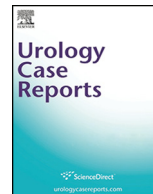




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Inflammation and infection

Testicular tumour, could it be benign? A clinical conundrum

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A B S T R A C T

Testicular vasculitis (TV) is a cause of testicular infarction (TI) which can lead to significant morbidity and rarely mortality. Polyarteritis Nodosa (PAN) is the most common vasculitis that leads to testicular infarction (TI). This case report describes the retrospective tissue diagnosis of autoimmune vasculitis in a middle aged Caucasian male who developed left unilateral orchalgia and a hard, palpable testicular mass.

Introduction

Testicular vasculitis (TV) is a cause of testicular infarction (TI) which can lead to significant morbidity and rarely mortality. Polyarteritis Nodosa (PAN) is the most common vasculitis that leads to testicular infarction (TI). This case report describes the retrospective tissue diagnosis of autoimmune vasculitis in a middle-aged Caucasian male who developed left unilateral orchalgia and a hard, palpable testicular mass.

PAN is a rare, autoimmune type of necrotizing, inflammatory vasculitis affecting middle sized vessels in men at the fourth to sixth decade of life.^{1–3} PAN can affect many organ systems, present with vague constitutional, flu-like symptoms and is often a retrospective diagnosis using biochemical, histological and radiological modalities.^{1–3}

Case presentation

A 35-year-old male presented with left testicular pain without systemic symptoms. He reported a medical history of childhood asthma and was a current smoker with a 23-year pack history. There was no regular medications and no pertinent family history. At presentation, his C-reactive protein (CRP) was 42 (< 5mg/L) and white cell count (WCC) was 14.2 (4–11x10⁹/L) with a neutrophilia of 10.11 (2–8x10⁹/L). Ultrasound of the testis revealed a heterogenous 2cm lesion in the left upper pole of the testes suspicious of epididymo-orchitis and an intratesticular abscess (Fig. 1a–b).

Subsequent presentation four months later with the diagnosis of right upper thigh and groin deep vein thrombus and a pulmonary embolism in the segmental branch of the right lung following a fall and subsequently warfarinisation four months prior. Computerised

tomography imaging excluded a retroperitoneal haematoma and thrombophilia screening excluded autoimmune thrombosis. CRP peaked at 272mg/L, WCC of 16.9 x10⁹/L and Neutrophilia of 15.23 x10⁹/L during this admission.

Further ultrasonography of the left testis again revealed a hard, palpable mass in the upper pole of the left testes and a marginal decrease in size suspicious for an inflammatory or malignant process. The tumour markers, alphafetoprotein, beta human chorionic gonadotropin and lactate dehydrogenase were all within normal limits.

Another two week USS found the lesion to be unchanged in size but had become hypoechoic in nature (Fig. 2); and radical orchidectomy was performed. CRP, WCC and Neutrophils normalized over three to four months post-orchidectomy. Histology on the removed testes showed a healed vasculitic process (Fig. 2a–b); areas of localized haemorrhagic infarct, arteries displaying fibro-intimal thickening with focal myxoid change and fragmentation of internal elastic intima and some evidence of re-canalisation and organization. Of note, no evidence of fibrinoid necrosis and granulomatous inflammation of giant cells were found. Acute inflammatory vasculitis was also found on re-sectioning of the specimen, with VVG staining demonstrating inflammation near artery branch point, and partial loss of elastic lamina in smaller involved branch (Fig. 3).

This patient subsequently tested negative for perinuclear-anti-neutrophil cytoplasmic antibody (pANCA) and positive for anti-nuclear antibody (ANA).

Discussion

Tissue biopsy following orchidectomy has been cited as the ideal diagnostic modality, clinical diagnosis of PAN is possible but difficult

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<https://doi.org/10.1016/j.eucr.2019.100981>

Received 5 March 2019; Received in revised form 23 July 2019; Accepted 26 July 2019

Available online 01 August 2019

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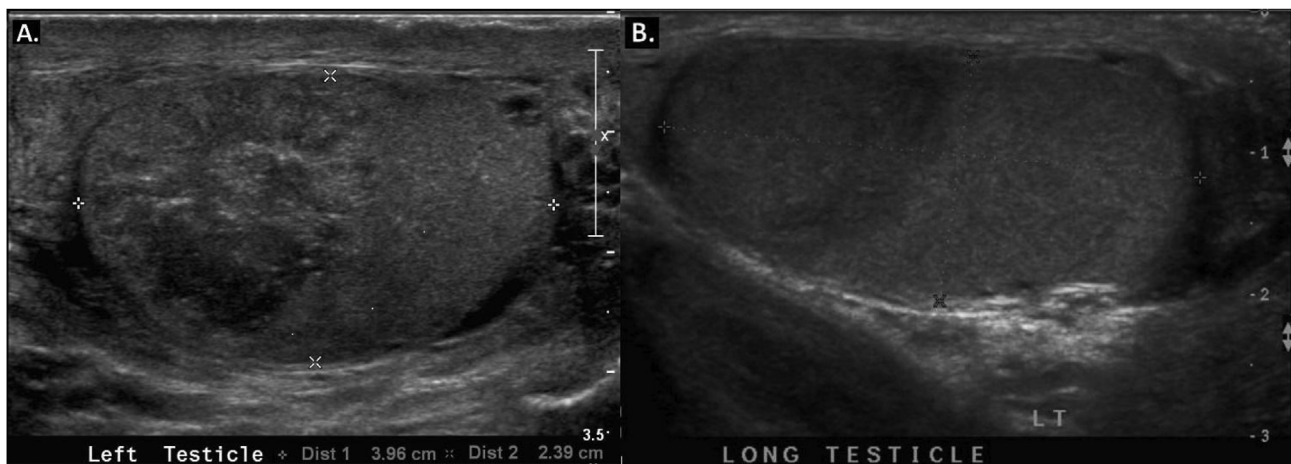


Fig. 1. (A) Ultrasound demonstrating heterogenous 2cm lesion in the upper pole of the left testis. Findings suspicious for epididymo-orchitis with an intratesticular abscess. (B) Interval ultrasound showing marginal decrease in lesion size with hard, palpable mass suspicious for inflammatory or malignant process.

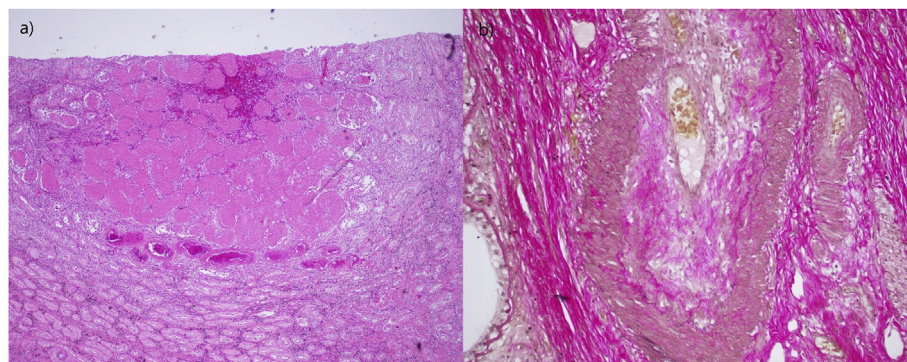


Fig. 2. (A) Testicular infarct at low magnification with H + E staining. (B) Scarred intratesticular vessel with VVG staining showing extensive loss of elastic lamina within vessel wall.

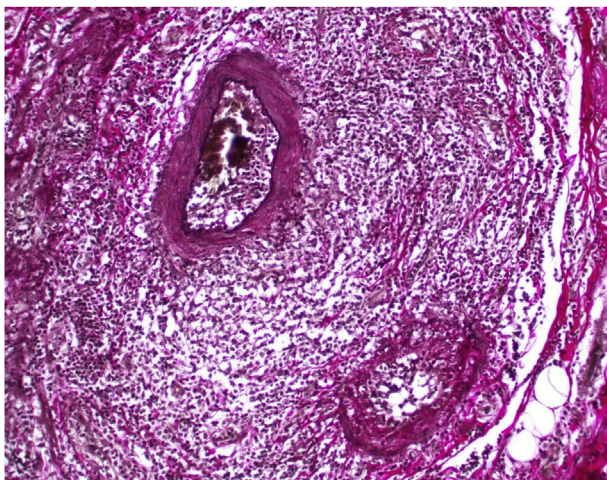


Fig. 3. Acute inflammatory vasculitis involving artery near branch point, with loss of elastic lamina in the smaller involved branch on VVG staining.

due to its variable disease presentation and progression.² Diagnosis has recently shifted away from using only the American College of Rheumatologist (ACR) Criteria and focuses on consideration of the ACR criteria, positive and negative disease associations, International Chapel Hill Consensus Conference Nomenclature of 2012, which unified the definitions of vasculitides internationally, and biochemical markers of inflammation.^{2,4} Although the patient studied didn't fulfill the ACR criteria for the diagnosis of PAN, the presence of many other features

such as inflammation and antecedent history does not exclude the diagnosis entirely.

Ultrasound is the imaging of choice in an unknown testicular lesion¹ and it's important to note that progressive ultrasound findings of heterogenous lesion being hypoechoic and unchanging in size⁵ is seen in both malignant and vasculitic processes which reflects the difficulty in distinguishing testicular inflammation from neoplastic disease.¹

Histologically, PAN affects various organs similarly and can contain a mixture of different pathological processes. Features of consistent with late stage, advanced vasculitic process were observed in our patient. fibro-intimal thickening, parenchymal congestion/haemorrhagic infarction, recanalization and organization.¹ Fibrinoid necrosis, giant cells and granulomas, present in more active and early disease, was absent^{1,2}

PAN typically causes arterial rather than venous thrombi.³ Although homocysteinaemia is likely contributing to thrombotic predilection; inflammatory markers suggest systemic PAN was possibly what unmasked the presentation in this patient. This prompted pANCA testing, with the negative result largely excluding various vasculitides such as Wegener's granulomatosis, Churg-Strauss Syndrome and Microscopic polyangitis (MPA).²⁻⁴

The differential of MPA typically affects the pulmonary, ENT and renal systems, again, the lack of constitutional, pulmonary and upper respiratory symptoms suggest limited disease³; which in MPA, is known to affect mainly gastrointestinal and cardiac systems.

Typical PAN therapy includes corticosteroids with/without cyclophosphamide.^{2,3} Use of the latter indicated by scoring ≥ 1 of the Five Factor Score (FFS),^{2,3} reflecting gastrointestinal, pancreatic, renal, CNS and cardiac effects of systemic PAN, with each point conferring an

additional 12% increase in mortality over five years,² if untreated. With treatment frequently limited by adverse effects and disease isolated to a single organ, patients with isolated disease would be unsuitable for medical therapy. Surgically, the lesion was too big for organ sparing therapy which fortuitously, lead to disease resolution demonstrated by normalization of inflammatory markers post-operatively, a frequently documented phenomenon.

Conclusion

PAN is the most common vasculitis that causes TI, a disease that is frequently idiopathic and can often lead to orchiectomies. It poses a diagnostic challenge due to its variable presentations, symptoms, as well as biochemical and histological findings and should be considered as a non-malignant differential of orchalgia and testicular lump.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://>

doi.org/10.1016/j.eucr.2019.100981.

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