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Letter to Editor

Sclerosing Sertoli cell tumor of the testis: a case report with review of the literature

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Sertoli cell tumor of the testis is a rare sex-cord stromal tumor composed of cells expressing varying degree of features of fetal, prepubertal or adult Sertoli cells [1]. This type of tumor accounts for less than 1% of all testicular tumors, and is classified into three variants by the World Health Organization Classification, namely Sertoli cell tumor not otherwise specified (NOS), large cell calcifying Sertoli cell tumor, and sclerosing Sertoli cell tumor (SSCT) [1]. SSCT is an extremely rare variant of Sertoli cell tumor, first described by Zukerberg *et al*. in 1991 [2-8], and only 16 cases with histopathological features have been reported in the English literature [2-8]. Herein, we report an additional case of this extremely rare tumor with detailed immunohistochemical analyses and review of the literature.

A 29-year-old Japanese male presented with an asymptomatic nodular lesion in his left testis. Physical examination revealed a relatively well-circumscribed elastic hard nodule in his left testis. Magnetic resonance imaging demonstrated a well-circumscribed nodule in the inferior and dorsal side of his left testis (**Figure 1**). Laboratory tests revealed that tumor markers were within normal ranges (alpha-fetoprotein was 1.3 ng/mL (range <10) and human chorionic gonadotrophin was <0.4 ng/mL (range <0.4)). Extirpation of the left testis tumor was performed.

Histopathological study of the resected specimen revealed a relatively well-circumscribed and unencapsulated nodule in the testis (**Figure 2A**). The nodule was composed of proliferation of nests or trabeculae of neoplastic cells with relatively rich slightly eosinophilic cytoplasm and round nuclei containing a small nucleolus (**Figure 2A**, **2B**). These neoplastic cell nests or trabeculae were separated by sclerotic stroma (**Figure 2A**, **2B**). No mitotic figures were noted. At the periphery of the nodule, the neoplastic nests interdigitated between residual seminiferous tubules (**Figure 2A**). Neither germ cell nor teratomatous component was present.

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [9-11]. **Table 1** summarizes the immunohistochemical results of the present case. Synaptophysin and CD56 were strongly positive in the tumor cells (**Figure 3**), however, inhibin-alpha and chromogranin A were negative. In addition, CD10 was also strongly expressed (**Figure 3**). Ki-67 labeling index was 0.3%.

Accordingly, an ultimate diagnosis of SSCT of the testis was made.

The post-operative course was uneventful, and no tumor recurrence or metastasis has been observed during 4 months of medical follow-up.

In this report, we described the 17th documented case of SSCT of the testis with histopathological and immunohistochemical analyses. SSCT is a distinct histopathological variant of Sertoli cell tumor, characterized histopathologi-

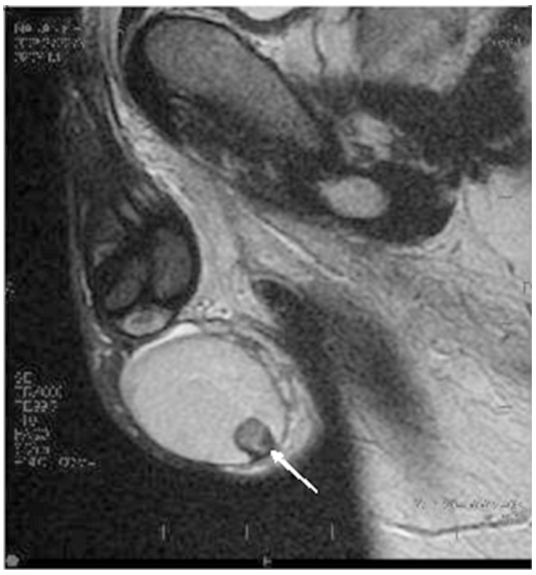

Figure 1. Magnetic resonance imaging showing a relatively well-circumscribed nodule in the testis, measuring 13 x 11 mm in diameter (arrow).

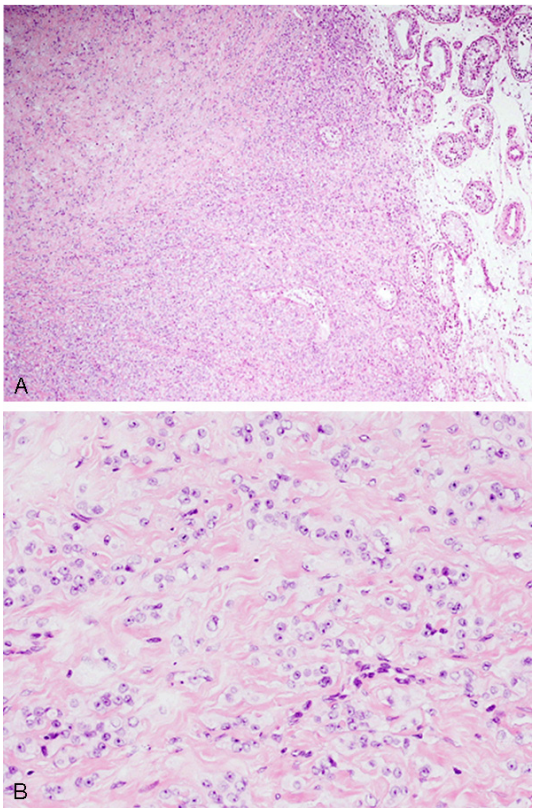

Figure 2. Histopathological features of the testicular tumor. A: Low-power view showing a relatively well-circumscribed tumor. At the periphery of the tumor, residual semiferous tubules are present within the tumor. HE, x 40. B: The tumor is composed of cord or trabeculae growth of neoplastic cells with relatively rich slightly eosinophilic cytoplasm and round nuclei containing a small nucleolus, that are separated by sclerotic stroma. HE, x 200.

Table 1. Immunohistochemical results

Antibody	Source	Results
Cytokeratin (AE1/AE3)	DAKO	-
Cytokeratin (CAM5.2)	Becton Dickinson	Focally +
Cytokeratin 7	Novocastra	-
Cytokeratin 20	Novocastra	-
Epithelial membrane antigen	Novocastra	-
Vimentin	Novocastra	+
S-100 protein	Nichirei	+
Chromogranin A	DAKO	-
Synaptophysin	Novocastra	+
CD56	Novocastra	+
Inhibin-alpha	Thermo Scientific	-
C-kit	DAKO	-
CD99	DAKO	-
CD10	DAKO	+
Ki-67 (%)	Novocastra	0.3

cally by the presence of a relatively uniform pattern of tubules, cords and aggregates of Sertoli cells separated by extensive sclerotic stroma [2]. **Table 2** summarizes the clinicopathological features of the previously reported cases as well as the present one. This tumor mainly affects in the 3rd decade of life (**Table 2**), however, a case of an 80-year-old has been documented (range 18-80 years) [2]. Most of the patients presented with a painless testicular nodule, however, sometimes pain was accompanied. Unlike the other previously described subtypes of Sertoli cell tumor NOS and large cell calcifying Sertoli cell tumor, no hormone production syndrome has been recorded [2, 3, 7, 8]. Most of the lesions were small in size (less than 2 cm), however, a large lesion (7 cm) has been documented [6]. The prognosis of this tumor is excellent because no tumor recurrence or metastasis has been reported.

The typical immunohistochemical characteristics of SSCT are as follows: vimentin, synaptophysin, and CD56 are positive, whereas chromogranin A is negative [2, 7]. The expression of cytokeratin is usually negative, although focal positive immunoreactivity for CAM5.2 has been reported [7], which was also seen in the present case. Inhibin-alpha is consistently negative [7, 8]. In addition, germ cell tumor markers,

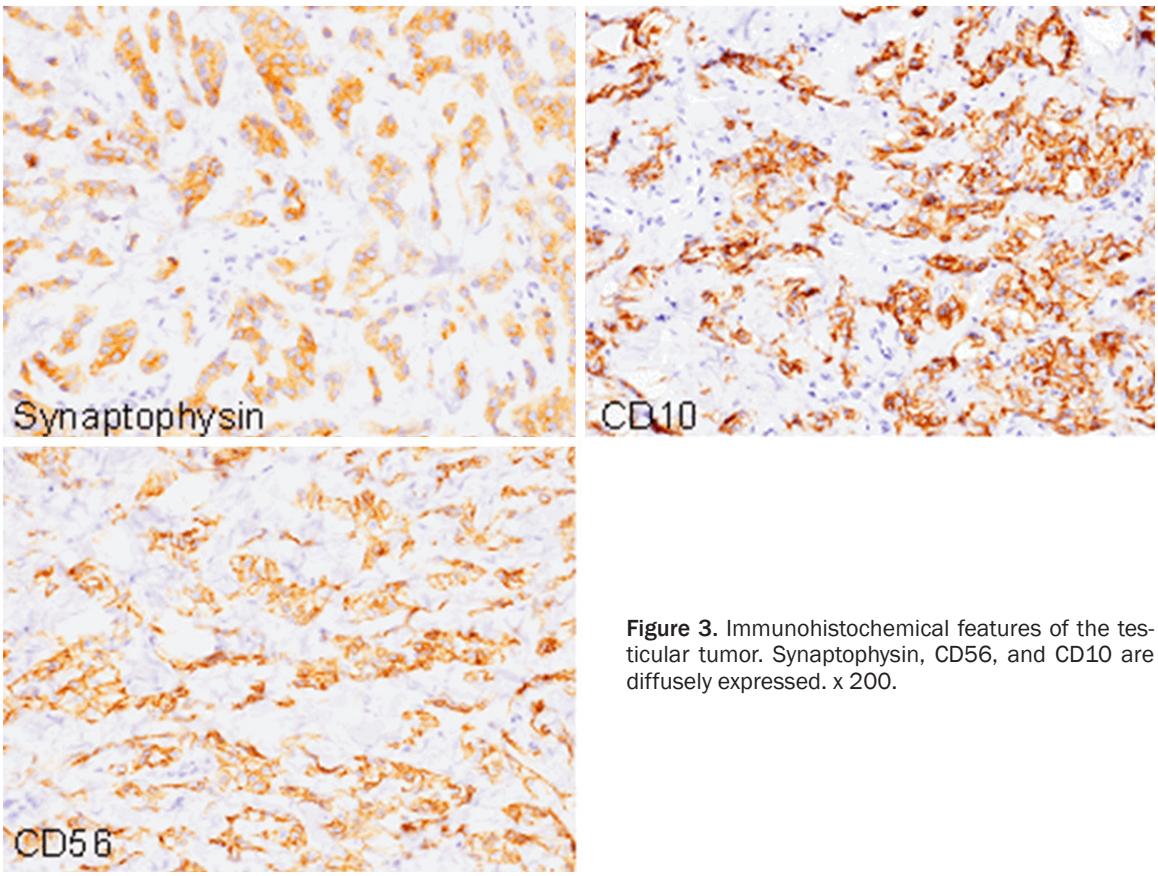

Figure 3. Immunohistochemical features of the testicular tumor. Synaptophysin, CD56, and CD10 are diffusely expressed. x 200.

Table 2. Clinicopathological features of sclerosing Sertoli cell tumor of the testis

Case No.	Age (years)	Size (cm)	Immunohistochemical characteristics	Outcome	Reference
1-10*	18-80 (median 30)	0.4-1.5 (8 cases) 4 (2 cases)	Cytokeratin (-), vimentin (+), chromogranin (-)	No recurrence for a mean of 5.8 years	[2]
11	35	0.4	Cytokeratin (-)	No recurrence for 9 months	[3]
12	18	1.5	Vimentin (+), neuron specific enolase (weakly positive)	Not available	[4]
13	34	2.7	Cytokeratin (-), alpha-fetoprotein (-)	No recurrence for 10 months	[5]
14	33	7	Cytokeratin (-)	No recurrence for 6 years	[6]
15	33	0.5	Synaptophysin (+), CD56 (+), inhibin (-)	No recurrence for 3 months	[7]
16	38	Not available	Vimentin (+), inhibin (-)	No recurrence for 6 months	[8]
Present case	29	2	Synaptophysin (+), CD56 (+), CD10 (+), inhibin (-)	No recurrence for 4 months	

*Only summary of the clinicopathological information was available.

such as c-kit and D2-40, are not expressed [7]. The immunohistochemical results of the present case corresponded to the above-mentioned characteristics.

Oliva *et al*. investigated CD10 expression in stromal and sex cord/stromal tumor of the ovary [12]. In their series, four of 9 cases of Sertoli cell tumor showed positive immunoreac-

tivity for CD10. This is the first report to clearly show CD10 expression in SSCT of the testis, and further analysis is needed to clarify the expression of CD10 in Sertoli cell tumors of the testis, including SSCT.

Differential diagnostic considerations for SSCT include carcinoid tumor of the testis, Leydig cell tumor, and metastatic prostatic carcinoma [2, 7]. SSCT lacks insular and acinar growth pattern, which is observed in carcinoid tumor of the testis. Further, carcinoid tumor of the testis is often associated with other teratomatous components [2]. Moreover, carcinoid tumor of the testis is usually strongly positive for chromogranin A [2]. SSCT lacks crystals of Reinke, which are observed in approximately 30-40% of Leydig cell tumor. In addition, Leydig cell tumor typically shows positive immunoreactivity for inhibin-alpha and CD99 [13]. Moreover, immunostaining for prostate specific antigen is useful for differentiation from metastatic prostatic cancer. These features aid in distinguishing the differential diagnostic considerations of SSCT.

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