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Testicular granulomatous vasculitis mimicking testicular torsion in an anti-neutrophil cytoplasmic antibody–associated vasculitis patient

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Abstract

Testicular vasculitis is uncommon and can be easily misdiagnosed. Early identification and treatment are essential for patient care. A 63-year-old man, presenting with testicular pain and swelling, had been treated with antibiotics for weeks. A month later, he developed severe left testicular pain and systemic symptoms. Scrotal ultrasound was suggestive of testicular torsion due to no blood flow. Pathology of the orchiectomy specimen demonstrated testicular granulomatous vasculitis involving small- to medium-sized arteries. Additional work-up of blood tests contained positive antinuclear, anti-proteinase 3 and anti-myeloperoxidase antibodies. Erythrocyte sedimentation rate and C-reactive protein were also elevated. Diagnosis of anti-neutrophil cytoplasmic antibody–associated vasculitis was made and prednisone was started. During more than 1-year follow-up, the patient's systemic symptoms were resolving gradually with no involvement of the other testis.

Keywords

Testicular granulomatous vasculitis, anti-neutrophil cytoplasmic antibody, prednisone

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Introduction

Testicular vasculitis is defined as inflammation and consequent pathological destruction of the blood vessels in the testis, which can be seen in either systemic or isolated diseases.[1] Systemic vasculitis such as polyarteritis nodosa (PAN), Henoch–Schönlein purpura (HSP), systemic lupus erythematous (SLE) and anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis has been reported to cause related testicular vasculitis, of which PAN is the most common form and affects two-third of the patients.[2–5] Isolated testicular vasculitis is rarer and the majority of the cases are confirmed to herald the onset of certain systemic vasculitis during long-term clinical follow-up.[4,6]

Testicular vasculitis is a great mimic due to nonspecific clinical presentations, laboratory tests and ultrasound findings. It can be easily misdiagnosed as infection, testicular torsion or tumor, especially when it presents as isolated disease or the first manifestation of systemic disease at an early stage. Many affected patients ended up with unilateral or bilateral orchiectomy because of misdiagnosis or testicular infarction caused by the late stage of disease.[7,8] Therefore, early identification and appropriate treatment are essential for patient care. Here, we report a case of ANCA-associated systemic vasculitis with testicular involvement as the first manifestation.

Case presentation

Clinical presentation

A 63-year-old man presented to the emergency room with testicular pain and swelling. He had a 2-month history of increased urinary frequency and testicular swelling and had been diagnosed as epididymo-orchitis and treated with antibiotics with no mitigation of the swelling. Urine analysis was negative for infection. Scrotum ultrasound showed no

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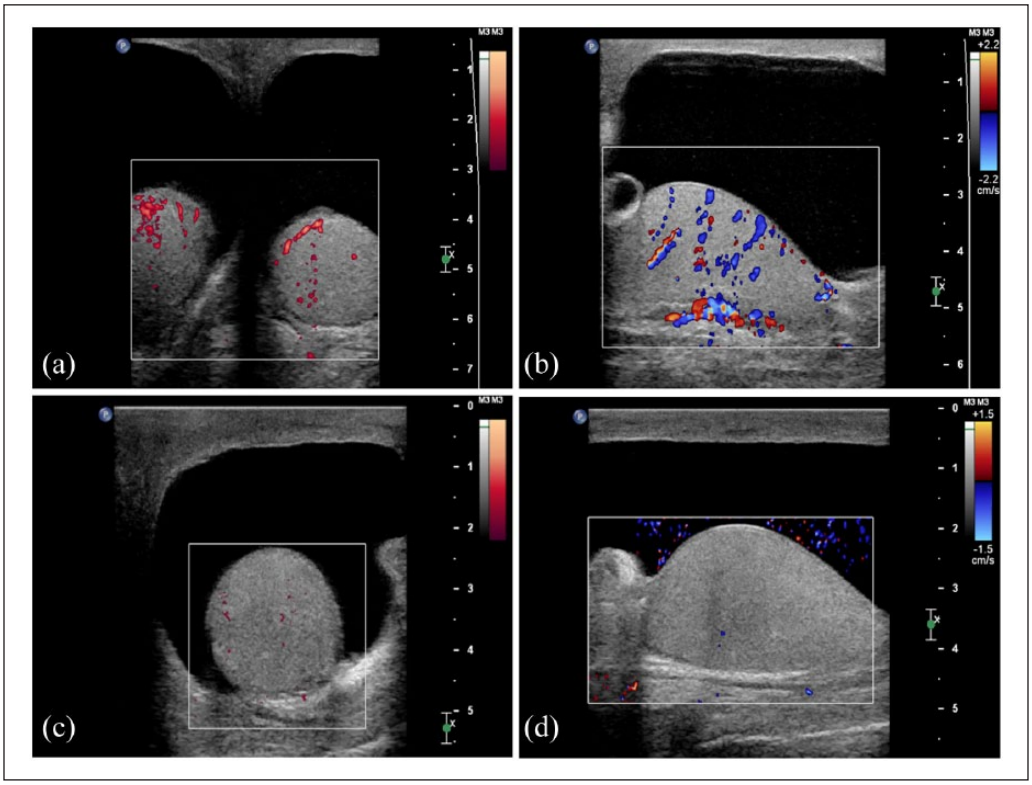

Figure 1. Scrotal ultrasound images during the first and second presentations of testicular pain and swelling. (a, b) Normal bilateral and left testicular blood flow during the first presentation: (a) transverse Doppler image of bilateral testes and (b) sagittal Doppler image of the left testis; (c, d) absence of blood flow in the left testis during the second presentation: (c) transverse Doppler image of the left testis and (d) sagittal Doppler image of the left testis.

signs of continued infectious process or testicular torsion (Figure 1(a) and (b)). The patient was discharged and advised to continue to follow-up with a urologist and complete the planned course of antibiotics.

A month later, the patient presented to the hospital with significant weight loss (25 lbs in the last 6 weeks), fatigue, bilateral leg pain and swelling. He was found to have bilateral deep venous thrombus (DVT), mediastinal and right infrahilar lymphadenopathy, anemia, leukopenia and positive hepatitis B virus (HBV) serology (hepatitis B surface antigen (HBsAg) negative, hepatitis B surface antibody (HBsAb) negative, hepatitis B core antibody (HBcAb) positive, hepatitis B e antibody (HBeAb) positive; and HBV DNA copies 2070 IU/mL). During the 7th day of hospitalization, he developed sudden onset of severe left scrotal pain (8/10) with no dysuria or fever. Emergent scrotal ultrasound demonstrated no flow to the left testicle (Figure 1(c) and (d)) and he was brought to the operating room for urgent operative treatment. During the scrotal exploration, the left testis was noted to be pale with no distinct necrosis or ischemia. No obvious torsion of the cord was seen. Examination of the left proximal cord revealed good pulsation, but it vanished 1 cm proximal to the left testis. The right testicle was unremarkable with normal blood flow. Left simple orchiectomy was performed.

Pathologic findings

Macroscopically, a 68.8-g, $6.0 \times 3.6 \times 3.0\,cm^3$ left orchiectomy specimen (consisting of a testicle: $3.5 \times 2.8 \times 1.6\,cm^3$, an epididymis: $3.0 \times 1.7 \times 0.8$ and an attached spermatic cord: $4.0 \times 0.6\,cm^2$) was received. The tunica vaginalis was tan-brown, shaggy and diffusely thickened, measuring 5 mm in thickness. The cut surface of the testicle was pale and focally hemorrhagic.

Microscopically, the left testicle and spermatic cord showed multiple foci of vasculitis ranging from small- to medium-sized arteries in a patchy distribution; most showed advanced features with fibrinoid necrosis and surrounding mixed inflammation including macrophages, giant cells, small lymphocytes, plasma cells, neutrophils and eosinophils (Figure 2). Rare early lesions were seen with only partial involvement of the vessel wall. The seminiferous tubules showed extensive infarct-type necrosis with occasional foci of neutrophils. There were maturation arrest, thickened basement membranes and paucity of Leydig cells in the less necrotic areas. The thickened tunica vaginalis also showed numerous foci of vasculitis, often with multiple associated giant cells (Figure 3). Verhoeff–Van Gieson (VVG), a special stain for elastic fibers, was negative in most of the involved arteries.

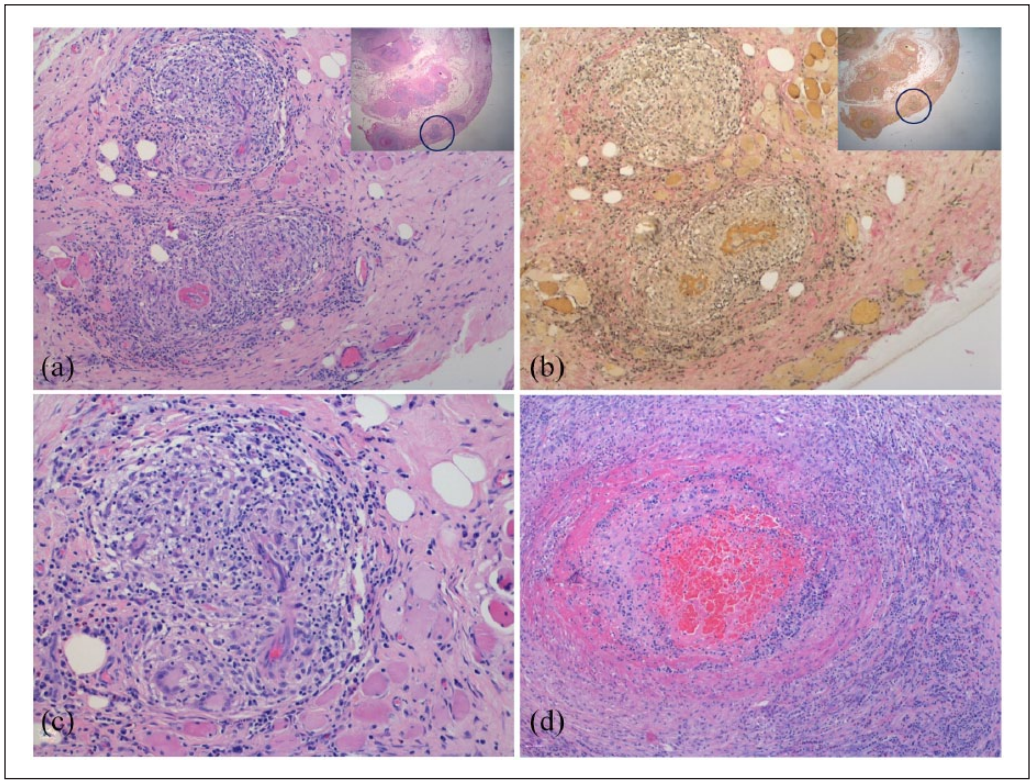

Figure 2. Multiple foci of granulomatous vasculitis in the left spermatic cord: (a, c, d) H&E sections show small- and medium-sized arteries with fibrinoid necrosis and surrounding mixed inflammation; (b) Verhoeff–Van Gieson (VVG) is negative in the involved arteries.

Clinical follow-up and management

Given the pathological findings, a rheumatology consult and additional work-up to assess underlying systemic vasculitis were obtained. Antinuclear antibody (ANA) was positive (1:320) with a speckled pattern. Anti-proteinase 3 (PR3-ANCA) and anti-myeloperoxidase (MPO-ANCA) antibody testing by enzyme-linked immunosorbent assay (ELISA) was both positive (MPO: 18.5 IU/mL, reference range with negative <10 IU/mL; proteinase 3 (PR3): 19.4 IU/mL, reference range with negative <10 IU/mL). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were also elevated. Anti-ds DNA and anti-Smith antibody were negative with normal C3 and C4. Cryoglobulin was not detected. Sputum culture showed normal flora and bronchoalveolar lavage was negative for organisms. Mediastinal lymph node biopsy was negative for malignancy, with normal lymphoid population. Chest computed tomography (CT) with contrast demonstrated bilateral pulmonary ground glass opacities (GGOs) with multiply calcified granulomas. Diagnosis of ANCA-associated vasculitis with the testis and possible lung involvement was made. Prednisone was started 40 mg daily and gradually tapered off completely. On the last follow-up (April 2018), the patient was doing well with complete resolving of the pulmonary GGO.

Discussion

To our knowledge, our case is the first to report testicular involvement as the first manifestation in an ANCA-associated vasculitis patient. In the setting of the emergency room, testicular pain and swelling due to testicular vasculitis can be easily misdiagnosed, which may lead to inappropriate treatment and disease progression.

Laboratory results, in addition to pathological findings, are crucial for establishing a specific vasculitis diagnosis. PAN is the most common systemic vasculitis with testicular involvement and is often associated with positive HBsAg and HIV serology.[9] In our case, PAN was excluded due to positive ANCA antibodies and the clinical picture, although the patient had positive HBsAg. ANCA positivity is helpful in identifying certain small vessel vasculitis; granulomatosis with polyangiitis (GPA) usually is positive for cytoplasmic pattern (c-ANCA) by indirect immunofluorescence (IIF) and PR3 positivity by ELISA; microscopic polyangiitis (MPA) is positive for a perinuclear pattern (p-ANCA) by IIF and MPO positivity by ELISA. Our patient had ANCA positivity of both PR3 and MPO, which have been repeated twice by ELISA.[10] Therefore, ANCA-associated vasculitis without specifying a certain type was determined to be the patient's final diagnosis.

Also, secondary ANCA-associated vasculitis due to multiple drugs, such as hydralazine, propylthiouracil and

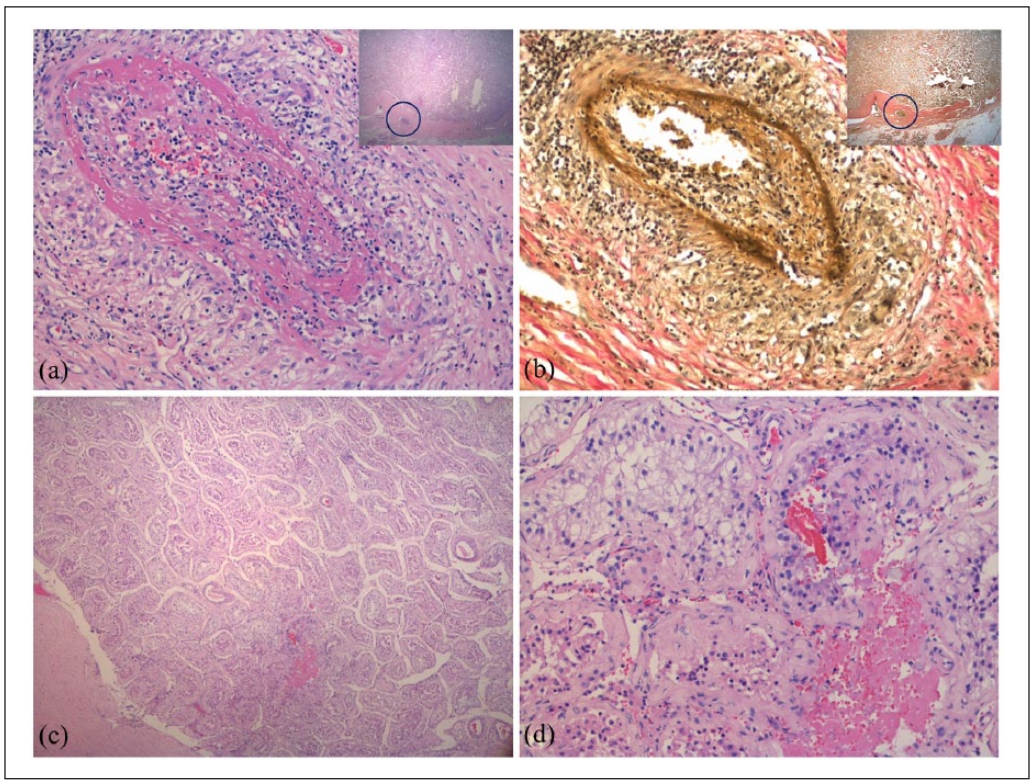

Figure 3. Involvement of tunica vaginalis and testicular parenchyma by granulomatous vasculitis (a, b). The thickened tunica vaginalis shows numerous foci of vasculitis (a), which is negative for Verhoeff–Van Gieson (VVG) special stain (b); (c, d) the seminiferous tubules show extensive infarct-type necrosis with occasional foci of neutrophils.

minocycline, has been reported and can be associated with segmental testicular infarction.[3] Our patient had never been treated with the drugs listed and secondary ANCA-associated vasculitis was not considered.

Systemic ANCA–associated vasculitis can involve many organs, such as the kidney, lung, skin and rarely the testis. Patients may have different symptoms as the first presentation. Early detection and prompt initiation of treatment are essential. Immunosuppressants combined with corticosteroid are considered as standard therapy for induction of remission, although our patient was treated with prednisone only due to his leukopenia and HBV infection. He responded very well and prednisone was tapered off completely.

In summary, testicular vasculitis is a rare entity, which can be easily overlooked. It is important to include it as a differential diagnosis for a patient presenting with testicular pain or swelling even without systemic symptoms. For pathologists, immediate recognition of this entity on biopsy or resection specimen and communicating with clinicians can help achieve accurate diagnosis and appropriate treatment.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

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