Case Report

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# Sex cord stromal tumour not elsewhere classified: a case report and review of the literature

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## 1. Abstract

This case report represents one of the fews present in the scientific literature dealing with sex cord-stromal tumours. They are rare in the paediatric population and their incidence represents less than 5% of the testicular tumours in children and adolescents, and as a consequence little is known in the scientific community about them and how should be treated.

In the following case report a five-month-old caucasian child in completely well-being was diagnosed with sex cord stromal tumour not elsewhere classified (NOS) and underwent orchifunicolectomy with inguinal approach. During the clinical and radiological follow-up no recurrence was diagnosed.

Therefore, our case report could be a useful clinical and surgical example for paediatric surgeons in order to successfully treat a sex cord stromal tumour not elsewhere classified (NOS).

**2. Keywords:** sex cord-stromal tumour; testicle; surgery; orchiectomy

## 3. Introduction

Sex cord-stromal tumours are rare in the paediatric population, comprising a range of subtypes with different clinical characteristics and biological behaviour. Approximately 10% of cases are malignant.

These tumours predominantly manifest as a solid mass in the testicular region and signs of masculinization have also been documented in some cases. It is notable that the clinical prognosis is significantly influenced by factors such as the tumour subtypes and the patient's age.

## 4. Case Presentation

A five months old child came to our attention for a right testicular mass noted by his mother.

At palpation the right testicle appeared enlarged and hard, no presence of hydrocele or inguinal enlargements and lymphoadenomegaly was not identified. Contralateral testicle was normal.

A testicular ultrasound revealed a well-defined, vascularized neoplasm measuring 13mm within the gonadal parenchyma (Figure1)

Tumour markers were the following: LDH 468 U/L (140-435U/L), alpha-fetoprotein 91.4 ng/ml (20 ng/ml- 400ng/ml), beta-human- chorionic-gonadotropin 0.1mlU/ml (<5mlU/ml), and ferritin 23 microg/l (n 6-24 microg/l).

Based on the clinical, laboratory and radiological data, testicular exploration with inguinal approach were performed. The spermatic funicular cord was isolated and clamped, than, the testicle was brought out of the scrotum and the inguinal incision. A testicular specimen was taken for intraoperative frozen tissue analysis, which identified a non-germinal neoplasia with high mitotic index.

Spermatic cord was ligated at the internal inguinal ring and orchifunicolectomy was performed.

The final histological report confirmed sex-cord stromal tumour.

The histological specimen was fixed in 10% formalin, embedded in paraffin and stained with hematoxylin-eosin. Additional 4 mm thick sections were mounted on electrostatic slides and used for the immunohistochemical studies.

The sections of testicular parenchyma were characterized by a proliferation of monomorphic cells with apoptotic bodies with 40 mitosis/10 HPF; the cells were arranged in solid groove pattern with microcystic aspects and fibrous stroma (Figure 2).

The tumour cells were ovoid without visible nucleoli positive for CAM5.2, CD99, and WT1 (Figure 3) and negative for HCG, AFP, PLAP, Synaptophysin, CD30 and Desmin.

Nearby the neoplasia immature seminiferous tubules were observed.

During the postoperative period, the patient remained stable; an MRI of the thorax and of the abdomen was performed to define the tumour stage; metastasis were not identified.

Five years post-surgery the patient remains in good health. The testicular ultrasound resulted negative for metachronous tumours in the left gonad, abdominal ultrasound and thorax X ray were negative for metastases. A left orchidopexy with a scrotum approach was programmed.

## 5. Review of the Literature and Discussion

Testicular tumours can happen at any age, most often between the ages of 15 and 45.

They represent nearly 1% of the paediatric solid tumours; from 5% to 11% are tumour of gonadic stroma, frequently diagnosed in children younger than 6 months of age [1;2;3;4].

The recommended pathological classification of testicular tumours is based on the updated classification of the World Health

Organization (WHO), reported in The fifth edition of the World Health Organization (WHO) classification of urogenital tumours (WHO ‘‘Blue Book’’), published in 2022 [5] and containing significant revisions compared to the 2016 version [6]

Following the 2022 WHO classification, mixed and other sex cord-stromal tumours represent a

family of non-germinal cell testis tumours, together with Leyding cell tumour, the most common, followed by Sertoli cell tumour, granulosa cells tumour, fibroma-thecoma stromal tumour [5].

As already noted, Leyding cell tumour has an incidence of less than of 3% of all gonadal tumours in the general male population; in prepubertal children, especially between 6 and 9 years old, the incidence increases up to 9% of all primary testicular masses. [7, 8].

Next to the Leyding cell tumour there is the malignant form [5].

Sertoli cell tumour constitutes one of the more prevalent sex cord tumours in patient aged under 12 years, but it is the second most frequent in adult age [8, 9]. There are three forms: Sertoli cell tumour, Malignant Sertoli cell tumor and Large cell calcifying Sertoli cell tumour [5].

Large cell calcifying Sertoli cell tumours are frequently observed in patients ranging from their teens to early twenties [8, 9].

In the granulosa cell tumour family, it is possible to distinguish the adult and the juvenile type [5].

Juvenile granulosa cell tumour stands as the most common congenital testicular tumour, it is especially prevalent among neonates and infants, in the first 6 months of age [8]. It is uncommon in older children, an exception in adults. [9]..

In the mixed and other sex cord stromal tumour family there are the mixed sex cord-stromal tumour type, the signet ring stromal tumour type (SRST), the myoid gonadal stromal tumour type and the sex cord stromal tumour not otherwise identified (NOS) type [5].

It is noteworthy that around 50% of sex cord-stromal tumours NOS manifest in children and the pre pubertal males have a slightly higher risk; the remaining 50% being observed in men of various age [10, 15].

Approximately 5% of sex cord stromal tumours show malignancy, usually they are characterised by larger size, necrosis, nuclear atypia, vascular invasion, extension to outside of the testis and higher mitotic count per 5mm2 [(10 HPF sec WHO 2016 4th edition); in order to increase the accuracy, the fifth edition defined mitotic count in square millimetres, instead of high power field] [5,10].

Up to now in the literature there is not any case in the paediatric population of malignant evolution of Leyding cell tumour, whereas in the adult population it is observed up to 10%. [7]

Sertoli cell tumours and Large cell calcifying Sertoli cell tumours have a border line behaviour (5), but the last one has a greater probability to have a malignant nature with the increase of the age.

In the granulosa cell tumours, the Juvenile granulosa cell tumour are frankly benign [9,11], while the adult type could have a malignant evolution up to the 20% of cases [12]

It is difficult to predict the evolution of mixed and other sex cord stromal tumour family [13,14], indeed the mixed sex cord stromal tumour type and sex cord stromal tumour NOS type have a borderline behaviour, while signet ring and myoid gonadal stromal tumour type have a benign behaviour [5].

Usually, sex cord stromal tumours present with a intra -testicular palpable mass, as in our patient, of small volume and rarely masculinizing signs, precocious pseudo-puberty or gynecomastia are present too [3, 14, 15,16]. There are not tumour markers for the initial diagnosis and for the follow-up of these tumours; often, although its usage is not standardized [3], they can have a positive histochemical coloration for Inibhin which can be secreted by granulosa cell tumours.

Surgery represents the only treatment. The treatment of choice is orchiectomy with inguinal approach, preceded by funicular clamping at the internal inguinal ring [13]. It is recommended an extemporary biopsy, except cases in which alphaphetoprotein levels are greatly increased for the age of the patient [1]. Tumour excision is indicated for benign lesions and for malignant neoplasm if the dimension is inferior to one third of the gonad, without ilar testicular involvement [13, 15].

If at the initial radiographic images the retroperitoneal lymphnodes results normal, a surgical exploration of these is not suggested at first [13,14]. It is recommended, instead, the monolateral retroperitoneal lymphoadenectomy, if after chemotherapy metastatic lymphnodes persist [1,13 ,14]. Indeed, chemotherapy is employed in cases of metastasis, residues after excision and abnormal hormonal levels after surgery [13].

In the first year after surgery, patients defined as low risk, on the base of the initial TNM staging undergo clinical and lab exams (AFP, BHCG, LDH) every 4 months, MRI without mdc and thorax RX every 6 months and testicular ultrasound after 12 months from surgery [8,17]. High risk patients undergo the same follow up of low risk patient with adjunctional MRI without mdc and thorax RX at 4th and 8th month from surgery [8,17].

In the second year, imaging is limited at the 6th month for all patients and at the 12th month for intermediate and high risk patients [8,17]. Lab exam follow up is the same as the first year.

From the third year, MRI without mdc and thorax RX are reserved for high risk patients (6th and 12th month) and intermediate risk patients (12th month). Laboratory exams are reserved every 6 months.

In the fourth and fifth year after surgery, laboratory exams are performed at 6th and 12th month for all patients, while imaging is reserved to high risk patients [8,17].

It’s noteworthy, testicle ultrasound is repeated every year for each patient [8,17].

## 5. Conclusions

Sex cord-stromal tumours, in particular the NOS, are extremely rare in the paediatric age and in the literature are reported few clinical cases. The absence of standardized tumour markers makes difficult their diagnosis and follow-up. Even though genetic could be a useful diagnostic tool.

In the literature is possible to find papers exploring the possibility to identify tumour specific gene, such as the CTNNB1 exon 3 mutations are likely to be involved in the pathogenesis of Sertoli cell tumour with nuclear accumulation of β-catenin and affect

the expression of cyclin D1. [19] Moreover, a further chapter on genetic tumour syndromes is now described in the literature, such as intratubular hyalinising Sertoli cell tumour occurs exclusively in Peutz–Jeghers syndrome.

In contrast, large cell calcifying Sertoli cell tumour is frequently associated with Carney complex, but sporadic cases occur too. [20]

In conclusion, our diagnostic and surgical approach aligns with the recent literature, which recommends radical orchifunicolectomy via inguinal canal after extemporary biopsy.

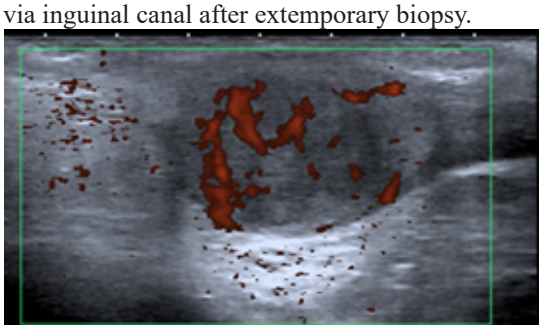

Figure 1a. Neoformation particularly vascularized of 13mm of diameter in the right testicular parenchyma.

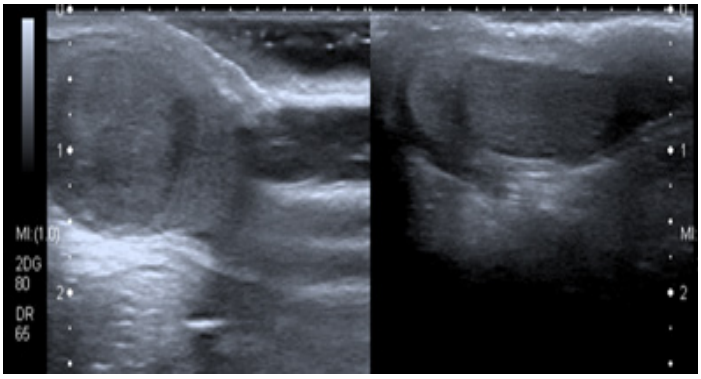

Figure 1b. Left testicle.

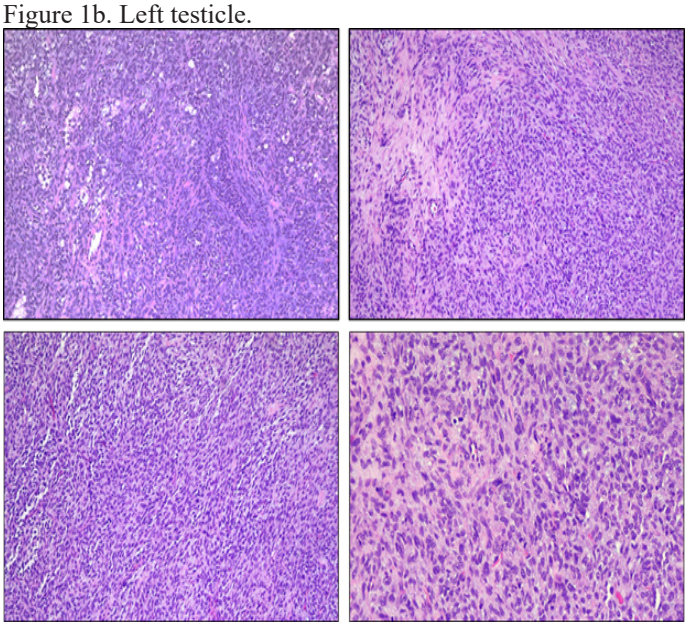

Figure 2. Proliferation of monomorphic cells arranged in solid pattern with microcystic aspects and fibrous stroma (A, B, C: Hematoxylin-eosin stain, original magnification x100); high mitotic activity (D: Hematoxylin-eosin stain, original magnification x200).

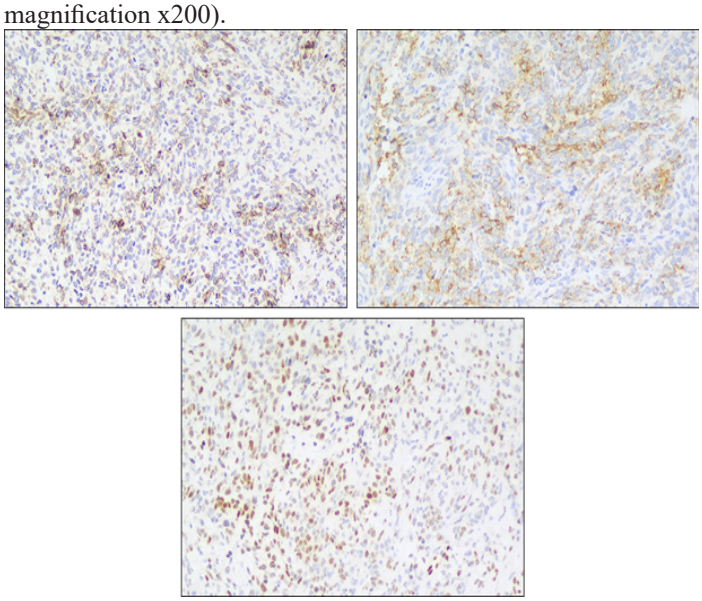

Figure 3. CAM5.2 (A), CD99 (B) and WT1 (C) were positive (Immunohistochemistry, original magnification x200).

## 6. Declarations:

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