Plasmacytoma of the testis in a patient with relapsed and refractory multiple myeloma: Case report and review of the literature

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Abstract

Testicular plasmacytoma, whether occurring as a primary lesion or as a reflection of underlying multiple myeloma (MM), is a rare disease. We report the case of a 38-year-old male with multiply relapsed MM, who was found to have a testicular plasmacytoma. He presented with a gradually enlarging scrotal mass. Following orchidectomy, pathologic examination of the specimen demonstrated a plasmacytoma. In the context of active MM, the specimen was also sent for cytogenetic analysis but this was unhelpful in guiding a chemotherapy regime, which still continues at time of reporting. Although a rare lesion, there remains no definitive treatment protocol for the management of testicular plasmacytoma representing an extramedullary manifestation of MM.

Key Words: Extramedullary plasmacytoma, multiple myeloma, plasmacytoma, testis

INTRODUCTION

Primary plasmacytomas are relatively uncommon lesions at diagnosis that may present as solitary lesions in bone (solitary bony plasmacytoma [SBP] or within soft tissues extramedullary plasmacytoma [EP]), but occur more frequently as a late manifestation of advanced heavily pretreated multiple myeloma (MM). Multiple solitary plasmacytomas are relatively rare and occur in up to 5% of patients with an apparently solitary plasmacytoma. Primary SBP and EP have been classified as distinct clinical entities within the plasma cell dyscrasia family by both the World Health Organization and International Myeloma Working Group¹² and have a relatively good prognosis with local radiotherapy alone with 50–72% of SBP and 0–36% EP 10 years progression to myeloma.³–¹³ Regardless of the association with underlying MM, plasmacytoma of the testis is very uncommon.¹⁴,¹⁵ Seventy-one cases of testicular plasmacytoma have been published up to 2008.¹⁶ The majority of these present as extramedullary manifestations of MM (eMM). When dealing with testicular plasmacytoma, the distinction between primary testicular EP and eMM is important given the differences in prognosis and treatment pathways.¹⁷

We report here the case of a 38-year-old male with testicular plasmacytoma on a background of aggressive MM with numerous extramedullary localizations.
CASE REPORT

A 38-year-old Indian male presented with a gradually increasing lump in his right hemiscrotum. He had a history of multiply relapsed MM, manifesting as multiple plasmacytomas with minimal marrow infiltration, initially treated with thalidomide based induction therapy, tandem autologous, followed by reduced intensity allogeneic transplantation and multiple lines of salvage therapy with novel agents (including lenalidomide, pomalidomide and bortezomib) and sequential hemiboody radiotherapy. Otherwise, his medical history was unremarkable and did not have any environmental or developmental risk factors. He did not complain of any other genitourinary symptoms although at the time of presentation had multiple soft tissue nodules reflecting active MM. Examination confirmed a mass in the right testis. This was noted to be metabolically active on a fluorodeoxyglucose positron emission tomography study, which incidentally demonstrated multiple avid lymph nodes [Figure 1]. Given his extensive burden of disease, several treatment options were discussed with the patient but in the end a right inguinal orchidectomy and lymph node dissection was performed to provide cytoreductive benefit along with the opportunity to run cytogenetic tests to guide further management.

Macroscopically, the right testis was 68 mm × 35 mm × 35 mm and weighed 53 g. Normal testicular tissue was replaced by lobulated tan and hemorrhagic tumor components [Figure 2]. Microscopically, there were visible sheets of cells with plasmacytoid morphology [Figure 3]. The tumor appeared to infiltrate the epididymis but did not extend into the tunica vaginalis or proximal spermatic cord. The inguinal lymph node was also infiltrated with plasmacytoid tumor cells, with evidence of extra-nodal extension.

Unfortunately, cytogenetic analysis failed but fluorescence in situ hybridization (FISH) was performed in conjunction with cytoplasmic immunoglobulin staining to positively identify plasma cells for analysis. There was no molecular cytogenetic evidence of the high risk (4;14), the t (14;16) or deletion of TP53 (17p13) abnormalities. However, FISH suggested an increased ploidy level in the plasma cell myeloma clone, with four IGH (14q32), three FGFR3 (14p16), three MAF (16q32) and 4 chromosome 17 centromere signals per cell in the majority (79–100%) of cells scored.

DISCUSSION

Testicular plasmacytoma, whether occurring as a primary EP or an eMM, is a rare clinical entity. As a proportion of all primary and secondary testicular tumors, plasmacytoma is estimated to have an incidence between 0.03% and 0.1%. Given its rarity, it is important that all cases of testicular plasmacytoma are reported, to not only improve the understanding of eMM and EP involving the testis, but also to better understand the distinctions between EP and eMM in general.

Although rare, the underlying cause of a testicular plasmacytoma has prognostic implications. The far more common secondary extramedullary spread into the testis from MM usually indicates aggressive disease and a poor clinical prognosis. In contrast, primary EP of the testis appears to have a better prognosis, which is in keeping with EP at other sites. However, given the small absolute number of cases of primary testicular EP reported, the overall prognosis needs to be confirmed by larger cohort studies.
In light of the prognostic differences, it follows that treatment protocols for EP and eMM would differ. Although treatment options for plasma cell neoplasms are constantly evolving, systemic therapy (with or without local radiotherapy to a dominant testicular mass) is usually necessary in the case of eMM, whereas primary testicular EP should be treated by local therapies such as radiotherapy or resection. The treatment of unifocal testicular relapse of MM is less clear, but extended periods of remission from local therapy alone have been reported.[22] However, as with other solitary EP, having primary testicular EP does not preclude disease progression to other plasma cell neoplasms and there are multiple case reports of primary EP progressing to MM but given the small numbers the exact rate is unknown.[13,23,24] The timeline for this progression can extend as far as several years and as such, these patients need to be closely monitored given the risk of developing subsequent generalized MM.[19,23,24]

Finally, despite the small incidence, eMM involving the testis may have a physiological basis. Testis involvement in myeloma and other hematological malignancies has been hypothesized to be partly attributable to the testes being a sanctuary site.[22] As has been noted by Rosenberg, this would be particularly important in the case of a solitary plasmacytoma in the testis without evidence of other myelomatous spread throughout the body. As an overall proportion, however, the absolute number of secondary solitary testicular plasmacytoma occurring as a manifestation of MM relapse is small [Figure 4]. The other interesting finding from the graph below is that although there were 14 cases of primary testicular plasmacytoma, seven of these went on to develop MM later and a further three were associated with plasmacytoma in other organs, making isolated primary testicular plasmacytoma very rare indeed.

However, even in cases like ours, where a patient presents with a testicular mass in the context of active systemic disease following extensive treatment cytogenetic testing from such testicular masses may assist in delineating clonal evolution of the underlying myeloma.

**CONCLUSION**

Testicular plasmacytoma is a very uncommon lesion. It appears to occur more commonly in the context of widespread MM in the context of aggressive end-stage disease rather than as a primary solitary clinical entity. Even when occurring in isolation, it remains important to screen and subsequently monitor patients with MM. Although it continues to carry a poor prognosis, cases of testicular plasmacytoma should be reported to facilitate the creation of a definitive treatment protocol.

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