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Microcystic stromal tumour of testis

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SUMMARY

Within the group of gonadal sex cord-stromal tumours, microcystic stromal tumour (MCST) is a rare entity. In the literature, most case series and reviews discussed MCST arising in the ovary, only one case-report concerned a testicular MCST. We present a Caucasian man in his late 30s, who presented with an MCST in his right testis. The tumour was encapsulated and composed of vaguely lobulated cellular nodules and cystic spaces with bland spindle cells and hyalinised fibrous stroma. By immunohistochemistry, the tumour cells expressed cluster designation 10, androgen receptor, steroidogenic factor-1 and nuclear beta-catenine, and there was focal nuclear expression of cyclin D1. Molecular diagnostics confirmed the presence of an exon 3 mutation (c.98C>T) in the *CTNNB1* gene. These features are similar to MSCT described in the ovary. Clinical follow-up (more than 1 year) was uneventful.

Although the clinical and radiological presentation was that of a possible malignant testicular lesion, this entity is benign.

BACKGROUND

We present this case to raise awareness on the possible outcome of a totally benign entity when a patient presents himself with a large testicular mass. The diagnosis microcystic stromal tumour (MCST) can be supported with molecular testing, to confirm a mutation in the *CTNNB1* gene. After definitive histopathological diagnosis, the patient can receive reassurance that his testicular tumour is benign and further treatment or follow-up are not required.

CASE PRESENTATION

A Caucasian man in his late 30s with no medical history presented at the urology department with a palpable mass in his right testicle. For years, the patient had noticed that his right testicle was somewhat larger and firmer than his left testicle. However, recently the size of the right testicle had increased, which prompted medical consultation.

Ultrasound examination showed an inhomogeneous mass with echogenic and echoic areas and cysts (figure 1). Tumour markers including alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-hCG) were normal.

A CT examination of thorax and abdomen did not show signs of metastatic disease.

An orchidectomy was performed. In the pathology department, the specimen was freshly received. On cut surface, the testicular tumour measured 4 cm and was sharply demarcated. There were nodular solid and macrocystic areas and white fibrous bands (figure 2).

The histology and immunohistochemical profile of the tumour is shown in figure 3. Histologically, the tumour was sharply demarcated and surrounded by a thick fibrous capsule. Solid and microcystic areas were composed of a monomorphic population of round to oval cells with monomorphic, round to oval nuclei with very fine chromatin and inconspicuous nucleoli. Mitotic activity was sparse and necrosis absent.

By immunohistochemistry, the tumour cells showed diffuse expression of cluster designation 10 (CD10, used here to distinguish sex-cord stromal neoplasms from smooth muscle neoplasms), beta-catenin (both cytoplasmic and nuclear, expression of beta-catenin reflects on germline mutations in the *APC* gene or in the *CTNNB1* gene), androgen receptor (AR, nuclear staining reveals the presence of androgenic hormones in cells) and steroidogenic factor-1 (SF-1, expressed in cells producing steroid hormones including a subset of sex cord-stromal tumours). There was focal positivity for cytokeratins (usually expressed in epithelial cells) and S100 (expressed in cells originating from the embryological neural crest).

Molecular diagnostics, using targeted next generation sequencing, confirmed a mutation in the *CTNNB1* exon 3 gene (c.98C>T).

INVESTIGATIONS

At clinical presentation, ultrasound examination of the testis was performed, followed by CT scan of the thorax and abdomen.

Blood markers concerning possible testicular germ cell tumours were measured (AFP and beta-hCG).

After surgery, at the department of pathology, routine macroscopic and microscopic examination of the tissue was performed, followed by immunohistochemical testing to create a marker profile of the tumour tissue.

Subsequently, tumour DNA was isolated and using next generation sequencing, a mutation in the *CTNNB1* exon 3 gene (c.98C>T) was confirmed.

DIFFERENTIAL DIAGNOSIS

When a patient presents with a testicular mass, a malignant testicular germ cell tumour is always on top of the differential diagnosis, including seminoma or non-seminoma or combined germ cell tumours.

TREATMENT

After surgical removal of the right testicle, no further treatment was needed.

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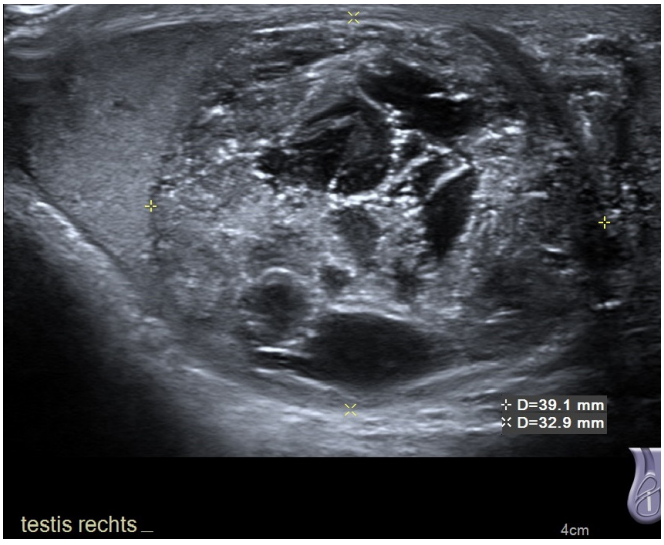

Figure 1 Ultrasound/echography image of the right testicle showed a mass in the right testicle, inhomogeneous with echogenic and echoic areas and cysts in it.

OUTCOME AND FOLLOW-UP

During follow-up, 12 months after surgery, the patient showed no local recurrence or any other disease symptoms.

DISCUSSION

In 2009, MCST of the ovary was first reported by Irving and Young.[1] Their cohort consisted of 16 ovarian neoplasms of stromal origin with distinctive microscopic changes. At that time, the immunohistochemical profile of these tumours was non-specific, showing expression of vimentin and CD10, whereas immunohistochemical staining for inhibin and calretinin was negative. In 2014, Yang *et al* reported a case of MCST with diffuse nuclear staining for beta-catenin[2] after which, in 2015, Irving *et al* reported nuclear accumulation of beta-catenin in 15 MCST cases, 8 of which showed point mutations in exon 3 of the *CTNNB1* gene. In addition diffuse expression of cyclin D1, FOXL2 and SF-1 was observed in the majority of MCST cases.[3] In a follow-up study reported in 2018, this group showed that the cohort of MCST cases lacking a *CTNNB1* mutation harboured an *APC* mutation. These *APC* mutations were mutually exclusive with *CTNNB1* mutations and might represent an extracolonic manifestation of familial adenomatous polyposis.[4]

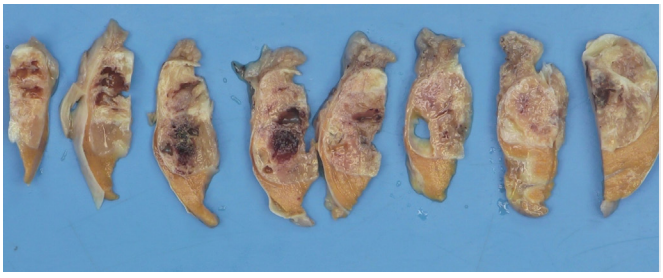

Figure 2 Macroscopy of the right testicle: on cut surface a sharply demarcated tumour was found, with both nodular and cystic growth, grey colour and white fibrous bands, contained to the testicular stroma. Tunica vaginalis and tunica albuginea were intact and unaffected, and there was no tumour extension into the hilus of the testicle. The largest diameter is 4 cm.

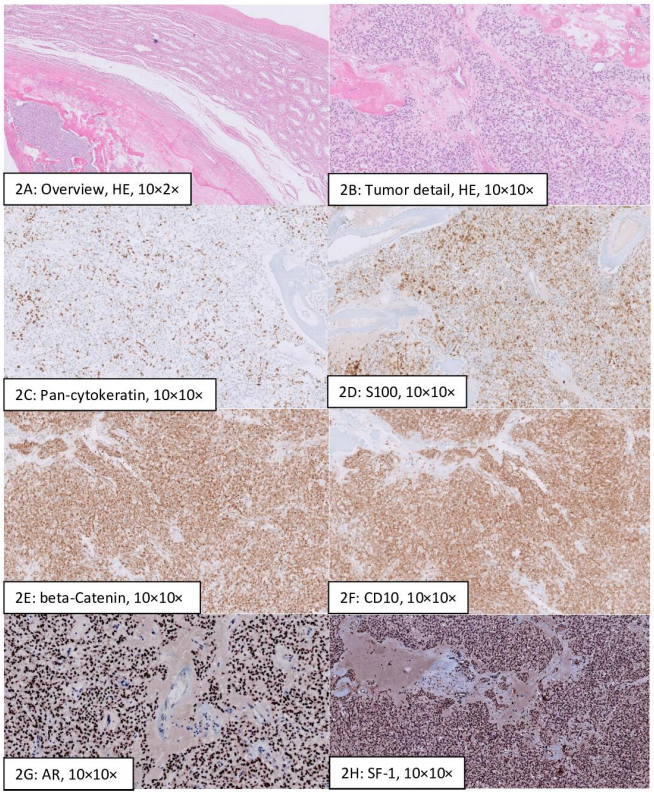

Figure 3 (A) and (B) Histomorphological examination in H&E staining showed a sharply demarcated, cellular proliferation surrounded by a thick fibrous capsule. The cellular areas showed a monomorphic population of round to oval tumour cells with monomorphic, dark round to oval nuclei. Nucleoli were inconspicuous and the cytoplasm was not sharply demarcated. The tumour cells were arranged in loosely solid fields and sometimes arranged in a reticular network and microcystic formations. Large nuclei, nuclear polymorphology or mitotic activity were sparse. There was no tumour necrosis. (C) Tumour cells were focally positive for cytokeratins. (D) Tumour cells were focally positive for S100 (cytoplasmatic and nuclear expression). (E) Tumour cells showed strong immunohistochemical expression for beta-catenin (cytoplasmatic and nuclear expression). (F) Tumour cells showed strong immunohistochemical expression for cluster designation 10 (CD10). (G) Tumour cells also showed was strong nuclear expression for androgen receptor (AR). (H) Tumour cells also showed was strong nuclear expression for steroidogenic factor-1 (SF-1).

The first and until now only case report on MCST in the testicle appeared in 2018, by Zhu *et al*.[5] They presented a 33-year-old Chinese man with a mass in his right testicle. Ultrasound and CT examination showed a solid and cystic tumour. Gross examination of the orchidectomy specimen revealed a well-circumscribed grey-white and solid nodule, 3 cm in diameter. Histologically, the tumour was composed of solid and microcystic areas of monomorphic stromal cells and intervening hyalinised fibrous bands. These stromal cells expressed vimentin, CD10 and nuclear beta-catenin. A *CTNNB1* gene mutation (c.110C>G) was detected with DNA sequencing.

Sex cord-stromal tumours may occur in both male and female gonads and include pure stromal tumours, pure sex cord tumours and mixed sex cord-stromal tumours. MCST is an exceptionally rare variant of pure gonadal stromal

tumours, which has been added to the 2014 WHO tumour classification.

There are few publications on MCST in female patients, often representing case reports or small case series with literature reviews. These MCST series vary between 1 and 16 cases (in the first report[1]).

To the best of our knowledge, to date, only one case of testicular MCST has been published.[5] Here, we have presented a second case with the distinct morphological features and characteristic immunohistochemical profile of MCST, including expression of vimentin, CD10 and beta-catenin. The observed expression of both AR and SF-1 in this case and FOXL2 in ovarian MCST case series[3] supports the notion that MCST arising in the testis and ovary is a tumour of sex cord-stromal origin.

Molecular testing showed an exon 3 *CTNNB1* point mutation (c.98C>T), different from the *CTNNB1* c.110C>G mutation detected in the Asian patient. However, these particular *CTNNB1* mutations have also been found in ovarian MCST.[3 6] Thus, based on overlapping immunoprofiles and molecular genetic abnormalities, testicular MCST may be considered as a counterpart of ovarian MCST.

Ovarian MCST may harbour either *CTNNB1* or *APC* point mutations. Therefore, it is conceivable that *APC* mutations may also be detected in future cases of testicular MCST lacking *CTNNB1* mutations.

Learning points

- When ultrasound imaging shows that a testicular mass is encapsulated and sharply demarcated and consisting of both (micro)cystic and solid areas, consider the possibility of microcystic stromal tumour (MCST).
- Not all testicular tumours are malignant.
- MCST is a rare gonadal stromal tumour, usually presenting in the ovary but rarely also in the testis.
- Mutations in the *CTNNB1* or *APC* gene are diagnostic for MCST.

MCST of the female and male gonads appears to behave in a rather benign fashion, which may justify limited clinical follow-up.

Contributors MH, first author and corresponding author was the pathologist who dissected and reported on this case. She wrote the template of the article and explained to the patient the reason for this case report and the importance of his informed consent on the publication of information and images. IB is the urologist who treated the patient. He provided the clinical information in this publication. He asked the patient for permission to be contacted by pathologist MH about informed consent and he reviewed the paper before submission. AS is the academical pathologist who reviewed the case before diagnosis, who ordered the molecular testing needed to prove the diagnosis. He also helped writing this paper and reviewed it before submission.

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Competing interests None declared.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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