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Adult granulosa cell tumour of the testis: an uncommon tumour

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SUMMARY

A male patient in his late 20s was admitted to the hospital after presenting with left abdominal, back and scrotal pain that had begun approximately 2 weeks earlier. He had a history of a stable left testicular mass for 3 years, and a physical exam revealed a non-tender, firm left testicular mass and a mild left varicocele. Testicular tumour markers were normal, but a scrotal ultrasound revealed a 2 cm hypoechoic left testicular lesion. Staging imaging showed no retroperitoneal adenopathy or pulmonary metastases.

The patient underwent left radical inguinal orchiectomy with no evidence of extratesticular or spermatic cord involvement. His surgical pathology revealed a left pT1a 2.3 cm adult granulosa cell tumour of the testis with no lymphovascular invasion. The tumour was positive for inhibin and negative for OCT3/4, supporting the diagnosis.

BACKGROUND

Testicular neoplasms have an annual age-adjusted incidence of 5.6 cases per 100 000 persons in the USA and, when diagnosed, are largely found to be germ cell tumours (GCTs).[1] GCTs comprise almost 95% of testicular tumours, while sex cord–stromal tumours account for approximately 5% of testicular neoplasms.[2] Of these sex cord–stromal tumours of the testis, Leydig cell tumours and Sertoli cell tumours are the most common subtypes, which account for 1%–2% and 0.1% of testicular tumours, respectively, and are sometimes of mixed type with both Leydig and Sertoli components.[3 4] The granulosa cell tumour represents a rare subtype of sex cord–stromal tumours that can be further divided into adult granulosa cell tumours of the testis (AGCTT) and juvenile type granulosa cell tumours of the testis.

AGCTT are rare, and since the first reported case of AGCTT by Laskowski in 1952, there have only been 73 well-documented cases recorded in the medical literature.[5] Among these cases, the majority of AGCTT are not malignant but are still treated using orchiectomies.[6] Improved differentiation between benign and malignant AGCTT, as well as an increase in testes-sparing surgery, can be accomplished by continually documenting and analysing AGCTT cases.

This case report will cover a non-metastatic AGCTT that was treated with a radical orchiectomy. Diagnosis of this tumour can be challenging and new instances of AGCTT must continually be recorded to expand the available data sets; physicians need to improve awareness and understanding of this type of cancer.

CASE PRESENTATION

A male patient, in his late 20s, presented to the hospital with back, abdominal and scrotal pain accompanied by pressure during urination that had developed 2 weeks earlier. The patient was found to have a history of ovarian cancer in his family. A subsequent physical exam revealed a non-tender, firm, left testicular mass.

INVESTIGATIONS

Following the physical exam, ultrasound imaging revealed a 1.3 by 1.8 cm hypoechoic, left testicular lesion (figure 1A). Doppler imaging revealed evidence of blood flow to the tumour (figure 1B). Additional chest and abdominal CT imaging revealed no evidence of the tumour beyond the left testicle.

Laboratory analysis

Laboratory work was normal and the GCT markers alpha fetoprotein (2.1 ng/mL, reference limits 0.9–9.0 ng/mL), beta-human chorionic gonadotropin (<1 mIU/mL, reference limits <5 mIU/mL) and lactate dehydrogenase (173 U/L, reference limits 116–250 U/L) were all within reference limits. A complete blood count and a basic metabolic panel were also normal.

Histopathological analysis

On histopathological evaluation, the tumour was well circumscribed and displayed a solid and diffuse growth pattern (figure 2A) consisting of monotonous cells with mostly scant cytoplasm, indistinct cell borders and round to oval nuclei with nuclear grooves (figure 2B). Occasional microfollicular (Call-Exner bodies) and palisading patterns were also present. Importantly, no features that have been associated with malignancy were identified, such as infiltrative borders, necrosis, lymphovascular invasion or extratesticular involvement.[7] Staining with OCT3/4 was negative (figure 2C), while diffuse staining with inhibin A was positive (figure 2D). As a result, the immunohistochemical profile supports a diagnosis of a sex cord–stromal tumour, while the morphology confirms the diagnosis of an AGCTT.

TREATMENT

The patient underwent left radical inguinal orchiectomy with no evidence of extratesticular or spermatic cord involvement. After surgical intervention, a 2.3×1.5×1.5 cm well circumscribed, firm fleshy non-encapsulated nodular structure was located 3 cm away from the inferior pole and 11.3 cm from the spermatic cord margin.

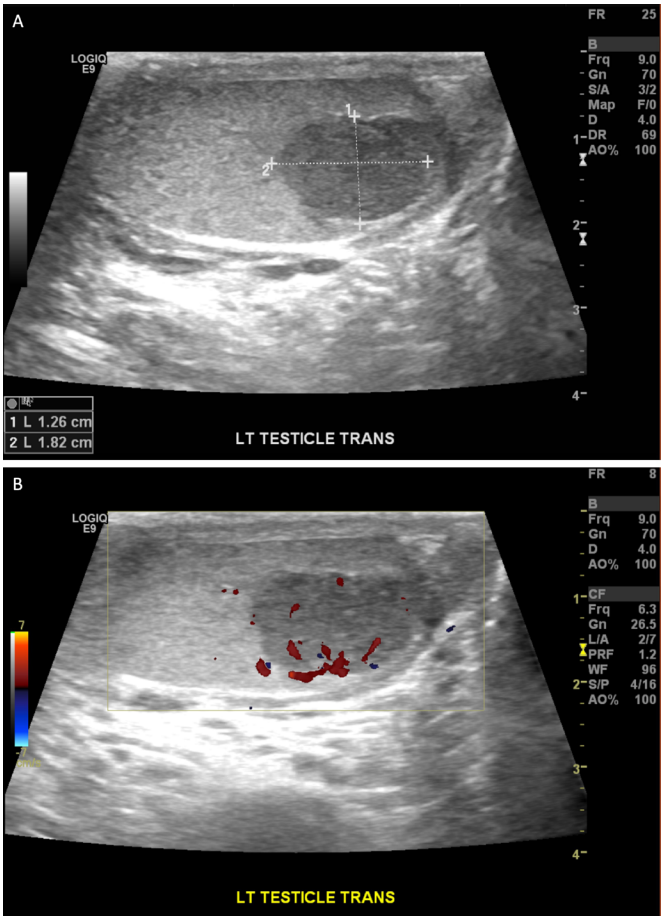

Figure 1 Representative ultrasound images of the testicular mass. (A) The mass is hypoechoic and measures about 1.3 by 1.8 cm in size. (B) Evidence of blood flow to the tumour on Doppler imaging.

OUTCOME AND FOLLOW-UP

The patient recovered from the surgery and has not required further treatment. No complications from the surgery or treatment were noted at follow-up appointments 3 years after the surgery, and the patient was able to return to work following the procedure.

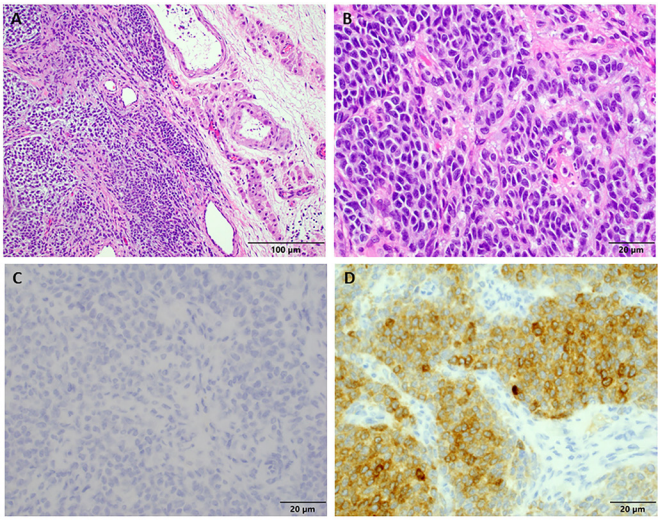

Figure 2 Images showing histopathological analysis of adult granulosa cell tumour. (A) The solid and diffuse growth pattern of the tumour is highlighted. (B) Monotonous cells with mostly scant cytoplasm, indistinct cell borders and round to oval nuclei with nuclear grooves. (C) Negative OCT3/4 staining. (D) Positive inhibin A staining.

DISCUSSION

AGCTT are rare neoplasms that are not commonly found in the medical literature. The first case of AGCTT was reported by Laskowski in 1952.[6] One of the first literature reviews of AGCTT cases occurred in 2014, when 32 unique AGCTT cases were recorded by Cornejo and Young.[8] After this literature review, more instances of AGCTT were published and in 2020, Grogg *et al* found 73 well-documented cases of AGCTT.[5] This growth in the reported number of AGCTT cases can be attributed to the lower misclassification rate of AGCTT due to increased medical knowledge, the addition of immunohistochemical markers and an increase in publication mediums through which new instances of the tumours can be documented.[6]

The patient discussed in this case report is in his late 20s and is younger than many of the patients found in the previous literature. Age is of considerable importance in the study of AGCTT, and a recent review by Grogg *et al* found the mean age at the time of diagnosis to be 42 years (±19 SD).[5] Among recorded cases, the youngest patient to be diagnosed with AGCTT presented to the hospital, in early adolescence, after a 5-year history of left scrotal mass enlargement.[9] However, the majority of AGCTT presented later in adulthood with the oldest recorded patient diagnosed at the age of 87.[8] Among the 91 AGCTT cases examined by Dieckmann *et al*, only 26 patients presented with AGCTT before the age of 30. Furthermore, of these 26 patients, only 14 patients have recorded documented follow-up visits.[6] Thus, this case advances knowledge regarding AGCTT cases in younger patients with documented follow-ups.

The differentiation of metastatic and nonmetastatic AGCTT cases has proved challenging due to the rarity of recorded literature about metastatic tumors. Grogg *et al* showed that the majority of recorded AGCTTs were non-metastatic (66/73, 90%), while the remaining cases were identified as metastatic (7/63, 10%).[5] Of these cases, the mean age of diagnosis for non-metastatic AGCTT patients was 42 years (±19 SD), and the mean age of diagnosis for metastatic AGCTT patients was 45 years (± 14 SD).[5] Of the metastatic AGCTT tumours in literature, the longest duration of symptoms prior to diagnosis was 8 years, and the shortest time frame was 7 months.[10 11] Additionally, AGCTT tumours have presented as incidental findings following metastatic spread to the liver, bones and retroperitoneal lymph nodes.[5] For non-metastatic tumours, the longest recorded time frame of symptoms before diagnosis was approximately 37 years with the shortest duration after just 2 weeks of pain.[12 13] As of now, age has not been found to be a predictive variable for differentiation between benign and metastatic AGCTT, and this case can be used to bolster existing cases regarding non-metastatic tumours.

Another possible differentiator between metastatic and non-metastatic tumours is the size of the tumour. Grogg *et al* found metastatic tumours are usually larger than non-metastatic tumours. The metastatic tumours had a median size of 70 mm (IQR 51–90 mm) compared with non-metastatic tumours, with median size of 24 mm (IQR 14–42 mm).[5] The tumour described in this case measured 23×15×15 mm, bolstering the existing literature suggesting that a smaller mass may indicate non-metastatic disease.[5]

Additionally, among the AGCTT cases identified by Grogg *et al*, only 41 of the 73 cases had summaries of the various clinical

presentations of the disease.[5] Of these recorded cases, testicular enlargement was the most common symptom (21/41, 51%) followed by a palpable testicular mass (15/41, 37%) and scrotal pain (6/41, 15%).[5] In this case, the patient presented with a testicular mass, but he also experienced pressure during urination, in addition to left abdominal, back and scrotal pain, which is relatively uncommon among recorded cases. Few recorded cases of AGCTT have presented with abdominal or back pain, and we hope this case draws attention to these uncommon symptoms.

After treatment with a radical orchiectomy—the intervention most used in cases analysed by Grogg *et al* (68/73, 93%)—histological analysis of the tumour revealed findings consistent with the previous literature.[5] Like other non-metastatic AGCTT tumours, this case contained a solid growth pattern with occasional microfollicular (Call-Exner bodies) and palisading patterns. Characteristic of this particular tumour, nuclear grooves imparting what is often referred to as 'coffee bean-like' tumour cells were apparent.[7] Inhibin A has been shown to be the best marker to establish a tumour as a sex cord–stromal tumour, which was positive in this case.[14]

Furthermore, ruling out a GCT with germ cell markers such as OCT3/4 or SALL4 can be helpful in the immunohistochemical workup.[14] Ultimately, with this staining pattern, the differential diagnosis includes other sex cord–stromal tumours. However, these can be ruled out based on epidemiological factors and histopathological features. For example, a juvenile granulosa cell tumour most commonly occurs in patients under 6 months of age and lacks nuclear grooves and a microfollicular pattern. In addition, a Leydig cell tumour classically contains tumour cells with abundant eosinophilic cytoplasm and enlarged nuclei with prominent nucleoli while also lacking nuclear grooves and a microfollicular pattern. Finally, Sertoli cell tumours are characterised by the presence of well-formed tubules, a pattern that is not seen in AGCTT; however, occasional nuclear grooves may be present. Ultimately, proper morphological and immunohistochemical evaluation should produce an accurate diagnosis in most cases.

The rarity of AGCTT cases increases the complexity of diagnosis in a clinical setting, and this case highlights the common and uncommon features of this presentation of AGCTT. Many cases that have been previously presented do not provide the in-depth clinical descriptions and symptoms that are needed to advance the knowledge of AGCTT. Most of the cases reported in the literature do not metastasise; however, there are limited data to accurately predict the clinical course based on clinical and pathological features. Therefore, in general, these patients should be monitored with serial imaging.

The standard treatment for AGCTT, in patients with a normal contralateral testis, is the radical orchiectomy. However, a partial orchiectomy can be considered for smaller tumours (<3 cm) in patients with synchronous bilateral tumours or tumours of solitary testis with sufficient testicular androgen production.[15] If testicular sparing surgery is performed, then intraoperative frozen section analysis must be used to differentiate between benign and malignant histology.[16] Following frozen section analysis, radiotherapy can be used on the residual testis to prevent residual germ cell neoplasia in situ (GCNIS) from transforming to AGCTT.[17] Continued publication of AGCTT cases, like the one detailed in this report, can help to refine the guidelines used for benign and malignant tumours and potentially increase the use of conservative surgical approaches.

Learning points

- Adult granulosa cell tumours of the testis is an uncommon stromal cell tumour of the testes in male adults but should be included in the differential diagnoses of testicular tumours in adults.
- Radical orchiectomy is the recommended treatment for any solid testicular tumour as imaging alone cannot accurately differentiate between subtypes.
- Partial orchiectomy may be considered in patients with a solitary testicle or an atrophic contralateral testicle.

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