POSTPUBERTAL YOLK SAC TUMOUR OF THE TESTIS. THE HISTOPATHOLOGIST'S POINT OF VIEW

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Abstract: *Yolk sac tumour of testis (YSTT) is an aggressive neoplasm that resembles the allantois of the embryo and becomes a difficult diagnosis in children, even in a pure form. We present the case of a- 16 year-old boy with a right scrotal swelling and haematocele that revealed due to microscopic examination a hepatoid – microcystic YSTT on a small testicular biopsy. The serum alpha-feto-protein (AFP) showed detectable levels as high as 3,7 ng/L, with negative values for β-hCG and CEA 125. Immunohistochemistry requires AFP, SALL4, Glypican 3 and cytokeratins.*

INTRODUCTION

Yolk sac tumour of testis (YSTT), also called endodermal sinus tumour of Teilum, the endoderm being the most inner layer of the yolk sac of the embryo, thus, resembling the yolk sac, the extraembryonic mesenchyme and the allantois. Pure YSTT is seen in children and infants, classified as malignant, representing almost 70% all testicular germ cell tumours. Increased serum α-fetoprotein is the most frequent preclinical clue to the diagnosis, while, clinical presentation is represented by testicular, painless, enlargement, sometimes as a frank, pseudo-traumatic, haematocele.(1) Although appearing as a benign condition, a scrotal, painless swelling, might be overlooked, the clinician should take in account that 15-50% of cases are associated with a testicular tumour and a thorough examination for a malignant pathology becomes mandatory.(2)

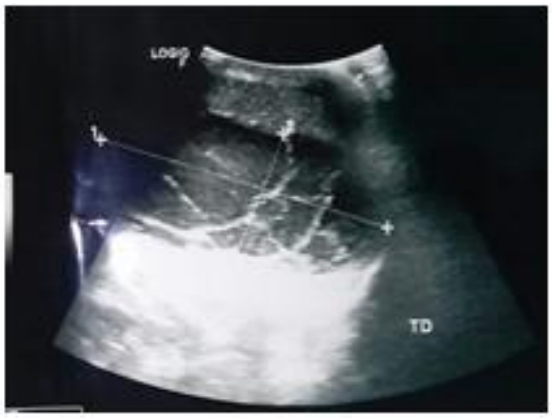
PURPOSE

The purpose of this article is to attract the clinician attention towards diagnostic issues frequently encountered in histological assessment of testicular germ cell tumours, especially in paediatric pathology, within small surgical biopsies.

MATERIALS AND METHODS

A 16-years old male patient was admitted with an enlarged painful, right testicle at the Surgery Department of our Hospital. During close inspection, the scrotum had a bluish, elastic appearance, with a liquid-like consistency during palpation. Screening laboratory tests proved negative for any acute inflammatory condition, although ultrasonography shows a tumour, apparently, as a extratesticular mass, with a multicystic appearance (figure no. 2), with maximum dimensions of 4/10,4 cm, that compressed the testis parenchyma (1,5/3,6 cm). Subsequently, blood samples were obtained for analysis of β-hCG, AFP (α-fetoprotein) and CEA 125 (carcinoembrionic antigen). Doppler ultrasonography proved intraparenchymal signal, raising the diagnostic suspicion of a YSTT. The left testis proved a homogenous structure, with dimensions within 2,7/4 cm, and a positive Doppler signal. No other clinical or radiologic anomalies were detected during immediate clinical follow-up. A surgical intervention was scheduled, with epidural anaesthesia.

Figure no. 6. Echographic aspect of the right testicle (TD). A septate, multicystic aspect of an enlarged, bulging mass can be observed



Thus, a testicular mass was discovered, with no gross clues for albuginea or vaginalis invasion. Afterwards, a quantity of 20 cc of haemorrhagic liquid inside the vaginalis exteriorised after incision, in a volume of 10-12 cc. Biopsies were sampled, from vaginalis, albuginea and parenchymal testis, and referred to the Pathology department in our hospital. The first biopsy (a) comprises an area of testicular parenchyma as well as albuginea testis with dimensions within 2,5/0,5 cm. The second (b) consists of thickened, loose, elastic, testicular vaginalis – 5/5/0,3 cm – with a brown, homogeneous colour. The latter fragment (c) from cremasteric muscle, with a brown colour and fragile appearance, had dimensions of 1/0,5 cm (figure no.1). These fragments were fixed in buffered formalin 4%, in order to preserve any lymphocytic distribution or molecular antigenicity. Afterwards, the fragments were processed in alcohol in successive grades, i.e. 70 and 80% concentration in the first day, three subsequent baths of 96% concentration alcohol, and the latter two baths of 99,96% and, respectively, another two isopropyl alcohol. Paraffin and wax impregnations were performed, followed by embedding and thin sections, 2-3 μm in

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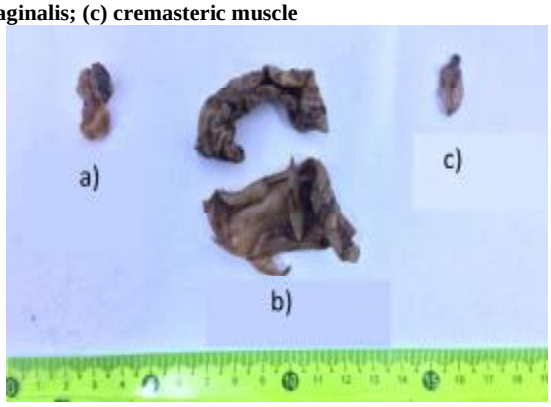
thickness. The obtained samples were stained with haematoxylin and eosin.

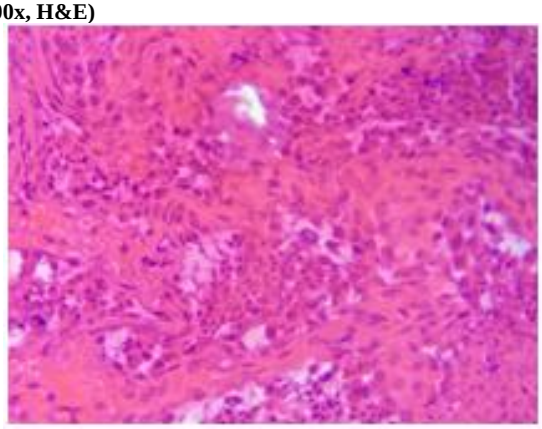
Figure no. 7. Macroscopic appearance of the tissue samples from the case: (a) testicular parenchyma; (b) testicular vaginalis; (c) cremasteric muscle



RESULTS

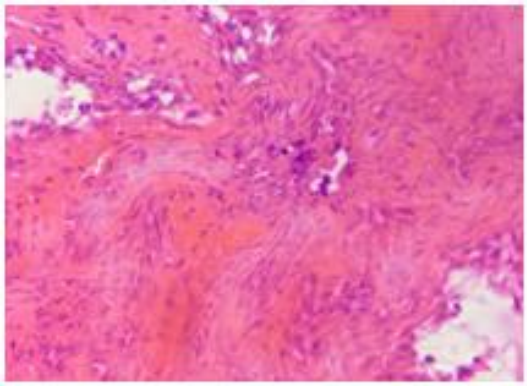
On the resulting slides we have observed a thickened albuginea testis with slight inflammation and scattered lymphocytes, fatty tissue areas with adipocytes and a thickened, haemorrhagic vaginalis. In the sampled testicular parenchyma we detected sarcoid, large-cell, polygonal shaped eosinophilic cells organised in inter-tubular sheets (figure no. 3), mostly arranged in a hepatoid fashion, with a perivascular distribution, focally solid and, eventually, reorganising in honeycomb-like laces, towards the albuginea, with epithelioid cell proliferation and capilar hyperaemia. Some cells proved to have a signet ring appearance.

Figure no. 8. Microscopic appearance of the testicular biopsy: diffuse spreading epitheliod cells between the tubuli; basal compartment of the tubuli with cells and vacuolization of Sertoli cells; central mitosis is visible (personal collection, 100x, H&E)



In the tumour aspect between the intermingled tubules, Leydig cells were appearing hyperplastic, almost with an invasive tendency in the basal compartment of the tubules (figure no. 4). The pampiniform plexus proved to be hyperaemic and having no signs of any vascular refraction whatsoever. However the plexiform appearance in some areas pleads for a mixed testicular tumour, either with a Yolk sac component, a non-germinative component. The blood samples revealed a negative β-hCG component, with a AFP level of 3,7 ng/L. This value, although indifferent from the laboratory point of view (normal value limit below 7 ng/L) cannot be ignored, regarding the spontaneous haematocele with no local traumatic or heavy effort history. Although Schiller-Duval bodies were not present, elements of intratubular germ cell neoplasia – like polychromasia, bland, vesicular, excentric nuclei – were encountered with a reticular and cord-like pattern, and moderately raised AFP, the diagnosis concluded to *hepatoid – microcystic Yolk sac tumour*.

Figure no. 9. Microscopic aspects of the tumour in case: sheets of cells with bland, vesicular nuclei, arranged in a perivascular fashion, with, areas of sarcoid differentiation; two tubuli with elements of intratubular germ cell neoplasia (100x, HE, personal collection)



DISCUSSIONS

Macroscopic aspect of YSTT is that of a nonencapsulated tumour, with a tan-white to yellow colour, soft texture and a gritty, friable on the cut surface, with frequent cystic change and gelatinous or mucoid appearance. The microcystic pattern seems to be the most frequent histological aspect, among the others aspects: macrocystic, glandular-alveolar, endodermal sinus, solid, myxomatous, spindled, hepatoid, papillary, parietal and polyvesicular or vitelline.(3) Sometimes, histological differentiation between sarcoid YSTT and choriocarcinoma testis might be difficult. It is generally accepted that choriocarcinoma of testis is a malignant germ cell neoplasm that might exhibit trophoblastic differentiation. Usually, it is detected as a component of a mixed TGCT, in pure form, comprising from 0,2% to 0,6% of all primary testicular tumours. The metastatic spread of the tumour would become, frequently, the first clinical sign either due to back pain – in retroperitoneal spread – gastrointestinal bleeding, neurological symptoms or haemoptysis in pulmonary metastasis. In laboratory screening, an elevated hCG would point to the diagnosis, extremely high levels leading to thyrotoxicosis, due to molecular similarities with thyroid stimulating hormone. Often, hCG levels are greater than 100,000 IU/litre. The average dimensions of a testicular tumour, in a study of 13 patients ranges from 1,5 cm to 10 cm, with a median of 7 cm, with haemorrhage and necrosis on cut-surface, also with haemorrhagic liquid in the vaginalis testis, being firstly diagnosed as a haematocele.(4) Microscopic diagnostic criteria in YSTT require the presence of polygonal cells, with eosinophilic cytoplasm, bland nuclei arranged in different patterns – reticular, papillary or cord-like. In some situation, Schiller-Duval bodies might be encountered, resembling primitive glomeruli having central capillaries surrounded by a visceral and parietal layer of cells, thus, similar to endodermal sinuses. Some authors report that YSTT, in childhood, have no mixed histologic pattern but rather a pure one, therefore, not becoming involved with any mixed germ cell tumour, like the

case of adults, however, in a postpubertal situation, it resembles more with the adult type.(5) Regarding tumour markers, serum alpha-feto-protein becomes a useful marker for early diagnosis of YSTT, used to check for complete remission or recurrence. Studies suggest that positive values of serum AFP are found in all patients with tumours that contain a YSTT area. However, it is speculated that preoperative serum AFP levels before initial resection surgery have no prognostic importance, while postoperative follow-up for AFP remain a good indicator for residual stages of neoplasia. Chemotherapeutic treatment with a good response would determine a lowering of AFP levels to a normal status. Elevation of β-hCG implies the presence of a germinal counterpart, probably choriocarcinoma, but values tend to become very high.

Immunohistochemistry requires AFP that becomes diffuse trough the cytoplasm and hyaline globules, although pediatric tumors are often AFP negative, with an almost indifferent serum AFP.(6) Cytokeratins, SALL4, Glypican 3, with a variable PLAP positivity might be helpful, when AFP remain negative, while intense CD117 is positive in the solid histological pattern of YSTT.(7,8)

CONCLUSIONS

Yolk sac tumour of testis, although with a rare incidence in scrotal pathology, is a very important condition that could be overlooked in current clinical practice, by the surgeon, paediatrician or pathologist. Differential diagnosis with other testicular tumours is mainly achieved through corroboration between histological and laboratory findings. A rapid involvement of a complete and competent medical team should avoid stage progressing or metastasis and, thus, an unfavourable prognosis.

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