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# Mixed sex cord stromal tumor of the testis composed of granulosa, Leydig, and Sertoli cell tumor components: a case report

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## Abstract

**Introduction** Mixed sex cord stromal tumor is defined as a tumor consisting of various combinations of sex cord stromal elements, and the tumor is extremely rare.

**Case presentation** A 76-year-old Japanese male visited our hospital complaining of left scrotal swelling. Magnetic resonance imaging of the mass showed a multilocular cystic pattern with different degrees of intensities in each cyst. The solid component was observed in part showing hypointensity on the T2-weighted image. Although there was no apparent evidence of malignancy in cytology of punctured fluid of the cystic tumor, malignant potential was not ruled out completely. Therefore, transinguinal radical orchiectomy was performed, and the tumor was diagnosed as mixed sex cord stromal tumor consisting of adult-type granulosa cell tumor, Leydig cell tumor and Sertoli cell tumor components. The patient recovered without any postoperative event. In addition, neither apparent recurrence nor metastasis was observed at 7 years after surgery.

**Conclusion** The tumor showed a multilocular cystic appearance with solid component, which was similar in appearance to previous reports of the same pathological features. Pathological findings of each component were compatible with those of mixed sex cord stromal tumor, and immunohistochemical analysis was useful for accurate diagnosis. The tumor was successfully resected, and no apparent recurrence was observed at 7 years after surgery.

**Keywords** Mixed sex cord stromal tumor, Testis, Adult-type granulosa cell tumor, Leydig cell tumor, Sertoli cell tumor

## Introduction

Mixed sex cord stromal tumor is defined as a tumor consisting of various combinations of sex cord stromal elements with differentiation toward Leydig, Sertoli, or granulosa cells admixed with stromal spindle cells per the World Health Organization (WHO) classification (urinary and male genital tumors) [1]. Sex cord stromal tumors are reported to be rare, comprising approximately 2–5% of testicular neoplasms [2]. Although tumors with mixed histologic types are common in the ovary, occurrence in the male gonad is extremely rare [3]. Here, we report a case of mixed sex cord stromal tumor consisting of adult-type granulosa cell tumor, Leydig cell tumor, and Sertoli cell tumor components.

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## Case presentation

A 76-year-old Japanese male visited to our department with a chief complaint of left scrotal swelling. The patient had been aware of the scrotal swelling for 4 years, and there was no evidence of enlargement. The left scrotal mass was soft and elastic without pain, and skin color was normal. Ultrasound examination revealed a 10 cm multilocular cystic mass with a solid component in part (Fig. 1A); however, apparent left testis could not be detected. T2-weighted images (T2WI) of the mass via magnetic resonance imaging (MRI) also showed a multilocular cystic pattern with different degrees of hyperintensities in each cyst (Fig. 1B, C). The solid component was observed as a hypointense area (Fig. 1B, C, arrow). Diffusion-weighted imaging (DWI) showed no significant decreasing apparent diffusion coefficient (ADC) value in the solid area (Fig. 1D, arrow). The results of laboratory examination including alpha-fetoprotein (AFP), human chorionic gonadotropin beta-subunit (βHCG), and lactate dehydrogenase were within normal limits (Table 1). We performed puncture of the cystic area, and the aspirated brown fluid was analyzed cytologically. Although there was no apparent evidence of malignancy in cytology, malignant potential was not ruled out completely. Since the patient consented to complete resection, transinguinal radical orchiectomy was performed. There were no specific findings including adhesion to surrounding tissue or intraoperative complications, and the patient recovered without any postoperative event. In

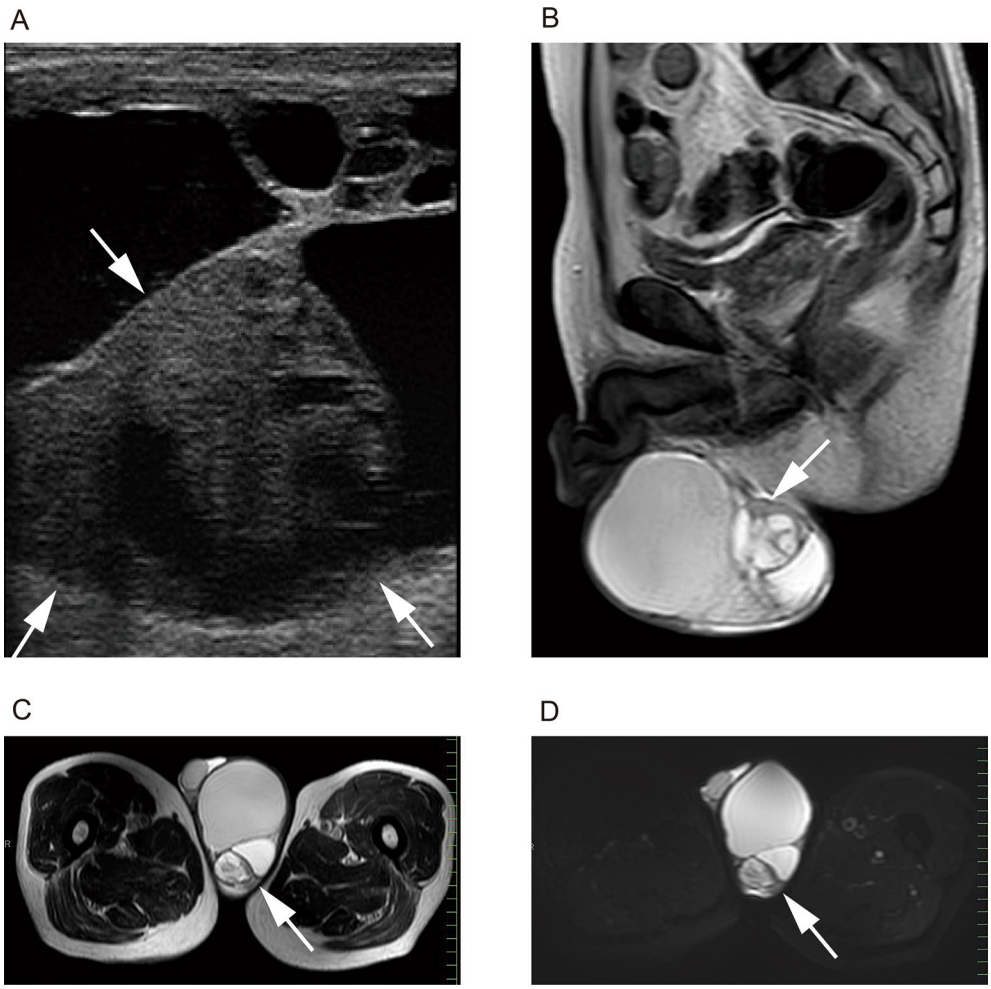


**Fig. 1** Appearance of ultrasound and magnetic resonance imaging. **A** Ultrasonography showed a multilocular cystic mass with solid components (arrows). The solid area revealed internal heterogeneity. The tumor showed clear demarcation. **B**, **C**. T2-weighted images (T2WI) via magnetic resonance imaging examination revealed a multilocular cystic mass. Each cyst showed different degrees of intensities, suggesting different concentrations of protein or blood. The solid component was observed as a low-intensity area (B [sagittal imaging], C [axial imaging], arrow). **D** Diffusion-weighted imaging shows no significant decreasing apparent diffusion coefficient value in the solid area of the tumor (arrow)

**Table 1** Summary of laboratory data on admission

| | |
|---|---|
| Complete blood count | |
| White blood cells | $7.8\times10^3$/μL ($3.3–8.6\times10^3$/μL) |
| Neutrophils | 65.5% (37–72%) |
| Hemoglobin | 15.3 g/dL (13.7–16.8 g/dL) |
| Hematocrit | 47.2% (40.7–50.1%) |
| Platelet counts | $191\times10^3$/μL ($158–348\times10^3$/μL) |
| Biochemistry | |
| Total bilirubin | 0.7 mg/dL (0.4–1.5 mg/dL) |
| Asparate aminotransferase | 20 U/L (13–30 U/L) |
| Alanine aminotransferase | 21 U/L (10–42 U/L) |
| Lactate dehydrogenase | 173 U/L (124–222 U/L) |
| γ-glutamyl transpeptidase | 26 U/L (13–64 U/L) |
| Alkaline phosphatase | 124 U/L (106–322 U/L) |
| Blood urea nitrogen | 13.1 mg/dL (8–20 mg/dL) |
| Creatinine | 0.66 mg/dL (0.65–1.07 mg/dL) |
| Total protein | 6.72 g/dL (6.6–8.1 g/dL) |
| Albumin | 4.13 g/dL (4.1–5.1 g/dL) |
| Na | 137 mmol/L (138–145 mmol/L) |
| K | 4.6 mmol/L (3.6–4.8 mmol/L) |
| Cl | 104 mmol/L (101–108 mmol/L) |
| Glucose | 99 mg/dL (73–109 mg/dL) |
| HbA1c | 5.6% (4.9–6%) |
| C-reactive protein | 0.05 mg/dL (0–0.14 mg/dL) |
| HBsAg | (–) |
| HCV-Ab | (–) |
| Tumor marker | |
| AFP | 4.2 ng/mL (0.89–8.78 ng/mL) |
| βHCG | 1.2 ml U/mL (–5 ml U/L) |
| sIL-2R | 251 U/mL (122–496 U/mL) |

HbA1c, glycated hemoglobin; HCV-Ab, hepatitis C virus antibody

addition, neither apparent recurrence nor metastasis was observed at 7 years after surgery.

The surgically resected specimen revealed a 10 cm multilocular cystic tumor with solid component. The solid area was tan-brown in color without hemorrhage or necrosis (Fig. 2A). Histologically, tumor cells proliferate in sheets, containing scant cytoplasm and oval- or round-shaped hyperchromatic nuclei with nuclear grooving (Fig. 2B, C). Cysts lined with flat cells were observed, and other cystic architectures lined with cuboidal or columnar epithelium were found. Small nests of tumor cells with clear cytoplasm were seen (Fig. 2C). In addition, tumor cells with eosinophilic cytoplasm similar with those of Leydig cells were seen in part (Fig. 2C). No apparent invasion into albuginea was found. Populations of the tumor cells were classified into three groups as follows: tumor cells with scanty cytoplasm and grooved nuclei (adult-type granulosa cell tumor-like appearance), tumor cells with eosinophilic cytoplasm (Leydig cell tumor-like appearance), and tumor cells with clear to slightly eosinophilic cytoplasm (Sertoli cell tumor-like appearance). Results of immunohistochemical staining are summarized in Table 2. All subtypes of tumor cells were positive for alpha-inhibin, calretinin (Fig. 2D, E), CD99, melan A, and vimentin, whereas all were negative for EmA. Tumor cells with scanty cytoplasm and grooved nuclei were positive for CD56 (Fig. 2F), which is consistent with adult-type granulosa cell tumor component (Fig. 2F). In addition, tumor cells with eosinophilic cytoplasm were positive for synaptophysin, suggesting a Leydig cell tumor component. Distinct nuclear staining of beta-catenin was observed in tumor cells with clear to slightly eosinophilic cytoplasm, which suggested a Sertoli cell tumor component (Fig. 2G, H). Based on these pathological findings, the patient was diagnosed with mixed sex cord stromal tumor consisting of adult-type granulose cell tumor, Leydig cell tumor, and Sertoli cell tumor components.

## Discussion

Sex cord stromal tumors are the second most frequent testicular neoplasm. They are composed of a histologically single or combinate tumor arising from granulosa cells, fibroblasts, theca cells, Sertoli cells, and Leydig cells [1, 2]. In our case, the tumor contained three sex cord elements, and was diagnosed as mixed sex cord stromal tumor. The tumor is reported to occur in patients of any age; however, they typically arise in middle-aged or elderly persons [1–3]. The etiology and pathogenesis

(See figure on next page.)

**Fig. 2** Gross and histological appearance of the tumor. **A** Gross findings (before formalin fixation) of cutting surface are shown. Similar to imaging findings, the tumor shows a multicystic appearance. Each cyst is separated by a slightly thick septum. Cut surface of the solid area is a heterogeneous tan-brown in color without hemorrhage or necrosis (white arrows). **B** Microscopically, tumor cells with hyperchromatic nuclei and scanty cytoplasm proliferate in sheets (hematoxylin and eosin staining[H&E], 100×). **C** Three types of the tumor cells are shown. Tumor cells with eosinophilic cytoplasm (Leydig cell tumor-like appearance, black arrow) and tumor cells with clear to slightly eosinophilic cytoplasm (Sertori cell tumor-like appearance, white arrow) proliferate in nests or tubular formation. And tumor cells with scanty cytoplasm (adult-type granulosa cell tumor-like appearance, lower right) are observed (H&E, 400×). The tumor cells with nuclear grooving are scattered (inset, arrow heads). **D**–**F**. The majority of the tumor cells are positive for calretinin (D, 100×), alpha-inhibin (E, 100×). Tumor cells with scanty cytoplasm and grooved nuclei are positive for CD56 (F, 100×), which is consistent with adult-type granulosa cell tumor. **G**, **H**. Tumor cells with clear cytoplasm are seen in part (G, arrows; H&E, 100×). The tumor cells show distinct nucleal staining of beta-catenin, suggesting a Sertoli cell tumor (H, arrows, 100×), whereas tumor cells with eosinophilic cytoplasm suggesting a Leydig cell tumor (G, arrow heads) show negative nucleal staining for beta-catenin

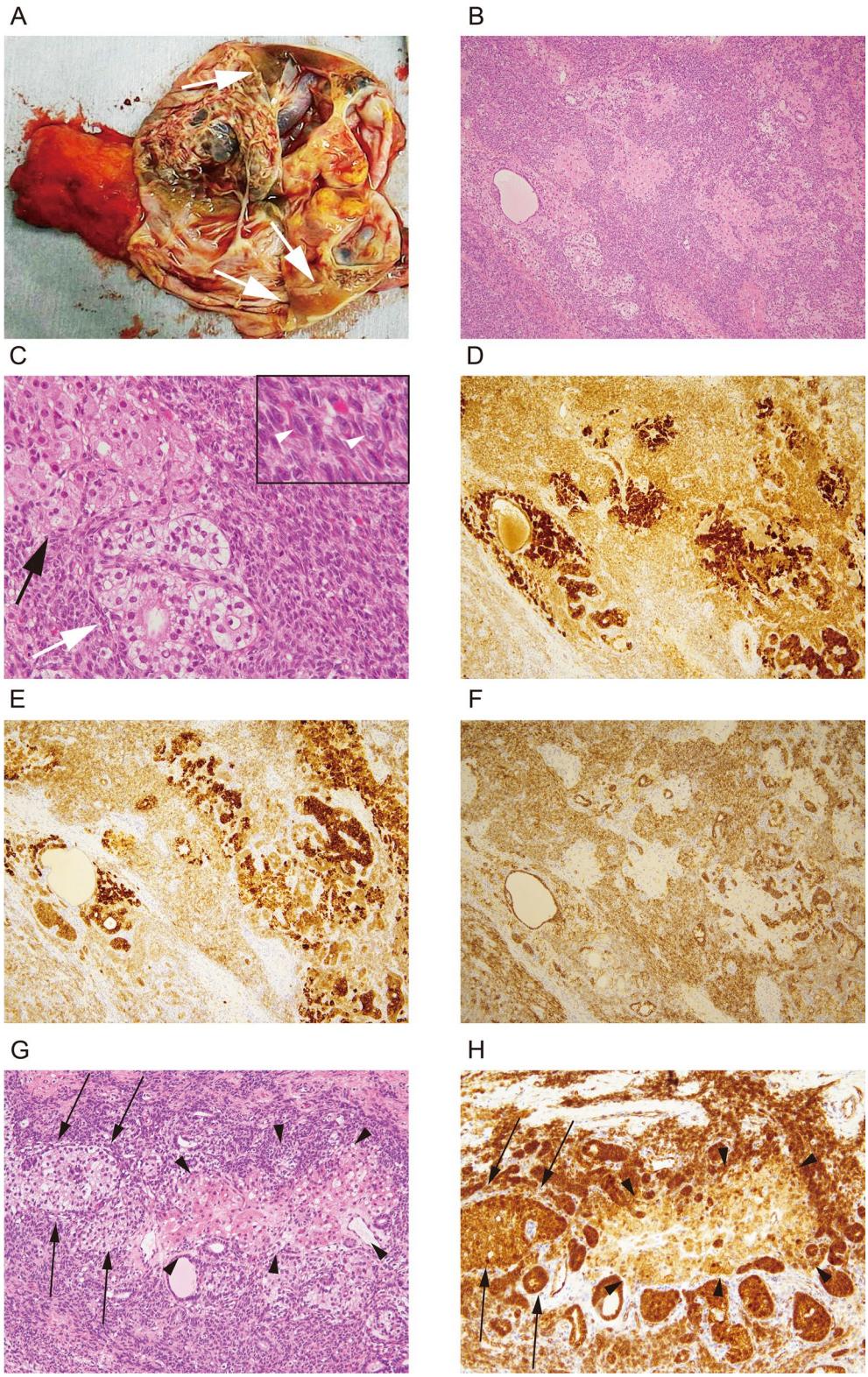


**Fig. 2** (See legend on previous page.)

**Table 2** Summary of immunohistochemical appearance compared with previous reports

| | Cells with grooved nuclei | Adult granulosa cell tumor | Eosinophilic cells | Leydig cell tumor | Clear to eosinophilic cells | Sertoli cell tumor |
|---|---|---|---|---|---|---|
| Alpha-inhibin [1–2] | + | + | + | + | + | + |
| Calretinin [1–2] | + | + | + | + | + | + |
| CD99 [1–2, 10] | + | + | + | + | + | + |
| Melan A [1–2] | + | N/A | + | + | + | ± |
| EMA [1–2] | – | – | – | – | – | – |
| Vimentin [1–2] | + | + | + | + | ± | ± |
| Synaptophysin [1–2, 10] | - | N/A | + | + | - | ± |
| CD56 [1–2] | + | + | ± | N/A | ± | N/A |
| Beta-catenin [1–2] (nuclei) | – | – | – | – | + | + |

are unknown. The most common presenting symptom is testicular enlargement, and approximately 10% of patents show gynecomastia [1–3].

It has been reported that 10–30% of the tumors have malignant potential with retroperitoneal lymph node metastasis and metastasis to abdominal organs and lung [1, 4]. Diagnosis of malignancy is based on the pathological appearance at the primary site; however, accurate evaluation of malignant potential is difficult in cases of Leydig cell tumor and Sertoli cell tumor [1, 5]. In such cases, the malignancy is confirmed by the presence of metastasis during postoperative follow-up (citation). As malignant features, tumor size (diameter of 5 cm or more), invasive growth pattern, vascular and/or lymphatic infiltration, nuclear atypia, high mitotic activity, increased cellularity, and the presence of necrosis have been reported [6, 7]; however, there are no definitive diagnostic criteria. In our case, there were no relevant pathological findings of malignancy except for tumor size (however, the tumor was mainly composed of multicystic architecture), and the patient has remained free of recurrence and metastasis for 7 years. The tumor cells with intermediate differentiation, the "incompletely differentiated subgroup in sex cord/gonadal stromal tumor" in the fourth edition of the WHO classification, were classified into "sex cord stromal tumor NOS" in the fifth edition [1].

Immunohistochemically, adult granulosa cell tumors are reported to be positive for calretinin, alpha-inhibin, SF1, CD99, vimentin, and CD56 [1, 2]. A morphological appearance, including scanty cytoplasm with grooved nuclei, is compatible with that of granulosa cell tumor, and immunohistochemical appearance is also consistent. The majority of Leydig cell tumors (more than 90%) are reported to be positive for calretinin, alpha-inhibin, SF1, melan A, and synaptophysin, whereas they are negative for nuclear beta-catenin [1, 2]. Sertoli cell tumors have been reported to show positive staining for nuclear beta-catenin and vimentin, and are less frequently positive (approximately 50%) for alpha-inhibin, calretinin, SF-1, and melan A [1, 2]. These immunohistochemical evaluations were also helpful for diagnosis of our case, and the results were compatible with those of morphological diagnosis (H&E staining).

Upon ultrasound examination, a Leydig cell tumor is reported as being a hypoechoic solid nodule [8]. And the tumor has been described as an isointensity mass on T1-weighted (T1WI) and hypointensity mass on T2WI compared with normal testis on MRI [8]. In contrast, Sertoli cell tumors have been reported to show a solid or multicystic, spoke-wheel-like appearance [8]. However, the findings of MRI are variable, and not sufficiently specific. There is a lack of information on imaging findings for male adult granulosa cell tumors. Our case showed multilocular cystic tumor composed of adult granulosa cell tumor, Leydig cell tumor, and Sertoli cell tumor components. Similar appearances on ultrasound and MRI imaging were reported in a case of Sertoli–Leydig–granulosa-cell tumor [9]. To the best of our knowledge, the current case is the second case report of this histological pattern containing the three components. Multilocular cystic appearance may be a specific finding of mixed sex cord stromal tumor including these elements; however, further study with a larger number of cases is needed. Since the presence of infection and chronic medical problem can worsen the clinical course at perioperative state, the management is important [11].

## Conclusion

We report a case of mixed sex cord stromal tumor with adult-type granulosa cell tumor, Leydig cell tumor, and Sertoli cell tumor components. The tumor showed a multilocular cystic appearance on ultrasound and MRI that was similar to a previous report of the same pathological

features. Pathological findings of each component were compatible with those of mixed sex cord stromal tumor, and immunohistochemical examination was useful for accurate diagnosis. The tumor was successfully resected, and no apparent recurrence was observed at 7 years after surgery.

**Abbreviations**

| | |
|---|---|
| T2WI | T2-weighted image |
| MRI | Magnetic resonance imaging |
| DWI | Diffusion-weighted imaging |
| ADC | Apparent diffusion coefficient |

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**Author contributions**
NW drafted the manuscript, performed the examination and observation and approved the final version of the manuscript. TM, MF, and TN performed examinations and surgery, cared for the patient, and approved the final version of the manuscript. MN and HT diagnosed and reviewed the pathological specimens, and approved the final version of the manuscript. SM and TK drafted the report and contributed the final version of the manuscript. All authors read and approved the final manuscript.

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**Availability of data and materials**
The supporting data and materials for this report are available on request from the corresponding author.

## Declarations

**Ethics approval and consent to participate**
This case report was approved by the Ethics Committee of Miyazaki University (approval number: C-0170). Consent to participant was obtained from the patient.

**Consent for publication**
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal.

**Competing interests**
The authors declare that they have no conflict of interest.

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**References**

1. WHO Classification of Tumours Editorial Board. WHO classification of tumours of urinary and male genital tumours. 5th ed. Geneva: WHO; 2022.
2. Lau HD, Kao CS, Williamson SR, *et al*. Immunohistochemical characterization of 120 testicular sex cord-stromal tumors with an emphasis on the diagnostic utility of SOX7, FOXL2, and SF-1. AM J Surg Pathol. 2021;45:1303–13.
3. Amin MB, Grignon DJ, Srigley JR, Eble JN. Urological Pathology, Wolters Kluwer, 2013
4. Morinaga S, Aoki S, Tsuzuki T, *et al*. Malignant testicular unclassified sex cord stromal tumor. J Med Case Rep. 2022;16:406.
5. Roth LM, Lyu B, Cheng L. Perspectives on testicular sex cord-stromal tumors and those composed of both germ cells and sex cord-stromal derivatives with a comparison to corresponding ovarian neoplasms. Hum Pathol. 2017;65:1–14.
6. Idress MT, Ulbright TM, Oliva E, *et al*. The World Health Organization 2016 classification of testicular non germ cell tumors: a review and update from the international society of urological pathology testis consultation panel. Histopathology. 2017;70:513–21.
7. Athanazio DA, Cruz AO, Farias GB. Mixed sex cord stromal tumor and incidental finding of perineural and intravascular extraparenchymal Leydig cells: a potential diagnostic pitfall. Int Urol Nephrol. 2020;52:693–5.
8. Cassidy FH, Ishioka KM, McMahon CT, *et al*. MR imaging of scrotal tumors and pseudotumors. Radio Graph. 2010;30:665–83.
9. Tahaineh S, Mughli RA, Fallatah M. Giant mixed Sertoli-Granulosa sex cord tumor of the testis; clinical, histopathological, and radiological features. Pan African Med J. 2017;27:51.
10. Lee W, Kim YM, Kim HJ. Adult-type granulosa cell tumor of the testis: a case report with immunohistochemical study. Urol Case Rep. 2021;38:101612.
11. Devaraj NK. Antibiotic resistance: a real menace. Oman Med J. 2017;32(6):531.

## Publisher's Note