued for five days. He made a slow recovery, with temperature becoming normal and a light diet started, but he remained in hospital for stabilization of anticoagulation. On the sixth postoperative day he became anorexic with increased abdominal pain. His temperature was 38°C and on examination he had lower abdominal tenderness and a small wound haematoma. Ultrasound showed no local or pelvic fluid collection. Intravenous fluids and antibiotics were started but after 24 hours he remained unwell and febrile, with signs of peritonitis in the lower abdomen. Reoperation was planned, but first the histology of the original specimen was reviewed. No inflammation of the

Figure 1 Medium-sized artery showing transmural inflammation with neutrophils, eosinophils and mononuclear cells. Note inflammation involving full thickness of the wall including the adventitia. There is striking fibrinoid necrosis

appendix was seen but several small blood vessels in the mesoappendix showed vasculitis of varying stages—fibrinoid necrosis, luminal occlusion, fibrosis, scarring and stenosis (Figure 1). Although lesions of this sort can be an incidental finding in the appendix, the extensive nature of the vasculitis suggested systemic polyarteritis nodosa. On closer questioning the patient revealed that for six months he had experienced vague abdominal pain, nausea and some weight loss; also, for 5 years he had had intermittent joint pains in the hands, feet, ankles and knees. Reoperation was cancelled and methylprednisolone 1 g intravenously was given for three days. The symptoms resolved completely. On subsequent autoantibody testing ANA, ANCA and rheumatoid factor were negative. Chest X-ray was normal. The urine contained small amounts of blood and protein, suggestive of renal involvement. He was discharged on cyclophosphamide 50 mg thrice daily and prednisolone 60 mg daily and remains well 2 years postoperatively.

COMMENT

Polyarteritis nodosa affects small and medium-size muscular arteries, typically renal (80–90%) and visceral but not pulmonary. Microscopically vessels show nodularity, aneurysmal dilatation, obstruction or infarction.¹ Laboratory investigations are often unhelpful, autoantibodies not being present. Clinical pointers are hypertension, fever and weight loss.² Although a third of patients have abdominal pain, complications requiring operation are rare.³ Renal infarction and intestinal perforation are rare serious

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sequelae. Gangrenous cholecystitis or appendicitis is reported in less than a dozen patients.⁴

In the present case, the clinical presentation reflected occlusion of meso-appendicular artery branches causing distal ischaemia of the appendix. The normal white cell count was surprising in a patient who proved to have pelvic sepsis and fever and it is possible that chronic autoimmune disease depressed his systemic inflammatory response. There was no hypertension. Antiphospholipid syndrome is itself associated with vasculitis, but antiphospholipid antibodies are seldom detected in polyarteritis nodosa.⁵ Prompt histological reporting spared this patient reoperation and led to effective long-term management.

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Uveitis in a patient receiving rifabutin for Crohn's disease

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Some clinicians are now treating Crohn's disease with rifabutin and a macrolide antibiotic^{1,2} because of evidence that *Mycobacterium paratuberculosis* contributes to the pathogenesis. In these circumstances, the development of uveitis may or may not be a rifabutin side-effect.

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CASE HISTORY

A Somali woman aged 22 with Crohn's disease developed redness, ache and a hypopyon first in the left eye then in the right eye, three weeks after starting treatment with rifabutin 300 mg daily and clarithromycin 250 mg twice daily. Her Crohn's disease had been diagnosed 10 years previously and treated for some years in the Middle East. On arrival in the UK at age 18 she was experiencing diarrhoea from severe colonic ulceration with painful perineal involvement and rectovaginal fistulating disease. The fistulae were laid open and seton drainage was established. For the next 2 years she took azathioprine 2 mg/kg but the disease did not respond. A defunctioning loop ileostomy was then fashioned and she came to proctocolectomy the following year. Subsequently there was global clinical improvement but she was troubled by an offensive discharge from a non-healing perineal wound cavity, communicating with the posterior wall of the vagina, for which she needed to wear a pad. MRI scanning of the pelvis confirmed inflammation within the proctectomy bed extending into the presacral space. At the time rifabutin and clarithromycin were started, she had never experienced ocular symptoms.

On ophthalmic examination she had bilateral anterior uveitis but good vision. Topical steroids were prescribed and the systemic medication was stopped, whereupon the symptoms resolved completely. About a month later, two days after restarting rifabutin and clarithromycin at the same dose as before, she reported sudden onset of pain and blurred vision in the left eye. On examination her visual acuity was 6/5 right eye and 6/18 left eye. A hypopyon was obvious in the left eye (Figure 1) and slit lamp examination showed numerous cells in the anterior chamber as well as in the vitreous. No retinal lesion was seen. Again the rifabutin and clarithromycin were stopped and the uveitis settled with topical steroids.

COMMENT

Patients with Crohn's disease can get uveitis as part of their disease process but hypopyon is unusual in these circumstances. Infection in any organ can also spread to the eye via the bloodstream and produce inflammation, often with a hypopyon, which takes many weeks to settle. In this patient, however, there are good reasons for thinking that the uveitis was drug-associated—namely, the onset soon after initiation of rifabutin and clarithromycin therapy, the rapid resolution when the treatment was stopped and the prompt recurrence when it was resumed.

Rifabutin-associated uveitis, which may be either unilateral or bilateral, typically presents as an anterior uveitis with a hypopyon. It can develop as early as two weeks and as late as nine months after the start of therapy and usually resolves within days when the drug is stopped