

TUBULAR SEMINOMA: CASE REPORT AND LITERATURE REVIEW

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Testicular neoplasms are classified into germ-cell and non-germ-cell neoplasms, with a predominance of the former, and a tendency to occur in young men.¹ Seminomas account for 40%-50% of all testicular germ-cell tumors,² and they have characteristic histological features, i.e., sheets of cells interrupted by fibrous septa containing lymphoplasmacytic infiltrate with occasional granuloma. When these classical features are not seen, diagnostic difficulties may arise. Tubular structures, a rarely encountered feature in seminoma, may lead to its confusion with other neoplasms, namely yolk sac tumors, embryonal carcinoma or Sertoli cell tumors. Tubular variant of testicular seminoma is a very rare entity with only eight cases reported in the English literature. We report here another case, emphasizing the diagnostic techniques utilized to differentiate it from other similar tumors.

Case Report

A 25-year-old Saudi male presented with left testicular swelling of a few months' duration which was confirmed by physical and ultrasound examination. The right testis was clinically normal apart from a small spermatocele. His serum β HCG level and alpha-fetoprotein (α FP) were not raised and his chest radiograph was free. Left inguinal exploration and frozen-section diagnosis of seminoma was followed by left radical orchidectomy with high ligation of the cord. Postoperative abdominal CT scan showed an enlarged para-aortic lymph node, putting the patient in stage IIa, for which he received radiotherapy and remained free from the disease over an 18-month follow-up period.

Patient and Methods

The patient was operated on in another hospital and a diagnosis of mixed germ-cell tumor (anaplastic seminoma and endodermal sinus tumor) was made for which he was referred to our hospital for further management. A review

of the histological material and histopathology report was done. The orchidectomy specimen was formalin fixed and paraffin embedded, and 4-5 μ m sections were obtained. Hematoxylin and eosin (H&E) and periodic acid-Schiff (PAS) staining were done. Immunohistochemical staining for vimentin, α FP, cytokeratin and placental alkaline phosphatase (PLAP) was performed on sections obtained from the available paraffin block.

Gross Pathology

The left orchidectomy specimen revealed a 5.5x5 cm testis with intact capsule harboring a homogenous fleshy, yellowish gray tumor replacing most of the testicular tissue. An attached 11 cm long unremarkable spermatic cord was identified. The tumor showed no extension to the surrounding structures.

Microscopic Findings

Most of the testis was replaced by malignant infiltrate with a few remaining seminiferous tubules that manifested intratubular germ-cell neoplasia. The tumor cells were arranged in sheets separated by connective tissue septa containing lymphocytic infiltrate in addition to areas of necrosis. This classic histologic architectural arrangement was seen in less than a third of the neoplasm. Most of the neoplastic cells were arranged in tubules of various sizes and shapes, with focal papillary formation. The cytological features of both classic and tubular areas were similar. The cells were round and large, with abundant clear cytoplasm, centrally located nucleus and inconspicuous nucleolus. PAS stain confirmed the presence of abundant cytoplasmic glycogen. No capsular or spermatic cord invasion was evident (Figure 1).

Immunohistochemical Findings

Immunohistochemical studies revealed diffuse strong reactivity for PLAP (Figure 2) and focal strong staining for vimentin in both classic and tubular areas. No staining was seen with α FP or cytokeratin.

Discussion

Germ-cell tumors account for 90% of all testicular neoplasms. The classification of germ cell tumors into seminomas and non-seminomas has great therapeutic implication. Treatment strategies, whether surveillance

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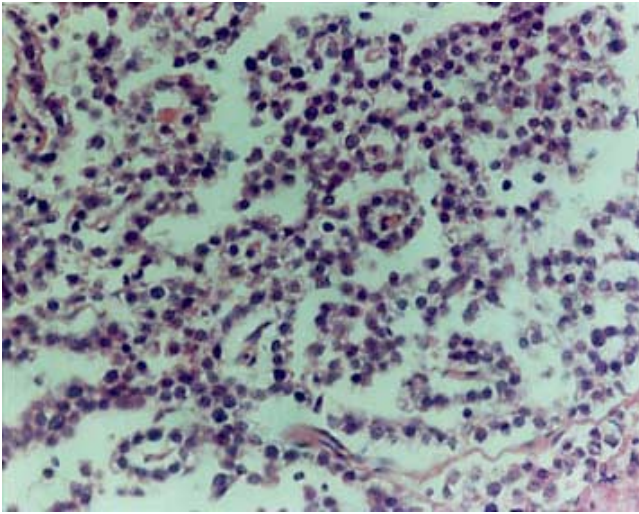


FIGURE 1. Tubular seminoma, where tumor cells are arranged in tubules and papillae (H&E, 25x).

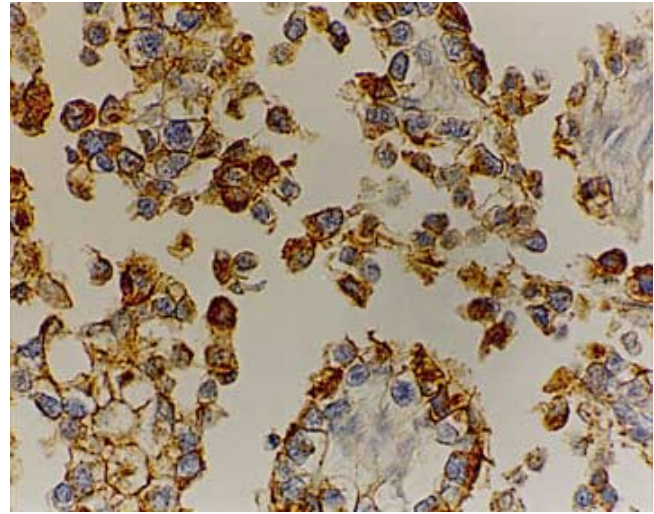


FIGURE 2. Immunohistochemical staining for placental alkaline phosphatase (40x).

TABLE 1. Summary of important immunohistochemical findings in tubular seminoma and its differential diagnosis.

Antibody	Tubular seminoma	Yolk sac tumor	Embryonal carcinoma	Sertoli cell tumor
PLAP	+	+/-	+	-
αFP	-	+	-	-
Cytokeratin	-	+	+	+
Vimentin	+	-	-	+
EMA	-/+	+	-	-/+

PLAP=placental alkaline phosphatase; αFP=alpha-fetoprotein, EMA=epithelial membrane antigen.

radiotherapy or chemotherapy, depend on both the histologic type and stage of the disease. Seminomas are well known for their dramatic response to radiotherapy, while non-seminomatous germ-cell tumors (NSGCT) are less sensitive and treated differently. Stage I disease occurs when only the testis is involved; stage II occurs when infradiaphragmatic lymph nodes are affected, and according to the size of the mass it is divided into IIa and IIb in seminomas, while in NSGCT, it is subdivided into four categories according to serum tumor markers and size of the involved lymph node. In stage III, supradiaphragmatic lymph nodes or distant metastases occur in both groups, including metastases of 10 cm or more in NSGCT. The treatment for stage II seminoma has been radiation therapy, with a survival rate of 95% for stage IIa, and 64% for stage IIb, as shown by Zagars and Babaian.³ The treatment for stage II non-seminomatous germ-cell tumors include retroperitoneal lymphadenectomy followed by adjuvant chemotherapy.⁴

The histological differential diagnoses of tubular seminoma include pagetoid spread of seminoma into the rete testis, yolk sac tumor, embryonal carcinoma, and Sertoli cell tumor. The recognition of a tubular seminoma pattern and its distinction from other testicular neoplasms

with similar pattern is fundamental to treatment decision. Secondary involvement of rete testes via pagetoid spread of seminoma is known to occur. The hilar location and presence of residual rete testicular tissue are helpful differentiating clues.

Yolk sac tumors are polymorphous neoplasms characterized by organoid arrangement of epithelial and mesenchymal elements with microcystic, glandular or papillary formation. Perivascular Schiller-Duval body is another distinct histologic feature. In addition, there are hyaline intracytoplasmic and extracytoplasmic round inclusions which are PAS-diacetate positive and reactive for αFP. PLAP staining results are variable, while cytokeratin is diffusely positive.

Embryonal carcinomas are, on the other hand, composed of sheets of undifferentiated pleomorphic cells, with occasional differentiation towards embryonic structures in the form of papillary and glandular formation.⁵ These cells are reactive for 43-9F and CD30. PLAP and cytokeratin immunohistochemical staining is positive in most of the cases, while they are characteristically epithelial membrane antigen (EMA) negative.

The last important but less frequently encountered differential diagnosis is Sertoli cell tumor that may present clinically with estrogenic symptoms such as gynecomastia and impotence. A typical histology is that of tubules lined by elongated cells with abundant clear or vacuolated cytoplasm, oval nuclei and moderate-sized nucleoli. Immunohistochemically, they show dual positivity for both vimentin and cytokeratin.

Seminomas are characterized by the presence of fibrous septa rich in lymphocytes, plasma cells or occasional granuloma separating tumor cells into sheets. Only rarely are tubular structures encountered. The tumor cells are large, uniform with abundant clear cytoplasm, large centrally located nucleus and inconspicuous nucleolus.

Cytoplasmic glycogen is best demonstrated by PAS staining. Immunohistochemically, the cells are reactive for PLAP and vimentin while cytokeratin staining is generally negative (Table 1).

Young et al.⁵ and Talerman⁶ each reported a case of tubular seminoma. Four additional cases⁷ have been reported with similar immunohistochemical results to our case. In that study, flow cytometric analysis revealed DNA aneuploid histogram in both seminoma components, namely classical and tubular patterns. This finding indicates that tubular pattern is only a different histologic appearance and not a genetically different neoplasm.

Unfortunately, we were not able to carry out either flow cytometric or cytogenetic studies due to technical difficulties and inavailability of fresh tissue. An additional case of tubular seminoma has recently been reported,⁸ which might reflect an increasing awareness of this rarely encountered entity. A question that still needs to be answered is whether tubular pattern could represent a fixation or processing artifact? The answer is most probably not, due to the rarity and focality of this pattern in a commonly encountered testicular tumor, however, more studies are needed to clarify this issue.

In conclusion, it is important for pathologists to be aware of the tubular pattern in classic seminoma and its resemblance to other germ-cell tumors, namely embryonal cell carcinoma, yolk sac tumor and Sertoli cell tumor. Immunohistochemical studies and DNA flow cytometry may help in settling the diagnosis and alleviating confusion.

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