Spermatocytic Seminoma

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Spermatocytic seminoma is a rare germ cell tumor distinct from classical seminoma, both clinically and pathologically. It affects older men, has not been associated with a history of cryptorchidism, and has no known counterpart in ovary or any other site. Pathologically, it is characterized by 3 distinct cell types, lack of cytoplasmic glycogen, and scant to absent lymphocytic infiltrate. Gain of chromosome 9 is the most consistent genetic abnormality. There have been few case reports of sarcomas arising in spermatocytic seminoma and only an occasional report of metastasis. It is important to differentiate this condition from its frequent mimics, such as classic seminoma and embryonal carcinoma, because patients with spermatocytic seminoma may not require further treatment after surgery.


Testicular germ cell tumors represent the most frequent solid malignancy in young white men between the ages of 20 and 35 but are relatively uncommon among African Americans.1–4 Epidemiologically, clinically, and histologically, 3 entities of germ cell tumors can be distinguished in the human testis. The first group includes teratomas—yolk sac tumors, which become manifest usually within the first 4 years of life and almost always before puberty. The second group comprises seminomas and nonseminomatous germ cell tumors, which manifest after puberty. The third group comprises spermatocytic seminomas, which usually affect older men.5 These groups differ in their presentation, treatment, and prognosis. Seminoma is the most common testicular tumor (50% of the germ cell tumors and 40% to 45% of testicular neoplasms) and the only one that is commonly treated with radiation.1

Spermatocytic seminoma was first described by Masson et al6 in 1946. It is a rare tumor, with a frequency varying from 1.3% to 2.3% for all patients with seminoma.7,8 According to an Australian study, the age-standardized incidence rate of spermatocytic seminoma is 0.4 cases per million and comprises 0.61% of all testicular germ cell tumors and 1.1% of the seminoma group.9 There is no race predilection among the 3 germ cell tumors, all being more common in whites.2

HISTOGENESIS

The origin of seminomas and spermatocytic seminomas of the adult testis remains debatable. It is thought that spermatocytic seminomas originate from cells capable of maturing at least to the stage of spermatogonia-pachytene spermatocyte. This theory is supported by the presence of proteins encoded by genes SCP1 (synaptinemal complex protein 1), XPA (Xeroderma pigmentosum type A), and SSX (synovial sarcoma on X chromosome) in spermatocytic seminomas. The genes SCP1 and XPA are expressed normally in the primary and pachytene spermatocyte stage, and protein encoded by the SSX gene is found normally in spermatogonia and primary spermatocytes, as well as in germ cells from the 17th week of intrauterine development. The absence of these proteins in conventional seminomas points to the embryonic germ cell as the cell of origin.10 The expression profiling of 156 microRNAs with quantitative polymerase chain reaction demonstrated that the spermatocytic seminoma cluster is in the same branch as the more differentiated tissue like normal testis and teratomas.11 MicroRNA in seminomas and dysgerminomas also cluster with embryonic carcinomas.12

CLINICAL FEATURES

Most spermatocytic seminomas occur in older white men, in their sixth decade of life.7 They usually manifest as a unilateral, painless swelling of variable duration without an associated history of cryptorchidism and have a negative tumor marker profile.7,8 However, a younger age group and bilateral presentation does not preclude the diagnosis. It is unique in occurring exclusively in testis, with no known counterpart in the ovary and elsewhere.7

MACROSCOPY

The tumor size ranges from 2 to 20 cm with an average of 7 cm.8 Grossly, spermatocytic seminomas are often homogeneous, solid, pale grey, soft, well-circumscribed, lobulated, cystic, hemorrhagic, edematous, and even necrotic with bulging mucoid cut surfaces. Most tumors are confined to the testis with few showing invasion or penetration of the tunica.7

HISTOPATHOLOGY

The tumor is well-circumscribed and encapsulated with rare extension into the paratesticular soft tissue. The tumor cells are noncohesive with little or no intervening stroma. Collagen bands, when present, may enclose tumor compartments, but lymphocytic infiltration and granulo-
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IMMUNOPROFILE

Many of the markers useful in other types of germ cell tumor are generally negative in spermatocytic seminoma, including OCT3/4, AE1/AE3, and CD30 (Table). c-Kit staining has been shown to be positive in around 40% of the spermatocytic seminomas, suggesting that at least some of the spermatocytic seminomas originate from primordial cells. VASA, a specific germ cell lineage marker, is expressed in normal spermatogonia, spermatocytes, and spermatids and is negative in Leydig cells, Sertoli cells, stromal cells, and spermatozoa. It is reactive in seminomas, dysgerminomas, and spermatocytic seminoma. The intensity of staining for spermatocytic seminoma is greater than that for seminomas and comparable to that found in more differentiated germ cells. In contrast, nonepithelial tumors, independent of the histology and the cell lines derived from them, have lost their VASA expression. Placental alkaline phosphatase has been observed in isolated or small groups of tumor cells. The cancer-specific antigen NY-ESO-1 is found in 50% of spermatocytic seminomas but not in other germ cell tumors. Other stains like α-fetoprotein, human chorionic gonadotropin, carcinoembryonic antigen, S100 protein, vimentin, epithelial membrane antigen, leukocyte common antigen, neuron-specific enolase, and human placental lactogen are not demonstrable in spermatocytic seminoma.

### Table: Immunostains for the Differentiation of Spermatocytic Seminoma From Classic Seminoma and Embryonal Carcinoma

<table>
<thead>
<tr>
<th>Stain</th>
<th>Classic Seminoma</th>
<th>Spermatocytic Seminoma</th>
<th>Embryonal Carcinoma</th>
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<td>OCT3/4&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>VASA&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Positivity less intense</td>
<td>Than spermatocytic seminoma</td>
<td>Diffusely positive</td>
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</table>

Abbreviations: CD, Cluster of differentiation; PLAP, placental alkaline phosphatase.

<sup>a</sup> 40% stain positively.
ANAPLASTIC AND SARCOMATOUS CHANGE

Anaplastic change is heralded by presence of prominent nuclei in the 3 cell types seen in spermatocytic seminoma. Cells with vesicular nucleus resembling embryonal carcinoma, bizarre giant cells, areas of necrosis, and frequent mitosis, including abnormal forms and blood vessel invasion, are also seen. These features are not absolute and can be rarely seen in conventional spermatocytic seminoma. On immunohistochemistry, p53 expression has been shown to be increased in some of the cases.18

Sarcomatous change in spermatocytic seminoma is characterized by the presence of 2 components. One component is typical spermatocytic seminoma. The second component usually comprises undifferentiated sarcomatous elements and, occasionally, more differentiated sarcoma such as rhabdomyosarcoma. Such change confers a worse prognosis and is often lethal.19–21 Some authors view the sarcomatous elements and, occasionally, more differentiated sarcoma as a part of the same entity and, therefore, only sarcomatous elements have been seen to metastasize in these cases.19 Only rarely has the conventional spermatocytic seminoma been shown to metastasize.22–24

ULTRASTRUCTURE

The most important ultrastructural features are prominent nucleolus with dispersed nucleolone and specialized cell junctions of the zonula adherens type, true intercellular bridges, identical to those normally found between spermatocytes and between spermatids. Comparison of these findings with ultrastructure of classic seminomas suggests that both originate from the same cell type but also indicates that spermatocytic seminoma is a tumor distinct from the former by virtue of its greater differentiation.25

DIFFERENTIAL DIAGNOSIS

Spermatocytic seminoma is most commonly misinterpreted as typical seminoma, embryonal carcinoma, or lymphoma. The distinction of spermatocytic seminoma from other forms of testicular germ cell tumor is important because spermatocytic seminomas, unless complicated by sarcomatous transformation, lack the capacity to metastasize and therefore are adequately treated by orchectomy alone without any form of adjuvant therapy.7 Spermatocytic seminoma lacks the features of classic seminoma including a fibrous stroma, lymphocytic and/or granulomatous stromal reaction, cells with abundant glycogen, positivity for placental alkaline phosphatase, and intratubular germ cell neoplasia component. Unlike many usual seminomas, the cytoplasm in spermatocytic seminoma is typically dense and amphophilic rather than clear. Lymphoma has a predominant interstitial growth pattern with a relatively monotonous cell population that lacks the lacy chromatin distribution. Relative monomorphic examples of spermatocytic seminoma may particularly be misdiagnosed because they have a sheetlike arrangement of large tumor cells with round nuclei, prominent nucleoli, and frequent mitotic figures but they are negative for leukocyte common antigen.17

Embryonal carcinoma lacks the 3 different types of cells described in spermatocytic seminoma. Also, the nuclei are much more crowded in embryonal carcinoma. Furthermore, additional sampling of monomorphic spermatocytic seminomas usually reveals more typical areas.

GENETICS

The gain of chromosome 9 appears to be a consistent finding in all spermatocytic seminomas, which is not found in classic seminomas.26 Other genetic abnormalities include gain of X chromosome. Classic seminomas, in contrast, reveal a consistent structural chromosomal abnormality of isochromosome 12p.27 Stage-specific markers of germ-cell maturation, including SCP1, SSX, and XPA, have been demonstrated in spermatocytic seminoma.28

TREATMENT AND PROGNOSIS

Spermatocytic seminomas rarely metastasize and hence orchidectomy alone is indicated for treatment.27

SUMMARY AND CONCLUSION

Spermatocytic seminoma is a rare testicular tumor that poses a diagnostic challenge. It should be considered, especially while evaluating germ cell tumor in older men. It is distinct in its histologic appearance with 3 different cell types, lack of cytoplasmic glycogen, and sparse or absent lymphocytic infiltrate. Since it rarely metastasizes or undergoes sarcomatous differentiation, correct histologic diagnosis can have great impact on treatment and prognosis.

REFERENCES


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