Testicular pain as an atypical presentation of sarcoidosis

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ABSTRACT

Sarcoidosis is a systemic granulomatous disease, with genitourinary tract involvement being very rare (0.2% of all sarcoidosis cases). Genitourinary sarcoidosis may present with a scrotal mass with or without testicular pain, often mimicking epididymo-orchitis or malignancy. Only 8 cases of genitourinary sarcoidosis have been reported in the literature in the last 14 years. We describe the case of a 25-year-old man who was referred with testicular pain. Scrotal ultrasonography demonstrated multiple bilateral hypoechoic testicular lesions that were of similar size and distributed unusually throughout the testicular parenchyma. Computed tomography detected a nodule in the middle lobe of the right lung, multiple small volume nodes in the retrocaval and left para-aortic regions, and enlarged bilateral external iliac and inguinal nodes, similar to those found in metastatic testicular cancer. Following ultrasound guided excision of one of the lesions, histopathological examination confirmed granulomatous inflammation consistent with sarcoidosis.

KEYWORDS

Testicular pain – Sarcoidosis – Testicular cancer

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Sarcoidosis is an idiopathic granulomatous disorder with a wide spectrum of organ involvement affecting patients of both sexes worldwide. Non-caseating granulomas are the hallmark histological feature. Involvement of the genitourinary tract is rare and this may present with a scrotal mass with or without testicular pain, mimicking infection or malignancy.

Case history

A 25-year-old man was referred with right-sided testicular pain. There was no preceding history of genitourinary infections, surgery or trauma and no risk factors for testicular cancer. He denied any contact with tuberculosis patients or recent travel abroad. Ultrasonography of the scrotum revealed multiple round hypoechoic lesions bilaterally. On clinical examination, the testicles were normal in volume and shape.

Investigations

Scrotal ultrasonography showed normal testicular volumes of 18cc and 20cc. Both testicles contained multiple well defined solid hypoechoic foci measuring up to 7mm, with some internal vascularity. The lesions did not lead to distortion of the testicular parenchyma (Fig 1).

Testicular tumour markers (alpha-fetoprotein [AFP], beta-human chorionic gonadotrophin [β -hCG], lactate dehydrogenase [LDH]) were within normal ranges.

Contrast enhanced computed tomography of the chest, abdomen and pelvis detected a small indeterminate soft tissue density in the right middle lobe, measuring 3mm in size. Multiple small volume retroperitoneal nodes were detected, measuring up to 1cm in the short axis diameter. Bilateral external iliac and inguinal nodes were seen, measuring up to 11mm in diameter.

Differential diagnoses

The differential diagnoses for unilateral testicular pain and bilateral hypoechoic testicular lesions in a young man are germ cell tumours, gonadal stromal tumours, testicular lymphoma, leukaemia, tuberculosis, sarcoidosis and schistosomiasis.

Treatment

The patient was counselled for ultrasound guided excisional biopsy of one of the testicular lesions. He subsequently underwent exploration of the right testicle through an inguinal incision with intraoperative ultrasound localisation, which targeted two 5mm lesions. Following needle localisation, the lesions were excised from the testicular

Figure 1 Testicular Doppler ultrasonography showing multiple well defined solid hypoechoic lesions (arrowed) with some internal vascularity and no distortion of the parenchyma.

parenchyma, and the tunica albuginea was closed and the testicle returned to the scrotum.

Outcome and follow-up

Histopathological examination showed testicular tissue with a central fibrous nodule containing numerous well formed non-necrotising granulomas. A rim of seminiferous tubules was seen and the majority of these appeared to contain mature sperm. There was no evidence of a germ cell tumour or germ cell neoplasia in situ. The appearances were consistent with foci of granulomatous orchitis. Immunohistochemistry results for placental alkaline phosphatase were negative on all sections, excluding the possibility of a seminoma. Special staining for acid-fast bacilli and fungi were negative. The histopathological findings were consistent with sarcoidosis (Figs 2 and 3).

Figure 2 Cross-section of lesion showing central fibrous nodule with granulomatous inflammation. A rim of seminiferous tubules at the periphery contain mature sperm.

Figure 3 Haematoxylin and eosin stained section of fibrous nodule containing well formed non-necrotising granulomas.

The patient was referred to a respiratory medicine specialist. His lung function tests were normal and serum angiotensin converting enzyme (ACE) was negative. In light of the results, the patient is being managed conservatively with regular clinical assessments and has not been commenced on steroid therapy as yet.

Discussion

Sarcoidosis is a granulomatous disorder that can involve a number of organs. The aetiology is unknown but has been linked to an immune response in individuals with a genetic predisposition after exposure to specific environmental or infectious antigens. Antigen mediated T helper cell activation leads to clonal proliferation, expression of chemokines and cytokines, accumulation of histiocytes and subsequent granuloma formation.¹

The most common manifestation of sarcoidosis is respiratory involvement, seen in more than 90% of patients.² Computed tomography is highly sensitive in the detection of thoracic sarcoidosis, the most common findings being symmetrical involvement of hilar lymph nodes followed by lung parenchymal involvement. In 75–90% of cases, lung parenchymal involvement is visualised as micronodules with a perilymphatic distribution. Pleural involvement is seen in only 1–4% of thoracic sarcoidosis cases.¹

Up to 70% of patients also develop extrathoracic sarcoidosis.³ Commonly involved sites comprise skin, eyes, lymph nodes, liver, spleen and central nervous system. Genitourinary sarcoidosis is seen in less than 0.2% of all clinically diagnosed cases, with the epididymis and testicles being the most commonly involved genitourinary organs.⁴ In this case, extrathoracic sarcoidosis was present in the testes and in the retroperitoneal, external iliac and inguinal nodes. To our knowledge, only eight cases of genitourinary sarcoidosis (including this case) have been reported since 2004.

It has been noted that the diagnosis of sarcoidosis is more likely to be made during follow-up review for testicular cancer, possibly as a sequela of testicular malignancy or its treatment.⁵ Moreover, sarcoid reaction (a non-caseating

granulomatous response to disintegrated tumour antigens) is frequently associated with malignancies.⁶

The major differential diagnosis of a scrotal mass is testicular malignancy. It is important to differentiate sarcoidosis (which is usually a benign and self-limiting disease) from testicular malignancies. The incidence of both diseases peaks in men aged 25–35 years. Laboratory tests for serum tumour markers associated with germ cell testicular malignancies (AFP, β -hCG, LDH) and serum ACE can be helpful in differentiating testicular cancer from sarcoidosis. Serum ACE levels are increased in 75% of untreated patients with active sarcoidosis.² Cases of testicular sarcoidosis with elevated tumour markers (eg LDH) have also been reported.²

Imaging does not differentiate between genitourinary sarcoidosis and malignancy. With scrotal ultrasonography, the most common finding in genitourinary sarcoidosis is a hypoechoic mass in the testicles or epididymis. However, as this is not specific to genitourinary sarcoidosis, a coarsened testicular echotexture is also looked for.

Histological examination remains the most reliable way to confirm the diagnosis of testicular sarcoidosis although classical seminoma can have a heavy sarcoidal granulomatous infiltrate, which can even obscure the seminoma cells in small specimens. In our patient, seminoma was excluded by negative immunohistochemistry for placental alkaline phosphatase on all sections and the absence of germ cell neoplasia in situ. European Association of Urology guidelines on testicular cancer recommend that every patient with a suspected testicular mass should

undergo inguinal exploration with exteriorisation of the testis.⁷ In cases where the diagnosis is not clear, a testicular biopsy (and enucleation of the intraparenchymal tumour) is taken for histological examination. This allows a formal histological diagnosis and if malignancy is confirmed, then an orchidectomy can be performed through the same incision.

Conclusions

A differential diagnosis of sarcoidosis should be considered when ultrasonography detects multiple atypical lesions in the testicle. Rather than proceeding to an inguinal orchidectomy, ultrasonography guided excision of the lesion allows an accurate diagnosis and preservation of the testicle.

References

1. Iannuzzi MC, Fontana JR. Sarcoidosis: clinical presentation, immunopathogenesis, and therapeutics. *JAMA* 2011; **305**: 391–399.
2. Gupta R, Senadhi V. A diagnostic dilemma: metastatic testicular cancer and systemic sarcoidosis – a review of the literature. *Case Rep Oncol* 2011; **4**: 118–124.
3. Wasfi YS, Rose CS, Murphy JR *et al.* A new tool to assess sarcoidosis severity. *Chest* 2006; **129**: 1,234–1,245.
4. Ricker W, Clark M. Sarcoidosis; a clinicopathologic review of 300 cases, including 22 autopsies. *Am J Clin Pathol* 1949; **19**: 725–749.
5. Paparel P, Devonec M, Perrin P *et al.* Association between sarcoidosis and testicular carcinoma: a diagnostic pitfall. *Sarcoidosis Vasc Diffuse Lung Dis* 2007; **24**: 95–101.
6. Brincker H. Sarcoid reactions in malignant tumours. *Cancer Treat Rev* 1986; **13**: 147–156.
7. European Association of Urology. Testicular cancer. <https://uroweb.org/guideline/testicular-cancer/#5> (cited February 2019).