CASE REPORT

Testicular plasmacytoma misdiagnosed as orchitis

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SUMMARY

Testicular plasmacytomas are rare, accounting for only 1.3% of all extramedullary plasmacytomas. The infrequency in which it is encountered, coupled with its non-specific clinical and sonographic presentation, makes its diagnosis a challenge. We present a case of a 70-year-old man with multiple myeloma, which was systemically responding to chemotherapy, who developed testicular swelling, erythema and pain. Ultrasound findings were concerning for infection, although urine and serum testing were unremarkable. The patient did not improve after several rounds of antibiotics prompting further evaluation. The patient underwent radical orchiectomy which revealed testicular plasmacytoma. Fluorescent in situ hybridisation (FISH) of the testicular tissue noted mutations which had not been present in the FISH analysis of bone marrow. Positron emission tomography scan later revealed new retroperitoneal plasmacytomas involving the new clone and his chemotherapy regimen needed to be adjusted for treatment.

BACKGROUND

Extramedullary plasmacytomas (EMP) represent ~6% of all plasma cell neoplasms and they can occur in a variety of anatomic sites including the respiratory and gastrointestinal tracts, lymphoid tissue, soft tissue and rarely the gonads.^{1–5} EMP can occur as an isolate presentation, but it is more commonly associated with multiple myeloma (MM). Extramedullary soft tissue involvement of myeloma is common in advanced disease, with autopsy studies citing 65%–71% of patients with myeloma being affected; however, testicular involvement remains a rare occurrence.^{6–7} Overall, testicular plasmacytomas account for only 1.3% of EMP and 0.03%–0.15% of all testicular tumours.^{8–10} The infrequency in which it is encountered, coupled with its non-specific clinical and sonographic presentation, makes diagnosis of testicular plasmacytoma a formidable challenge.

CASE PRESENTATION

A 70-year-old man presented with a 2-week history of erythematous, non-tender swelling of his right testis while undergoing salvage therapy for his relapsed IgG lambda MM. His MM had been diagnosed 4 years earlier and he had previously undergone induction therapy with six cycles of bortezomib, cyclophosphamide and dexamethasone (CyBorD) followed by autologous stem-cell transplantation. Subsequently, he had received maintenance immunotherapy with lenalidomide for 2 years until he developed a sternal plasmacytoma and an increase

in his monoclonal (M) protein from 0.2 to 0.4. He was then retreated with CyBorD which resulted in shrinkage of the sternal plasmacytoma and a 50% decline in his serum M protein. After his fifth cycle of CyBorD he developed the aforementioned right testis symptoms. He reported no pain at the testis and normal urination. Urinalysis (UA) revealed trace leucocyte esterase but was otherwise negative. Ultrasound (U/S) revealed an enlarged right testis with heterogeneous echotexture and increased vascularity, consistent with a diagnosis of orchitis. Oral quinolone was prescribed with no response and the patient returned 1 week later with testicular pain and dysuria. He was admitted to the hospital with presumed sepsis, meeting the Systemic Inflammatory Response Syndrome (SIRS) criteria, and was started on broad-spectrum antibiotics.

INVESTIGATIONS

Repeat UA was negative. The patient underwent several testicular ultrasound (U/S) during his admission which continued to yield hypoechoic signal of the testis favouring infection versus inflammation. U/S did reveal an absence of associated epididymitis, raising concern for possible viral or atypical pathogens (figures 1 and 2). Cultures, gonorrhoea and chlamydia PCR, mumps serology, urine and sputum Acid-Fast Bacillus (AFB), and quantiferon testing were all negative. Biochemical tests showed no evidence of systemic relapse of myeloma.

TREATMENT

Due to his immunocompromised state, the presumed diagnosis was orchitis and he was treated with a prolonged course of intravenous antibiotics for 3 weeks. The testicular pain resolved, however the swelling persisted for an additional 2 months after completing antibiotic therapy. It was initially suspected that he was suffering from reactive hydrocoele related to the orchitis, but the lack of improvement led to biochemical marker screen for germ cell tumours, all of which were negative. Serial U/S imaging remained unchanged. During this time period, his chemotherapy was being held and he developed another sternal mass, prompting a FDG-PET/CT scan to be completed to evaluate for relapse of myeloma. FDG-PET/CT revealed an enlarged, diffusely hypermetabolic right testicle (figure 3). As he had undergone empiric antibiotic treatment for orchitis 2 months prior to the scan and evaluation for atypical causes of orchitis had been negative, the hypermetabolic activity in the testicle was concerning for malignancy. Due to the FDG-PET/CT findings and lack of improvement with antibiotics, the patient underwent radical

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Figure 1 Ultrasound reveals enlarged right testis with heterogeneous echotexture, scattered hypoechoic regions and associated hydrocoele.

orchiectomy as it was believed that his testicular symptoms were related to his myeloma and not from orchitis. The gross specimen revealed pink-tan, fleshy cut surfaces that replaced the entire testicular and spermatic cord parenchyma. Histological evaluation showed diffuse sheets of pleomorphic plasmacytoid cells that obliterated the seminiferous tubular architecture and filled the surrounding extratesticular adnexa and spermatic cord up to the surgical margin. The tumour cells were positive for CD138 and lambda light-chain restricted (figure 1). These findings were compatible with a testicular plasmacytoma.

OUTCOME AND FOLLOW-UP

While recovering, the patient underwent FDG-PET/CT scanning which noted pelvic and retroperitoneal adenopathy with hypermetabolic signal. Fluorescent in situ hybridisation (FISH) of the testicular tissue showed t(11;14)(q13;q32), which was not present in the FISH analysis of bone marrow. He subsequently was started on carfilzomib and later daratumumab and pomalidomide but these were discontinued due to lack of response and side effects, respectively. He is currently receiving treatment with dexamethasone, bortezomib, etoposide, cisplatin,

Figure 2 Ultrasound with Doppler reveals enlarged right testis with marked hyperaemia.

Figure 3 FDG-PET/CT image shows an enlarged right testicle that is diffusely hypermetabolic with a focal area of intense FDG avidity laterally. PET, positron emission tomography.

cyclophosphamide and doxorubicin (VDPACE). He has undergone a repeated FDG-PET/CT scan with no uptake in the testis and improvement in his retroperitoneal plasmacytoma size.

DISCUSSION

This case illustrates the difficulties in diagnosing testicular plasmacytoma, as imaging studies such as U/S or CT scans are not specific. Sonographic greyscale imaging of testicular plasmacytomas are either homogeneous or heterogeneous, primarily hypoechoic and are associated with hypervascularity on Doppler.^{11 12} These findings can be seen in cases of the more prevalent primary testicular neoplasms, including germ cell tumours, sex cord-stromal tumours and mesenchymal tumours, as well as secondary testicular neoplasms from lymphoma and leukaemia, testicular haematomas, infarctions and abscesses.^{13 14}

The main differential diagnoses of isolated testis enlargement are infections and tumours. While infectious aetiology is more common, the negative microbiology workup and lack of response to antibiotics are clues to a non-infectious course. However, autoimmune granulomatous orchitis as well as atypical infectious causes, such as syphilis, tuberculosis, mumps and viral aetiologies, like EBV and parvovirus, remain on the differential.

Fluorodeoxyglucose (FDG)-PET/CT imaging is a standard staging tool for myeloma and is particularly helpful to identify plasmacytoma evidenced as intramedullary or extramedullary hypermetabolic lesions. However, hypermetabolic lesions are not always malignant in nature, as shown in this particular case. FDG-PET/CT cannot differentiate between orchitis and testicular plasmacytoma. In case of multiple hypermetabolic lesions, the diagnosis favours multiple plasmacytomas rather than infection. Diagnostic gold standard remains a biopsy of the hypermetabolic sites. If the biopsy is technically difficult and treatment either with antibiotics for infection or chemotherapy for presumed relapsed myeloma is initiated presumptively, a follow-up FDG-PET/CT is needed to document a resolution of the hypermetabolic lesions. In case of lack of response, a biopsy is needed to rule out other aetiologies. Needle aspirate should be avoided though, as skin seeding can occur in cases of germ cell tumours and there is risk of false negatives in the case of lymphoma or testicular plasmacytoma. Transinguinal orchiectomy is the most recommended surgical approach. It offers both diagnosis and treatment, particularly in patients with isolated testicular plasmacytoma. In our case, at the time of presentation with isolated testicular enlargement, the hypermetabolic activity on FDG-PET-CT was limited to the testis. Together with the absence of detectable monoclonal protein, which suggested for

Figure 4 H&E stains of the radical orchiectomy specimen showing an atypical plasma cell infiltrate diffusely replacing the testicular parenchyma underneath the tunica albuginea (A, $\times 400$ magnification). Sheets of plasma cells diffusely infiltrate between efferent ducts (B, $\times 200$ magnification). Immunohistochemical staining shows that tumour cells express CD138 (C, $\times 20$ magnification) and lambda light chain (D, $\times 20$ magnification), which mark for lambda clonal-restricted plasma cells.

an ongoing remission, and the immune suppressive side effects of chemotherapy, the testicular lesion was presumed to be infectious in nature. However, the lack of response to the antibiotics led to the orchiectomy, which confirmed plasmacytoma. The histological appearance is that of either small mature or large and atypical plasma cells. The pattern of spread can be diffusely obliterative, as in the current case (figure 4), or exhibit seminiferous tubular entrapment with or without invasion of the tubules.

EMP represents a subclone of bone marrow-independent tumour cells. Therefore, EMP can develop despite systemic

remission of myeloma, as presented in our case. The blood–testis barrier may limit tissue penetration of chemotherapy and testes represent a sanctuary site for relapse. $t(11;14)(q13;q32)$ in plasmacytoma has been shown to carry poor survival.¹⁵ While systemic involvement of myeloma is through haematological spreading, testicular plasmacytoma may follow the pattern of other testis cancers and lymphoma, via lymphatic spreading—as noted in our case. By the time of orchiectomy, our patient unfortunately developed lymphatic spreading, as evidenced by retroperitoneal adenopathy. Systemic therapy with chemotherapy is required once systemic involvement occurs.¹⁶

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Learning points

- ▶ Testicular plasmacytoma is rare. It can occur as an isolate presentation, but is more commonly associated with multiple myeloma, and often at later stages of disease when the cancer cells are more aggressive and not relying on bone marrow for survival.
- ▶ Imaging studies including ultrasonogram and FDG-positron emission tomography-CT cannot differentiate infection from testicular plasmacytoma. Tissue diagnosis is required particularly in the absence of response to antibiotics started presumptively for orchitis.
- ▶ Blood–testis barrier may limit penetration of chemotherapy. Orchiectomy with or without radiation is the standard treatment.
- ▶ Testicular plasmacytoma may spread via lymphatic channels to the regional lymph nodes and subsequently to distant sites, similar to lymphoma or germ cell tumour. This pattern is different from myeloma which typically spreads to multiple bone sites via haematological spreading.

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