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American Society of Clinical Pathologists

SURGICAL PATHOLOGY II, VOLUME 24, NUMBER 1, 2000, ISSN-1091-8663

Surgical Pathology II No. SPII 00-1 (SPII-253)

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Learning Outcomes

Upon completion of this exercise, the participant should be able to

- describe the morphologic and immunohistochemical features of testicular plasmacytoma.
- recognize and differentiate the lesions that may closely mimic testicular plasmacytoma.
- recognize the importance of a careful clinical evaluation of a patient with testicular plasmacytoma.

HISTORY

A 45-year-old man with Down syndrome developed an acute-onset left-sided testicular swelling. He was evaluated with ultrasonography which showed a complex lesion of the left testicle, as well as a hydrocele. He then underwent a left orchiectomy.

Questions to be considered

1. What is the diagnosis?
2. What is the differential diagnosis?
3. How may immunohistochemical studies help in the diagnosis?
4. What is the treatment and prognosis?

TESTICULAR PLASMACYTOMA

Pathological Findings

The specimen was composed of a left testis with a well-defined, firm tumor 3 cm in greatest diameter. Its cut surface was tan-white to tan-pink, smooth, glistening, and homogeneous. It involved most of the parenchyma and extended to, but not through, the tunica albuginea. The tunica vaginalis and the spermatic cord were free of tumor.

Light microscopic examination showed sheets of slightly to moderately large tumor cells with eccentric nuclei and moderately abundant cytoplasm (**Images 1,2**). Scattered binucleated and multinucleated cells were seen. Bizarre multinucleated cells admixed with well-differentiated plasma cells were occasionally present (**Image 3**). There were areas with cells that possessed large vesicular nuclei and large pink nucleoli (**Image 4**). Mitotic figures were easily found. Angiolymphatic invasion was present (**Image 5**). Immunohistochemical studies were performed and malignant cells showed positive cytoplasmic kappa immunoglobulin expression (**Image 6**). Markers for B-cell antigen (CD20), T-cell antigen (CD3), and leukocyte common antigen (CD45RB) were negative.

Discussion

This is an example of a testicular plasmacytoma. Extramedullary plasmacytoma is a rare tumor that has been identified in the upper respiratory tract, oral cavity, intestines, kidney, and thyroid.[1] Plasmacytoma involving the testis is an extremely rare tumor. Less than 40 cases are published in the English literature.[2]

Testicular plasmacytoma may present as a solitary lesion or as part of multiple myeloma.

Testicular plasmacytoma is a neoplastic proliferation of plasma cells in the testicular parenchyma. It may present as a solitary lesion or as part of multiple myeloma. In a report by Levin and Mostofi,[1] the tumor occurred in men aged 22 to 66 years, while in a more recent report by Ferry et al,[2] the age range was 40 to 89 years. Most of the cases reported were unilateral with the majority presenting with testicular enlargement. Extratesticular symptoms preceding testicular enlargement were seen in some cases. Ultrasound usually reveals a heterogeneous, hypoechoic pattern.[3] In a review of literature and summary of 36 reported cases, Oppenheim et al[4] found that more than half of the cases had histories of multiple myeloma or developed multiple myeloma shortly after the diagnosis of testicular plasmacytoma was made. There were very few reported cases of patients manifesting testicular tumor without evidence of multiple myeloma.[5-9] However, the length of follow-up of these cases was insufficient, and Carson et al[10] believed that patients with the disease would eventually develop multiple myeloma with long-term follow-up.

Also see Check Sample SP 97-8, Testicular Lymphoma.

In the evaluation of patients with plasmacytoma of the testes, Terzian et al[7] proposed that a careful evaluation must be made to determine whether the lesion represents metastasis or primary disease. Routine laboratory tests as well as additional tests such as chest and abdominal computed tomographic scans, bone scan, bone marrow aspirate and biopsy, serum and urine immunoelectrophoresis should be conducted. Serum alpha-fetoprotein and beta-human chorionic gonadotropin levels should be measured before performing radical orchiectomy.

Serum alpha-fetoprotein and beta-human chorionic gonadotropin levels should be measured before performing radical orchiectomy.

The management of primary testicular plasmacytoma is radical orchiectomy with subsequent close clinical follow-up. However, Chica et al[8] considered these cases to be extramedullary manifestations of multiple myeloma and proposed combination chemotherapy. Radiotherapy may be added for symptomatic lytic bone lesions.

On gross examination, the tumor is described as firm, tan, tan-gray, and approximately 5 to 8 cm in greatest dimension. The tumor may involve the entire testicular parenchyma and may penetrate the tunica albuginea.

Microscopically, the tumor consists of sheets of plasma cells which are moderately larger than the normal plasma cells. They have eccentric nuclei and abundant cytoplasm. Some larger cells may not possess the usual cartwheel pattern, but may exhibit vesicular nuclei with large central nucleoli and less chromatin. Some areas may show binucleated or multinucleated cells with bizarre nuclei. Mitoses are easy to find. Sclerosis is not seen. Rare cases show invasion of the seminiferous tubules.[2] Others may show vascular invasion, as seen in this case.

Immunohistochemical examination shows that the tumor cells are strongly positive for monotypic cytoplasmic immunoglobulin. They are negative for B-cell markers, such as CD19 and CD20, T-cell markers such as CD3, and leukocyte common antigen (CD45RB). Tumor cells show variable expression with CD43, CD45RO, and epithelial membrane antigen.[2]

The differential diagnosis includes neoplastic as well as inflammatory lesions. Among the neoplastic lesions are malignant lymphoma (including large cell immunoblastic, Burkitt's and small noncleaved non-Burkitt's type lymphoma), seminoma, granulocytic sarcoma, and Leydig cell tumor.

Although malignant lymphoma cells have less abundant cytoplasm and lack a paranuclear hof, the cells of plasmacytoma may have large, vesicular nuclei and prominent nucleoli that resemble those seen in large cell immunoblastic type. Testicular Burkitt's lymphoma may exhibit a diffuse growth pattern with small to medium-sized cells, prominent nucleoli, basophilic cytoplasm, abundant mitotic activity, and occasional plasma cells that may be mistaken for testicular plasmacytoma. However, the extremely high mitotic rate and numerous tingible-body macrophages are more characteristic of Burkitt's lymphoma. Small noncleaved non-Burkitt's lymphoma involving the testis has cytologic features that may sometimes mimic testicular plasmacytoma, with

Small noncleaved non-Burkitt's lymphoma involving the testis has cytologic features that may sometimes mimic testicular plasmacytoma.

slightly enlarged cells, prominent nucleoli, and moderate cytoplasm. However, testicular lymphomas in general are almost always B-cell neoplasms and express the B-cell antigens, CD19 and CD20. These markers are usually negative in plasmacytomas. Testicular lymphomas are usually negative for monotypic cytoplasmic immunoglobulin while plasmacytomas are positive.

Seminoma consists of cells with more abundant cytoplasm and stromal infiltrate of benign lymphocytes. The tumor cells stain for glycogen and placental alkaline phosphatase.

Granulocytic sarcoma involving the testis has been misinterpreted as plasmacytoma.[11] This lesion may present with a prominent component of myelocytes exhibiting round, eccentric nuclei and moderately abundant cytoplasm. Because of the associated chronic inflammation with mature plasma cells, this could mimic a testicular plasmacytoma. However, this lesion is positive for myeloperoxidase, leukocyte common antigen (CD45RB), CD43, and lysozyme.

Leydig cell tumor may also be mistaken for testicular plasmacytoma because of the presence of cells with eosinophilic cytoplasm and eccentric nuclei. However, the tumor cells have more abundant cytoplasm than plasma cells. The cytoplasm is more granular and lacks paranuclear hof. Leydig cells usually grow in sheets, cords, and trabeculae, a feature not usually seen in plasmacytoma.

The inflammatory lesions that may mimic testicular plasmacytoma are nonspecific chronic orchitis and inflammatory pseudotumor. Chronic orchitis may resemble plasmacytoma. However, orchitis usually shows a mixed benign cellular infiltrate of lymphocytes, histiocytes, and plasma cells. Immunohistochemically, the plasma cells do not express monotypic cytoplasmic immunoglobulin staining.

The inflammatory lesions that may mimic testicular plasmacytoma are nonspecific chronic orchitis and inflammatory pseudotumor.

Inflammatory pseudotumor (plasma cell granuloma) consists of abundant plasma cells with admixed lymphocytes and histiocytes. Sclerosis is present and there is no nuclear atypicality.[2] Immunohistochemistry is also helpful in differentiating this from plasmacytoma which expresses the above-mentioned markers.

The prognosis for metastatic testicular plasmacytoma is poor and that for primary testicular plasmacytoma is unknown.[1]

Summary

Testicular plasmacytoma is an extremely rare tumor. It occurs in men aged 22 to 89 years. It may occur as a solitary tumor or as part of multiple myeloma. It is composed of sheets of neoplastic plasma cells with scattered binucleated and multinucleated cells and occasional bizarre giant cells. The malignant cells may sometimes possess large vesicular nuclei with prominent nucleoli. They are strongly positive for monotypic cytoplasmic immunoglobulin and negative for B-cell markers such as CD19 and CD20. Differential diagnosis includes malignant lymphoma, as well

as immunoblastic Burkitt's and small cell non-Burkitt's type seminoma, granulocytic sarcoma, Leydig cell tumor, and inflammatory lesions such as chronic orchitis and plasma cell granuloma. Solitary testicular plasmacytoma is managed with orchiectomy and subsequent observation, while those associated with multiple myeloma with symptomatic lytic bone lesions are treated with additional chemotherapy and radiation. The prognosis for metastatic testicular plasmacytoma is poor and that of primary plasmacytoma without subsequent multiple myeloma is unknown.

Key to Images

Image 1. Sheets of moderately large cells with eccentric nuclei and moderately abundant cytoplasm. (H&E, medium power)

Image 2. Moderately large plasma cells with eccentric nuclei and moderately abundant cytoplasm. (H&E, oil immersion)

Image 3. Bizarre multinucleated cells admixed with well-differentiated plasma cells. (H&E, high power)

Image 4. Sheet of cells with large vesicular nuclei and large pink nucleoli. (H&E, high power)

Image 5. Angiolymphatic invasion. (H&E, high power)

Image 6. Positive cytoplasmic kappa immunoglobulin expression. (Immunoperoxidase stain, high power)

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CME DOCUMENTATION QUESTIONS

1. The following are features of testicular plasmacytoma, except
   A) slightly to moderately large plasma cells.
   B) large cells with vesicular nuclei and prominent nucleoli.
   C) frequent mitoses.
   D) sclerosis.
   E) positive expression with monotypic cytoplasmic immunoglobulin.

2. The following immunohistochemical stains are helpful in differentiating testicular plasmacytoma from malignant lymphoma.
   A) Positive expression of B-cell markers
   B) Positive expression of epithelial membrane antigen
   C) Positive expression of monotypic cytoplasmic immunoglobulin
   D) Positive expression of leukocyte common antigen
   E) Positive expression of myeloperoxidase

3. Recommended treatment for testicular plasmacytoma with myeloma and symptomatic lytic bone lesions is
   A) radical orchiectomy alone.
   B) radical orchiectomy with chemotherapy.
   C) radical orchiectomy with combined chemotherapy and radiation.
   D) chemotherapy alone.

4. The prognosis for metastatic testicular plasmacytoma is
   A) good.
   B) excellent.
   C) poor.
   D) unknown.

Note: If you wish to receive CME credit, enter the answers to these test questions on your 2000 Check Sample Program Answer Sheet. Retain your answer sheet until the final exercise for this series has been distributed (there are 8 exercises in the Surgical Pathology II series). DO NOT SEND THE ANSWERS TO THE ASCP AT THIS TIME.

1

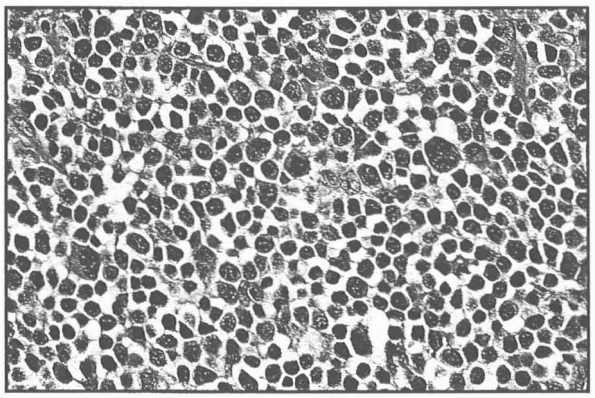

Image 1. Sheets of moderately large cells with eccentric nuclei and moderately abundant cytoplasm. (H&E, medium power)

2

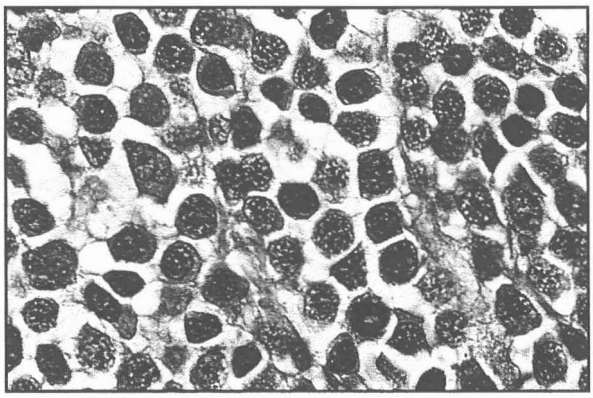

Image 2. Moderately large plasma cells with eccentric nuclei and moderately abundant cytoplasm. (H&E, oil immersion)

3

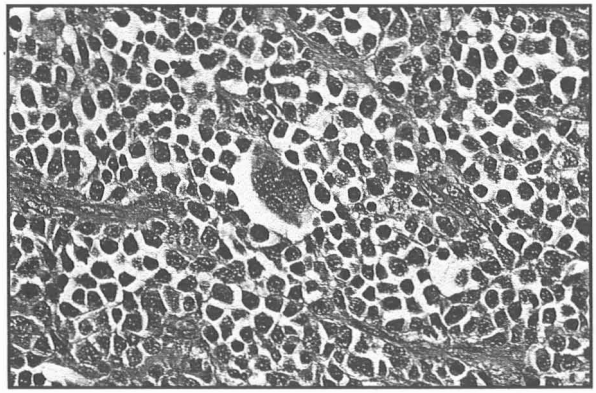

Image 3. Bizarre multinucleated cells admixed with well-differentiated plasma cells. (H&E, high power)

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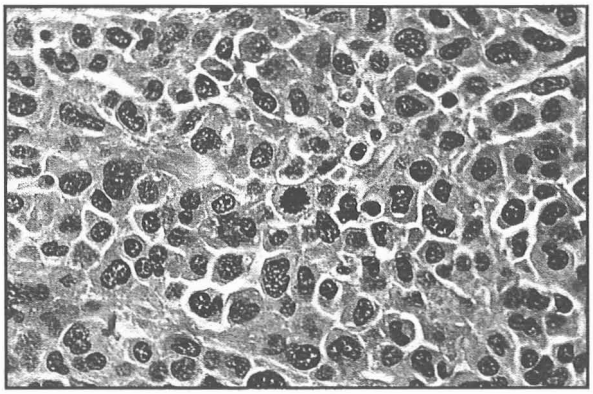

Image 4. Sheet of cells with large vesicular nuclei and large pink nucleoli. (H&E, high power)

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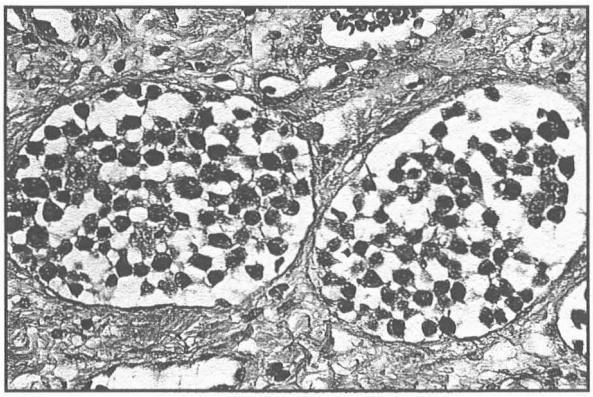

Image 5. Angiolymphatic invasion. (H&E, high power)

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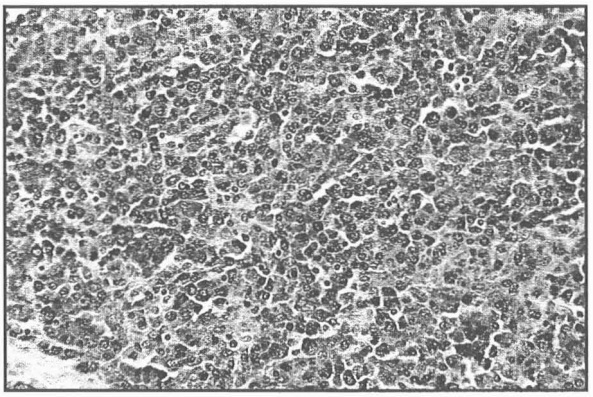

Image 6. Positive cytoplasmic kappa immunoglobulin expression. (Immunoperoxidase stain, high power)