CASE REPORT

Organ-sparing surgery for large cell calcifying Sertoli cell tumour in a patient with Carney complex

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SUMMARY

Carney complex is a rare genetic disease characterised by a complex of myxomas, spotty pigmentation and endocrine overactivity. At diagnosis, about one-third of male patients presents with testicular tumours, namely large cell calcifying Sertoli cell tumours, which are often multicentric and/or bilateral and have a low malignant potential. Although radical orchiectomy is the gold standard for the treatment of testicular neoplasms, a conservative approach with partial orchiectomy or tumourectomy may be the best treatment option for these patients, allowing the preservation of endocrine function, fertility and body image. We present a case of a 19-year-old man with a known history of Carney complex with early identification of a small testicular tumour treated with organ-sparing surgery.

under surveillance due to a 1 cm growth hormone (GH) pituitary adenoma and testicular microlithiasis.

INVESTIGATIONS

On physical examination, the testicles had normal volume, consistency and no palpable masses, and there were no signs of gynecomastia. After performing a follow-up scrotal ultrasound, an intraparenchymal calcified lesion with 5.80 mm in the upper pole of the right testis, suggestive of testicular cancer, was found (figure 1). Tumour markers (alpha-fetoprotein, beta-human chorionic gonadotropin and lactate dehydrogenase) and testosterone levels were within normal range. Thoracic and abdominopelvic CT had no signs of metastatic disease.

TREATMENT

After general anaesthesia, we proceeded to an inguinal approach of the right testicle, clamping of the spermatic cord and incision of the tunica vaginalis. An excisional biopsy of the tumour was performed after doing an intraoperative testicular ultrasound to find the intraparenchymal tumour. An intraoperative frozen section analysis revealed a well-defined lesion of undetermined nature and excluded a germ-cell tumour. Because a germ-cell tumour was excluded, the lesion was small and very likely to be benign in the context of a Carney complex, we decided to perform an organ-sparing surgery. Tunica albuginea and tunica vaginalis were closed and right orchidopexy performed. The patient had no postoperative complications and was discharged at postoperative day 1.

OUTCOME AND FOLLOW-UP

Final anatomopathological examination confirmed the diagnosis of a LCCSCT, with 5 mm and negative surgical margins (figure 2). Although there are no exact recommendations on surveillance, the possibility of recurrence, multifocality and bilateralism of these tumours leads to a close clinical and ultrasound monitoring. After a follow-up of 36 months, the patient is asymptomatic, has no palpable testicular masses and has no evidence of recurrence of a testicular tumour on scrotal ultrasound. Testosterone remains within the normal range levels. Concerning the 1 cm GH pituitary adenoma, he was submitted to endoscopic trans-sphenoidal surgery due to recent rise in GH levels.

BACKGROUND

Carney complex is a rare genetic disease characterised by multiple endocrine and non-endocrine neoplasia syndrome. Patients often have more than one endocrine gland affected as well as cardiac myxomas, skin lentiginosis and schwannomas.^{1–3}

About one-third of the male patients show testicular tumours at the time of presentation. Large cell calcifying Sertoli cell tumour (LCCSCT) is a very rare sex cord stromal neoplasm and is the particular testicular tumour found in Carney complex. Tumours usually present in adolescents and young adults and are often multicentric and bilateral, have a low malignant potential and are unlikely to proceed to metastasis formation.^{4,5}

This case report highlights the importance of surveillance, early identification and conservative treatment, whenever possible, of testicular tumours in patients with Carney complex. The low malignant-potential and possibility of bilateral tumours of LCCSCT may lead to unnecessary unilateral or even bilateral orchiectomy with severe consequences to endocrine function and infertility. We hereby present the management of a young man with Carney complex and testicular tumour.

CASE PRESENTATION

We present a case of a 19-year-old male patient, with familiar (mother) and personal history of Carney complex. He has skin pigmentation and had already been submitted to excision of atrial myxomas (at age 2 and 19), total adrenalectomy at age 7 due to Cushing's syndrome and excision of a dorsal cutaneous myxoma at age 17. He was also

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Figure 1 Scrotal ultrasound reveals an intraparenchymal calcified lesion with 5.80 mm in the upper pole of the right testis.

DISCUSSION

Carney complex, initially described by J Carney in 1985, as a complex of myxomas, spotty pigmentation and endocrine overactivity,⁶ is caused by inactivating mutations of the regulatory subunit type 1- α of the PRKAR1A gene.^{7,8} It is mainly inherited in an autosomal-dominant manner, but some cases can be sporadically and approximately 70% are familial.^{1,2}

It is a rare disease with unknown prevalence, and so far about 750 patients have been reported, with women and men being affected in 63% and 37%, respectively.^{9,10}

Clinical manifestations may be numerous and may vary between patients. Diagnostic criteria were reviewed in 2001 by Stratakis *et al.*² A patient is considered to have Carney complex if two major criteria are present (summarised below):

- ▶ Spotty skin pigmentation with a typical distribution; Histological confirmation of:
 - ▶ cutaneous and mucosal myxoma, cardiac myxoma or breast myxomatosis;
 - ▶ primary pigmented nodular adrenocortical disease;
 - ▶ acromegaly due to GH-producing adenoma;
 - ▶ LCCSCT;

Figure 2 Microscopic features of the 5.80 mm large cell calcifying Sertoli cell tumour.

- ▶ thyroid carcinoma;
- ▶ psammomatous melanotic schwannoma;
- ▶ blue nevus, epithelioid blue nevus (multiple);
- ▶ breast ductal adenoma (multiple);
- ▶ osteochondromyxoma.

Diagnosis can also be made if one of the major criteria is present and a first-degree relative is affected or an inactivating mutation of the PRKAR1A gene is present.² The clinical detection can be made as early as in the second year, but the median age at diagnosis is 20 years old.^{2,11} Our patient was diagnosed with Carney complex at a very early age (2 years old) and had multiple clinical manifestations, namely cardiac, adrenal, pituitary, cutaneous and testicular, leading to multiple hospital visits and surgical procedures.

Approximately 40% of affected male patients develop sex cord stromal tumours.¹⁰ These tumours account for 3%–4% of all testicular neoplasms, being the Leydig cell tumour the most common and Sertoli cell neoplasm extremely rare, accounting for 1% of all testicular tumours. Although there are numerous microscopic features of Sertoli cell tumours, Proppe *et al* described 10 cases of a distinctive Sertoli cell neoplasm (characterised by large cells with abundant eosinophilic cytoplasm and calcifications) with frequent unusual clinical associations, which they designated LCCSCT.⁵ These are the typical and almost exclusively testicular tumours encountered in patients with Carney complex.⁴ Unlike sporadic sex cord stromal tumours, LCCSCT are multifocal and bilateral in approximately 50%–60% of cases.^{4,5} They behave in a benign way although there are rare reports of malignant tumours,^{2,5} particularly when they are solitary, have more than 4 cm, necrosis, angiolymphatic invasion, extratesticular extension and occur in older patients (>20 years old).^{4,12}

An asymptomatic testicular mass is the most common presentation, but gynecomastia (due to increased P-450 aromatase expression) and precocious puberty, although rare, may be present.¹¹ LCCSCT can lead to replacement and obstruction of the seminiferous tubules,⁹ and patients with the null mutation of the PRKAR1A gene have teratospermia and reduced sperm count.¹³ In addition, the treatment of these tumours with orchiectomy contributes to the multifactorial origin of infertility in these patients. As our patient already had the diagnosis of Carney complex and was on surveillance, the solitary testicular tumour was diagnosed at an early stage by ultrasound image instead of presenting as asymptomatic testicular mass. LCCSCTs are usually detected by scrotal ultrasound as round, regular and hyperechoic lesions with acoustic shadow. But these specific elements may also be present in germ-cell tumours and benign lesions.⁹

Due to its generally malignant behaviour, the standard treatment for germ-cell testicular neoplasms is radical orchiectomy. However, in the last years, the management of these testicular tumours has evolved in favour to conservative surgery due to improvement of oncological outcomes and awareness of functional issues in survivors.¹⁴

An organ-sparing approach with intraoperative frozen section analysis may be an option for small bilateral malignant tumours, tumours in a solitary testis or suspected benign tumours, if the testosterone levels are within the normal range and the remaining testicular parenchyma is sufficient to maintain endocrine function.^{14,15} Thus, a conservative approach with partial orchiectomy or tumourectomy may be the best treatment option for patients with Carney complex because these patients may have multifocal and/or bilateral testicular tumours, often with low risk of aggressiveness and metastatic potential. This testis-sparing surgery

ensures the total excision of the tumour with low overall complication rates, while preserving the endocrine function, fertility as well as body image.¹⁶

Learning points

- ▶ The typical testicular tumour found in Carney complex is the large cell calcifying Sertoli cell tumour that is exceptionally rare, often multicentric and/or bilateral and has a low malignant potential.
- ▶ The standard treatment for testicular tumours is radical orchiectomy; however, an organ-sparing surgery is an option in selected cases like small bilateral malignant tumours, neoplasms in a solitary testis or suspected benign tumours.
- ▶ An organ-sparing approach is recommended, whenever possible, in patients with Carney complex. We can avoid unilateral or bilateral orchiectomy in young men whose endocrine function, fertility and body image are important to preserve.

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