Isolated testicular vasculitis mimicking a testicular neoplasm

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Abstract

A 19 year old man presented with unilateral testicular swelling and pain. An initial diagnosis of epididymo-orchitis was modified to a presumed testicular neoplasm following ultrasonography. The final diagnosis of isolated testicular vasculitis was established following histological examination of the orchidectomy specimen. Staining for anti-neutrophil cytoplasmic antibodies was negative. Despite immunosuppressive treatment, the patient developed further symptoms affecting the remaining testis one year later. He responded well to an increase in immunosuppressive therapy and has remained asymptomatic 18 months from diagnosis. Symptomatic vasculitis confined to the testis is extremely rare, but must be considered

in the differential diagnosis of testicular swelling and may be the presenting feature of a systemic vasculitis such as polyarteritis nodosa. The risk of progression to systemic disease in such cases is unknown. Immunosuppressive therapy must be considered carefully and long term follow up is important.

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Symptomatic vasculitis confined to the testis without clinical or laboratory evidence of systemic disease is extremely rare. It is difficult to diagnose clinically and to detect using non-invasive methods. We describe a case with an unusual presentation simulating a testicular neoplasm.

Case report

A 19 year old man presented to his general practitioner with left testicular swelling and was treated with oral antibiotics for presumed epididymo-orchitis. Over the next 10 days, the swelling increased, the testis became painful and he was referred for urgent urological assessment. Otherwise, the patient was in good health with no other symptoms and no relevant medical history.

On examination, the patient was afebrile and normotensive. The left testis was swollen and tender on palpation. Scrotal ultrasound examination revealed an abnormal left testis with a heterogeneous echo pattern including areas suggestive of cystic change. The right testis was clinically and sonographically normal. Urinalysis and culture were negative. Full blood count, serum electrolytes and liver function tests were normal as were serum α -fetoprotein and human chorionic gonadotrophin concentrations, and chest radiography. The initial clinical diagnosis was of a possible testicular tumour and left radical orchidectomy was performed via an inguinal incision.

The testis measured $4 \times 3 \times 2.5$ cm and contained scattered areas of haemorrhage, particularly around the lower pole (fig 1). The epididymis, investing membranes and spermatic cord seemed grossly normal.

Microscopy showed the presence of a patchy, necrotising vasculitis affecting medium and small calibre arteries. Several vessels showed frank fibrinoid necrosis of their walls with a transmural infiltrate of polymorphonuclear leucocytes and lymphocytes

Figure 1 The bisected testis shows cystic areas of haemorrhage, mostly within the lower half of the specimen ($\times 2.5$).

Figure 2 A small parenchymal testicular artery showing an intense segmental inflammatory cell infiltrate, perivascular inflammation and early fibrinoid necrosis (haematoxylin and eosin; $\times 180$).

(fig 2); others were partly occluded by immature fibroblastic tissue consistent with early healing. Aneurysms were not seen. The changes were confined to the testicular parenchyma and associated with focal haemorrhage and infarction. The tunical, epididymal and cord vessels were not involved. Examination of the entire specimen did not reveal any evidence of a neoplasm.

Further laboratory investigations revealed evidence of an acute phase response with a raised erythrocyte sedimentation rate of 100 mm/hour, C-reactive protein (CRP) concentrations were moderately raised at 18 mg/l (normal 0–10 mg/l) and von Willebrand factor marginally increased at 210 IU/l (normal 50–200 IU/l). Antineutrophil cytoplasmic antibodies (ANCA) were not detected by indirect immunofluorescence assay.

The overall features were thought to be consistent with a diagnosis of polyarteritis nodosa. Treatment was therefore instituted with oral cyclophosphamide for one month followed by azathioprine and oral prednisolone. The patient remained well on treatment with no clinical or serological evidence of disease activity until one year after diagnosis when he developed pain in his right testis. The von Willebrand factor was raised at 486 IU/l but CRP concentrations remained below 10 mg/l and staining for ANCA was negative. The patient was treated for a relapse with short term increase in the dose of prednisolone and azathioprine. Sperm counts were not performed. He has remained well and, 18 months from initial diagnosis, is clinically and serologically quiescent on low dose oral prednisolone.

Discussion

Vasculitis apparently confined to the testis without evidence of systemic disease is extremely rare. There are several previous reports of this condition presenting as pain or epididymitis, but presentation with clinical features suggestive of testicular neoplasm is exceptional.^{1,2} Other reported cases have shown clinical or laboratory evidence of disease in other organ systems on presentation or have subsequently developed them within a short space of time.³

Most cases of testicular vasculitis occur as part of a systemic disease, most commonly polyarteritis nodosa. Involvement is seen less frequently in other vasculitides including Wegener's granulomatosis, Henoch-Schönlein purpura, giant cell arteritis, and rheumatoid arthritis.⁴ Polyarteritis nodosa is a disease of unknown origin which, in its classic form, affects medium and small arteries of any organ, usually excluding the lungs. It may vary in severity from mild, focal disease to extensive multisystem involvement. The histological changes are virtually indistinguishable from the vasculitis seen in other systemic disorders. Postmortem studies suggest that the testis is involved in about 38–86% of cases of polyarteritis nodosa, but that less than 18% of these are symptomatic, and most will show other manifestations of polyarteritis nodosa.⁵

Isolated organ involvement in vasculitis is rare. Involvement of the testis, epididymis, appendix, uterus, cervix, gall bladder, synovium, and breasts have been reported,⁶ although involvement of the skin in polyarteritis nodosa⁷ and the respiratory tract in limited Wegener's granulomatosis⁸ is better recognised. Whether such cases represent truly isolated vasculitis or merely represent an unusual site of presentation with the risk of subsequent progression has yet to be determined from long term studies. Classic polyarteritis nodosa carries a significant mortality and morbidity rate, even with treatment, and has a high rate of relapse.⁹ It is not known whether isolated vasculitis has a better prognosis than systemic disease, although this may be true for polyarteritis nodosa confined to the skin and in limited Wegener's granulomatosis.

Testicular vasculitis may be impossible to diagnose clinically, without histological examination. Serological markers such as CRP and von Willebrand factor are possible indicators of endothelial injury in systemic vasculitis but may not reflect the activity in isolated organ disease. Whilst granular cytoplasmic ANCA (c-ANCA) staining is commonly seen in Wegener's granulomatosis and perinuclear (p-ANCA) staining is seen in up to half of patients with microscopic polyarteritis, staining for ANCA is usually negative in classic polyarteritis nodosa.¹⁰ Ultrasound examination may fail to show any abnormality. Magnetic resonance imaging is a more sensitive technique which can demonstrate focal testicular infarction,¹¹ but, at present, the diagnosis of vasculitis requires histological confirmation.

The pathogenesis of isolated organ vasculitis is unknown, as is why only one organ may be affected. Localised infection has been suggested in limited Wegener's granulomatosis. ANCA are now being found to have a pathogenetic role in some systemic vasculitides but the absence of ANCA in most cases of classic polyarteritis nodosa suggests that cell mediated immunity may also be important.

To treat this patient with potentially toxic immunosuppressive therapy with the added risk of sterility, despite the lack of clinical and objective laboratory evidence of systemic disease, was a difficult clinical decision. In view of the high relapse rate associated with polyarteritis nodosa, long term follow up is essential. The absence of serological markers of disease activity, however, may make monitoring of any future relapse difficult.

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Lymphocytic gastritis, gastric adenocarcinoma, and primary gastric lymphoma

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Abstract

A series of primary gastric lymphomas and adenocarcinomas was reviewed to assess the prevalence of lymphocytic gastritis in these conditions. Lymphocytic gastritis was more prevalent in patients with gastric adenocarcinoma (16 of 130 cases; 12.3%) and primary gastric lymphoma (six of 45 cases; 13.7%) than in unselected patients undergoing endoscopy (0.83-2.5%). This suggests that these two disparate gastric tumours may share an immunological dysfunction or a common pathogenesis, and this is of interest given that *Helicobacter pylori* is thought to have a role in the evolution of gastric adenocarcinoma and lymphoma.

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varioliform gastritis on endoscopy.¹ Serological evidence of *Helicobacter pylori* infection is present in most, but not all, of these cases,² but the precise link between *H pylori* and lymphocytic gastritis is unknown. A hypertrophic form has been recognised and distinguished from Menetrier's disease.³ Lymphocytic gastritis also occurs in a substantial proportion of patients with coeliac disease.⁴ The disorder affects the whole stomach⁵ and occurs with an incidence of between 0.83 and 2.5% in unselected patients undergoing endoscopy,⁶ and of 4.5% in those with chronic gastritis.²

Concurrent lymphocytic gastritis and primary gastric tumours in resection specimens prompted us to review a series of primary gastric lymphomas and adenocarcinomas to assess the prevalence of lymphocytic gastritis in these conditions.

Methods

Specimens were retrieved from the archives of Leeds General Infirmary and St James's University Hospital, Leeds, and from the Yorkshire Regional Lymphoma Panel. A total of 52 gastric lymphomas were examined, 45 of which had features associated with primary gastric mucosa associated lymphoid tissue (MALT) lymphoma.⁷ We also examined 130 cases of primary gastric adenocarcinoma.

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