

Unclassified sex cord/gonadal stromal testis tumor with a “pure” spindle cell component: a case report

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Key words

Sex cord/gonadal stromal tumors • Spindle cells • Immunohistochemistry

Summary

Unclassified sex cord/gonadal stromal tumors (SCSTs) composed predominantly of spindle cells are rare. Very few cases have been documented to date. Here, we report a case of “pure” spindle cell tumor of the left testis in a 83-year old man whose morphological

and immunohistochemical findings were consistent with a diagnosis of unclassified SCST and review the literature. Owing to the spindle cell pattern, the differential diagnosis with other benign and malignant spindle cell lesions is discussed.

Introduction

The occurrence of benign and malignant spindle cell tumors of the testis is rare. Apart from the well-known possibility that soft tissue and immune accessory-type spindle cell neoplasms can uncommonly arise from the male gonad, Leydig/Sertoli or granulosa cell tumors may only rarely contain spindle-shaped differentiation of the neoplastic elements^{1,2}. Conversely, a spindle cell predominant component has been reported in few cases of tumors belonging to the wide group of “unclassified sex cord-stromal tumours” according to WHO 2016 classification³. These rare neoplasms are usually predominantly composed of spindle cells with intermixed occasional epithelioid elements and/or Leydig cells^{4,5}. To date, only three (3 out of 6) of such cases were entirely formed by spindle cells^{4,6}. Herein, we report the clinical and pathologic features of a new case of “pure” spindle cell tumor arising in the testis, consistent with the designation of “unclassified sex cord-stromal tumor”; we discuss problems in the differential diagnosis, and review the pertinent literature too.

Case report

In February 2015, a 83-year-old man was admitted to the

Division of Urology of Hospital “San Giacomo”, Novi Ligure (AL), because of a slow-growing, painless, firm nodule in his left testis of several months’ lasting. Apart from diabetes mellitus and hypertension, he also had a past history of prostatic nodular hyperplasia, diagnosed by microscopic examination of the **specimen** obtained from transurethral resection. Urinalysis, liver enzymes, serum alpha-fetoprotein, and serum beta-human chorionic gonadotropin were all within normal limits. Scrotal ultrasound revealed a well-circumscribed, heterogeneous, prevalently solid with some cystic lacunes, nodular mass in the left testis, measuring 7 x 7 x 5,5 cm. A magnetic resonance imaging confirmed the presence of a mass with near-complete replacement of the left testis (Fig. 1). The patient underwent radical orchiectomy.

On naked eye examination, a well-circumscribed, rubbery, solid and cystic, firm, gray-yellowish in colour, testicular mass measuring 7 cm in its maximum diameter was identified in the specimen. Microscopic examination of hematoxylin-eosin stained sections showed a highly cellular lesion arranged in long fascicles of spindle-shaped cells with varying degrees of hyalinized collagen bundles in the background, focal storiform and nodular growth patterns and intermixed oedematous and cystic areas (Fig. 2A). Reticulin fibers were focally lacking around individual cells partially surrounding nests and aggregates of tumor cells of varying sizes (Fig. 3B).

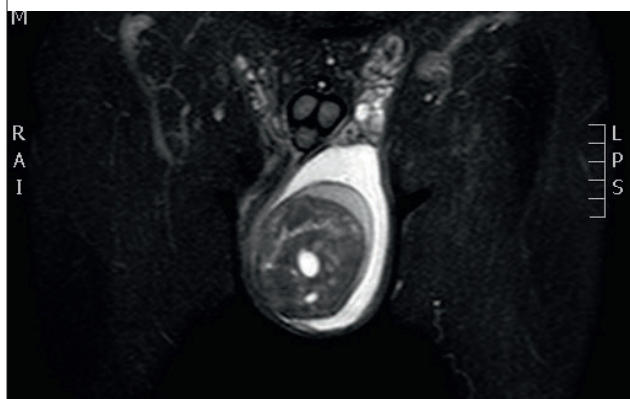
Authors’ note

This work was presented in abstract form (poster presentation) at the 7th Three-year Congress of Anatomic Pathology, Genova, Italy, November 23-26, 2016.

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Fig. 1. Preoperative MR image demonstrating a heterogeneous prevalently solid lesion with near-complete replacement of the left testis.



The neoplastic cells had indistinct pale to eosinophilic cytoplasm, and exhibited round to elongate, vesicular in appearance, nuclei with frequent tapered ends, inconspicuous to small nucleoli and occasional grooves (Fig. 3A). At times, small, tight clusters of tumor cells with more dark nuclei and scant cytoplasm stood out in some examined sections. Mitotic figures were occasionally observed, ranging from 0 to 1 per 10 high-power fields. At the periphery of the neoplasm seminiferous tubules were not trapped by the tumor cells and the surrounding testicular parenchyma appeared to be normal (Fig. 2B). There was no evidence of necrosis, hemorrhage and vascular invasion. At immunohistochemical examination, tumor cells stained brightly and diffusely for vimentin and S-100 protein; staining for smooth-muscle actin and **inhibin** was intense but more irregular, confirming the diagnosis of unclassified SCST with a “pure” spindle cell component (Figs. 4 A-D). Furthermore, the tumor had a low MIB-1 index (< 5%). Stains for epithelial markers (EMA, Cam 5.2 and AE1/AE3 cytokeratins),

desmin, CD34, CD99, **Melan-A** and PLAP were uniformly negative.

Follow-up after **45 months** was negative for recurrence or metastasis.

Discussion

Sex cord/ gonadal stromal tumors (SCSTs) are a heterogeneous group of neoplasms that account for approximately 5% of all primary testis tumors including various histologic subtypes as Leydig cell tumors, that are the most common, together with Sertoli cell tumors, adult and juvenile granulosa cell neoplasms and mixed tumors^{5,7}. There remains, however, a small group of neoplasms, predominantly spindle cell in their morphology, that are more difficult to classify and as a result, have been described under a variety of names, mostly under the uncommitted term “unclassified sex cord/stromal tumor”⁴⁻⁶. From the published data to date, including those of our patient, among the seven cases of SCST with a predominant spindle cell pattern, only four were completely formed by spindly elements (Tab. I)⁴⁻⁶. It is noteworthy that the histological and immunohistochemical features of spindle cell tumors similar to the present case, closely resemble those previously reported for “testicular myoepithelioma” and “testicular fibroma of gonadal stromal origin with or without minor sex elements”⁸⁻¹⁰. Taking the former into consideration, the term “myoepithelioma” was suggested for ultrastructural findings of a dual, epithelial and myoid (peritubular myoid cell) differentiation¹⁰. Following the original description in 1991 by Weidner¹⁰, Du et al.¹¹ and Kao et al.¹² further delineated a rare testicular neoplasm, distinctly different from other SCSTs, under the term “myoid gonadal stromal tumor”, with less than 10 examples reported to date^{3,10-12}. Discussion of the categorization of these tu-

Fig. 2. (A) The tumor displays a storiform and nodular pattern, a high degree of cellularity and intermixed large hyalinized collagen bundles; (B) The neoplasm shows a pushing border, sparing the seminiferous tubules.

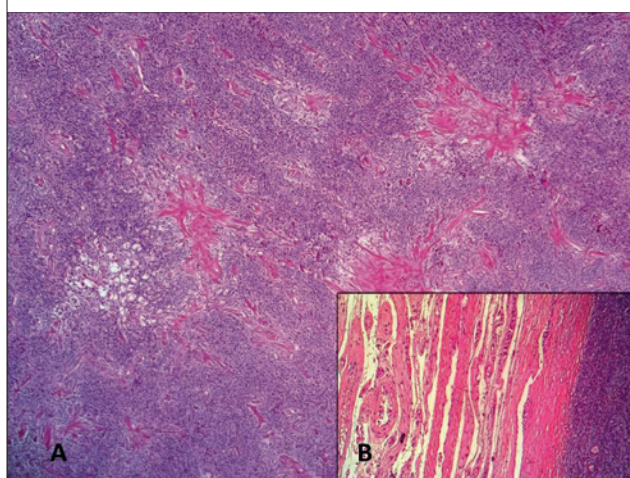


Fig. 3. (A) High-power view of the mass displaying cellular areas constituted by cells with spindle-shaped or oval-like nuclei, scant cytoplasm and occasional nuclear grooves; (B) Reticulin stain shows a nested pattern of the tumor cells (arrow) lacking reticulin fibers.

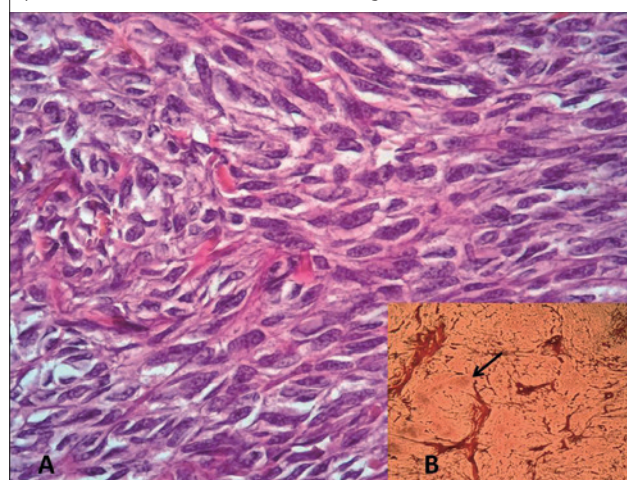
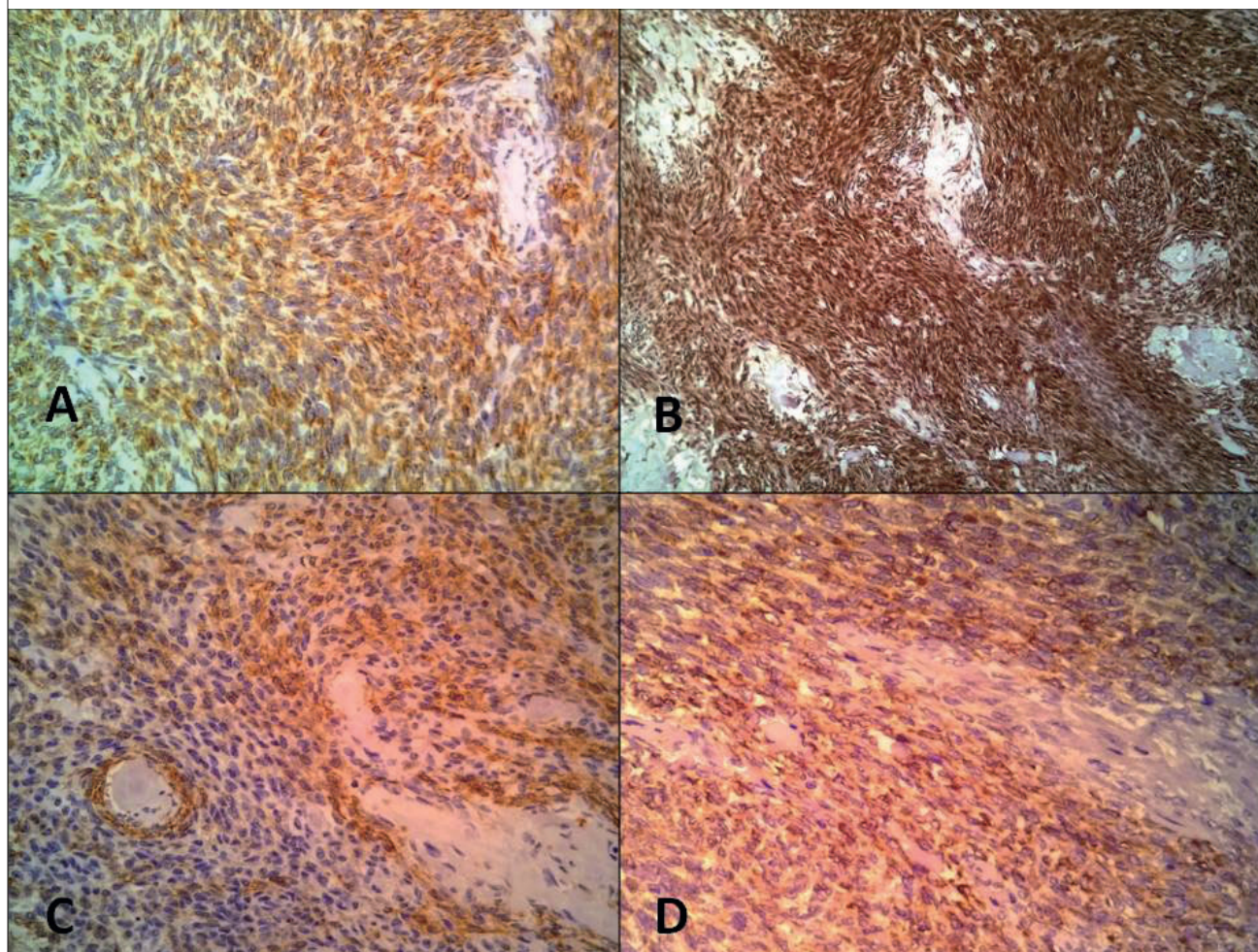


Fig. 4. (A) The spindle to ovoid cells are strongly positive for vimentin; (B) The neoplastic cells are diffusely positive for S-100 protein; (C) Tumor cells staining positive for anti α -smooth-muscle actin; (D) Tumor cells staining positive for inhibin.



mors is beyond the scope of this case report; however, it is also important to mention that the 2016 WHO classification of testicular non-germ cell tumors stated that myoid gonadal stromal tumors and unclassified spindle cell-predominant **SCSTs** were separate entities³. Reticulin stains might be helpful in distinguishing them as it envelops groups of sex cord cells (which may be morphologically inconspicuous) in the latter^{3,12}. In our case, microscopically, the testicular lesion seemed to fit the morphologic criteria for unclassified SCST with a “pure” spindle cell component, including reticular **framework**, immunopositivity for S-100 protein, smooth-muscle actin, and **inhibin**. Co-expression of S-100 protein (7/7) and smooth-muscle actin (7/7) is typical of unclassified SCSTs with predominance of spindle cells^{4,6}. Although **inhibin** expression was not often previously reported in this type of neoplasm, moderate to diffuse staining for this marker was recently noted in 3/3 studied cases, including the present one^{5,6}. In addition, these tumors were consistently negative for cytokeratins (AE1/AE3) (0/7), including the present case. It is deserving to be noted that nuclear grooves in tumor cells were often observed (5/7)^{4,6}.

As some morphological features of unclassified SCSTs with a spindle cell component predominance, mainly nuclear grooves, and their immunophenotype were almost identical to the phenotype of granulosa cell tumors, Renshaw et al.⁴ regarded the former as a poorly differentiated variant of the latter^{4,6}. Focal expression of Melan-A in two tumors was consistent with incomplete Leydig cell differentiation and, the co-existence, in one of them, of some morphological and immunohistochemical features indicative of granulosa cell differentiation was also found^{5,6}. The histogenesis of these tumors is still unclear and a larger number of studies is needed before a conclusion about this topic can be drawn.

Unclassified SCSTs with a predominant or pure spindle cell component need to be distinguished from a wide variety of benign and malignant monomorphic spindle cell tumors, analogous to their soft-tissue counterparts, rarely arising from the testis. Immunohistochemically, a moderate reactivity for **inhibin** was crucial in recognizing our case as unclassified SCST with a “pure” spindle cell component and, accordingly, in excluding benign tumors (leiomyomas, angioleiomyomas, benign periph-

Tab. I. Clinical and pathologic features of unclassified SCSTs with a predominant spindle cell component.

Case No.	Authors	Age (years)	Size (cm)	Fas-cicles	Nuclear grooves	Epithelioid cells	Treat-ment	Follow-up	S-100	SMA	Inhibin	Cyto-keratin	Melan-A	Vimen-tin
1	Renshaw et. al (4)	22	3	No	Yes	Yes	RO	ANED at 3 months	+	+	NK	-	NK	NK
2	Renshaw et. al (4)	50	0,9	No	Yes	Yes	PO	ANED at 12 months	+	+	NK	-	NK	NK
3	Renshaw et. al (4)	55	1	No	Yes	Yes	RO	ANED at 1 month	+	+	NK	-	NK	NK
4	Renshaw et. al (4)	45	2,1	Yes	No	No	RO	ANED at 60 months	+	+	NK	-	NK	NK
5	Tarjan et al (5)	35	1	Yes	No	No	PO	ANED at 4 months	+	+	+	-	+	(focal)
6	Magro et al (6)	23	2,2	Yes	Yes	No	RO	ANED at 13 months	+	+	+	-	+	(focal)
7	Present case	83	7	Yes	Yes	No	RO	ANED at 45 months	+	+	+	-	-	+

Abbreviations: ANED, alive with no evidence of disease; RO, radical orchiectomy; PO, partial orchiectomy.

eral nerve sheath tumors) and sarcomas with a bland-looking spindle cell pattern (low-grade fibrosarcomas, low-grade myofibroblastic sarcomas, inflammatory myofibroblastic tumors, follicular and interdigitating dendritic cell neoplasms)²⁻⁹. The remaining malignant high-grade spindle cell tumors, such as malignant fibrous histiocytoma and rhabdomyosarcoma, can be easily distinguished on the basis of overt cytological atypia, high mitotic index, atypical mitoses, necrosis and vascular invasion¹.

All the reported cases of testicular unclassified SCST with predominant or pure spindle cell component pursued an innocent course, even though one of them exhibited worrying histologic features (3 mitoses per 10 HPF)⁴. Follow-up information was available in all patients with unclassified SCST with predominance of spindle cell component for a mean period of **19,7 months** (range = 1 month to 60 months, median = 12 months)⁴⁻⁶. Pathologic findings suggestive of a high probability of malignant behaviour include large tumor size, infiltrative margins, evidence of lymphatic or vascular invasion, tumor necrosis and high mitotic rate¹⁷. Nevertheless, it is difficult to predict with certainty the clinical behaviour of unclassified SCST with predominant or pure spindle cell component based on histology, also because metastases may occur many years later⁷. Thus, as for other SCSTs, careful and long-term follow-up is mandatory for all cases.

Summing up, we report a case of unclassified SCST arising in left testis with a “pure” spindle cell neoplastic component. The clinical history, morphological findings, and immunohistochemical profile support the diagnosis, but the experience with this extremely rare tumor is, however, very limited and thus the proper prognostic features as well as optimal management and treatment have not yet been stated. Additional studies on more large series, collecting long-term follow-up results, are

needed to determine the behaviour of these tumors, as this category of SCSTs might have a more favorable prognosis.

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