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The Solid Pattern of Postpubertal Pure Yolk Sac Tumor: A Seminoma Mimicker. A Dangerous Pitfall - A Case Report and Literature Review

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Abstract

A case of rare pure postpubertal Yolk Sac Tumor with a predominant solid pattern, which mimicked a seminoma, is presented. However, upon closer examination of the morphology and immunohistochemical staining, the tumor was distinguishable as a YST due to the presence of hyaline globules, microcysts, and AFP expression in certain areas

1. Introduction

The WHO 2022 Classification of Yolk Sac Tumor(YST) distinguishes two distinct varieties depending on the age of onset: postpubertal and prepubertal: The first is placed among the non seminomatous Germ Cell Tumors derived from Germ Cell Neoplasia in Situ. The second among the Germ Cell Tumors Unrelated to Germ Cell Neoplasia in Situ. It can occur in the male and female gonads as well as in extra-gonadal sites: sacrococcygeal region, retroperitoneum, pelvic organs, mediastinum, brain, and very rarely, the head and neck area. The Tumor has a protean morphology and different patterns are described, rarely unique, often intermingled with each other. Ten patterns have been described: 1) Microcystic /reticular; 2) Macrocystic; 3) Myxomatous; 4) Sarcomatoid/spindle cell; 5) Solid; 6) Glandular/ alveolar7) Endodermal sinus/ perivascular; 8) Hepatoid; 9) Papillary;10) Parietal.

The Solid Pattern, when prevalent, poses serious problems in differential diagnosis with Seminoma with which it can be confused, specially in biopsies, with negative consequences on the therapeutic approach which is completely different for the two neoplasms. The observation of a case of this type has offered the opportunity to review the differential diagnosis criteria both on the basis of personal observation and on data from the literature.

2. Case Presentation

Patient: 47-year-old Caucasian male presenting with testicular swelling for several months. The patient underwent orchiectomy.

3. Material And Methods

Testis 8x6 cm. When cut, the normal testicular structure is not recognizable and appears replaced by a whitish material. Spermatic cord 7 cm. The sampling was conducted according the international standard from the testis, spermatic cord, and vaginal tunic. The material was fixed in buffered formalin and embedded in paraffin. The sections were stained with Hematoxylin-Eosin, subjected to PAS reaction and tested with a panel of antibodies. Table 1

Ck AE1-AE3	AFP	Cd117	D240	Cd30	PLAP	βHCG	Ki 67

Histopathology

In the examined material, no structures referable to normal didymal parenchyma are recognizable. The epididymis is recognized, separated by a thick tunica albuginea from a proliferative tissue with neoplastic characteristics. This is largely affected by coagulative necrosis. In the non-necrotic marginal part, still assessable, the tissue is mainly made up of a sheet of globose elements with predominantly rounded, hyperchromatic nuclei and amphophilic cytoplasm. Cells with anaplastic and squarred-off nuclei are

sporadically observed. In some areas, located at the margins of the necrotic area, there are groups of cells from extremely pale cytoplasm and very evident intercellular basal membranes. Roundish eosinophilic hyaline globules are abundantly and diffusely present. In the areas where the cells have pale cytoplasm, microcystic cavities of various sizes open up. A fairly lively mitotic activity is present. Angiolymphatic invasion is evident.

The results of the immunohistochemical investigation are reported in Table 2

Ck AE1-AE3	AFP	Cd117	D240	Cd30	PLAP	βHCG	Ki 67
+++	+++f	---	---	---	---	---	35%

The immunophenotypic expressivity for CK AE1-AE3 is intense and diffuse. As for AFP, the intense expressivity is limited to the areas in which microcysts and pale cytoplasmic cells with reinforcement of the intercellular basement membrane are present. The solid areas are completely negative. As well as clearly negative results are: 117, D240 (Podoplanin), Cd30, PLAP, βHCG

4. Discussion

The case we observed presents at glance as a solid proliferation (Fig.1a) composed of globose elements with fairly regular nuclei associated with a conspicuous coagulative necrosis (Fig.1b).

These aspects have brought to the forefront the diagnostic possibility of a Seminoma. A more careful observation, alongside the prevailing solid pattern, reveals the presence of very numerous hyaline globules (Fig.2a), finding that calls into question the original diagnostic hypothesis. Hyaline globules are reported in 65% of the YST cases [3,4,5,6], while they are not reported in seminoma. Scattered anaplastic nucei (Figg.1-c, d) (in contrast with the cellular monomorphism of classic of seminoma) are observable in the solid component. Cells with vacuolated cytoplasm and prominent intercellular basement membranes (Fig.2b) and sparse microcysts,right at the border with the necrotic area (Figs.2c,d,3a). These last aspects integrate the morphological pattern of microcystic reticular YST in a context of a prevalent solid pattern. The literature indicates that the solid pattern of YST with high frequency is associated with other morphologic patterns that participate to a greater or lesser extent in the formation of the neoplasm. The pattern that is associated with greatest frequency is the microcystic reticular one (90% of cases). Only 4% of cases present an exclusively solid pattern. [3].

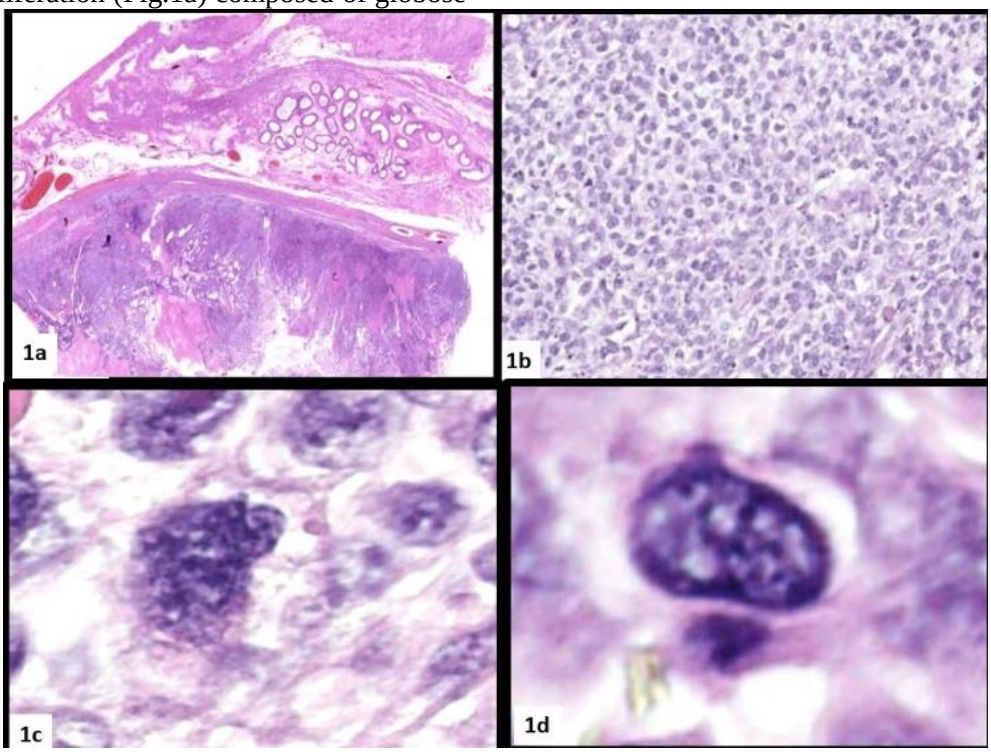

Fig 1- a) *Below the albuginea solid proliferation. Deep area of necrotic tissue. No recognizable didymal structures. Recognizable epdidymis (HE50X);* **b)** *Solid area. Globose elements with rounded nucleus, amphophilic cytoplasm (HE 175X);* **c-d)** *Anaplastic nuclei (HE 250 X).*

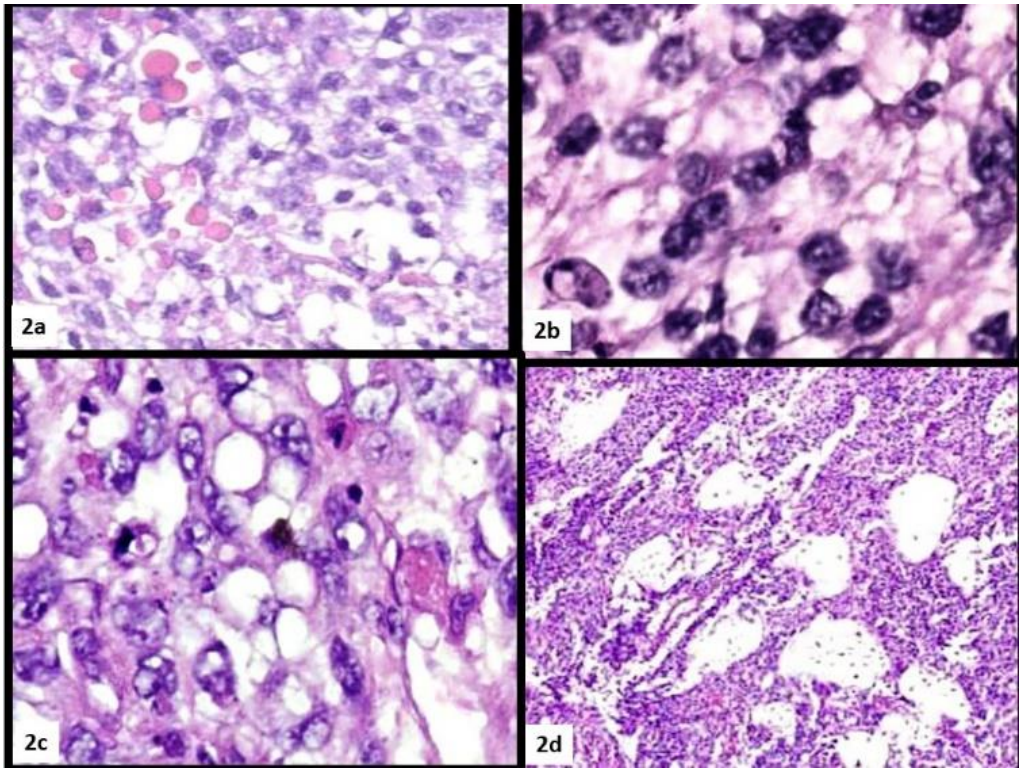

Fig 2–a) *Hyaline globules (HE 125 X);* **b)** *Reticular pattern : cells with pale citoplasm and prominent intercellulaar membrane (HE 250 X);* **c - d)** *Microcysts (HE 125-175X).*

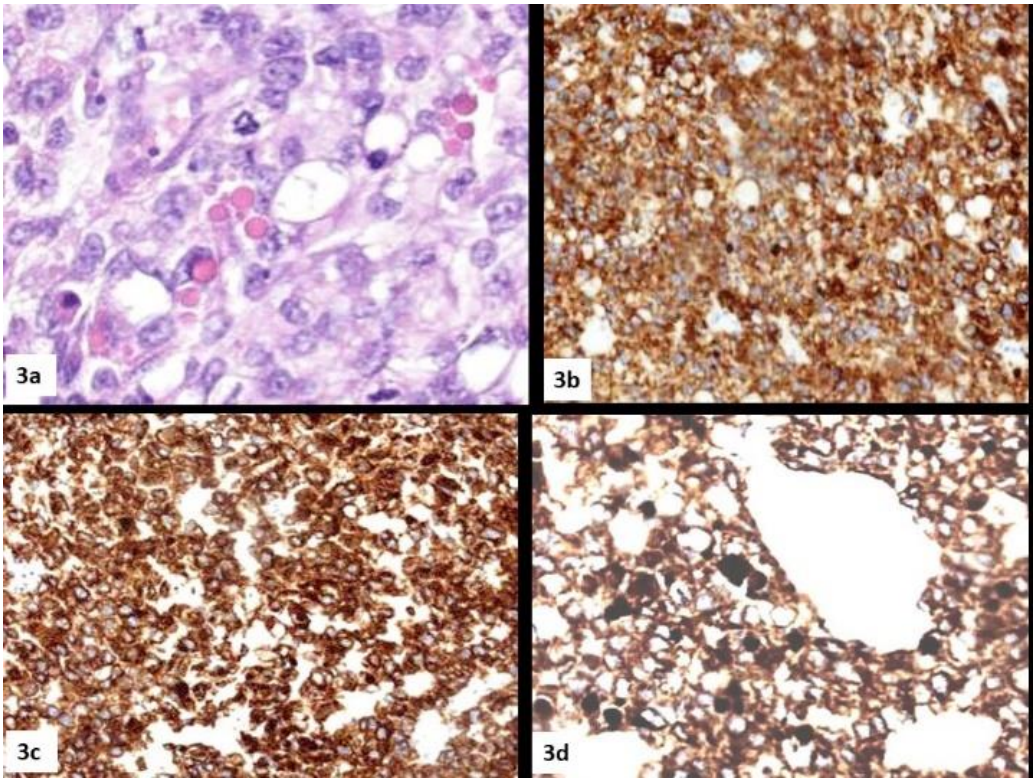

Fig 3–a) *Microcysts and Hyaline Globules (HE 175X);* ***b-c-d-)*** *Intense and diffuse expression of CK AE1-AE3. In-d- Hyaline globules intensely positive (125, 175X).*

Immunohistochemical research (Table 2) has highlighted an intense and diffuse expressivity for CK AE1-AE3 (Figs. 3 b,c,d). This is in accordance with what the literature reports regarding the expressivity in YSC, in contrast with the negativity or weak, scattered dot-like positivity in Seminoma [5, 6]. The solid component of the tumor is completely inexpressive with respect to AFP (fig.4a), whereas it is intensely expressed at the level of

the microcystic reticular pattern and in some yaline gobules (Figs. 4b, c,d). These data are widely supported in literature. In which it is found that in over 50% of the solid patterns there is no expression of AFP.[3,5] *"In EST(YST), AFP was found in all the various patterns, except in the cells in the myxoid stroma pattern and in the cells in the solid aggregates. The cells of the vacuolated network, the lining cells of the various cystic patterns and the liver trabecula-like cells were usually heavily stained "(Jacobsen, 1986)* [7]

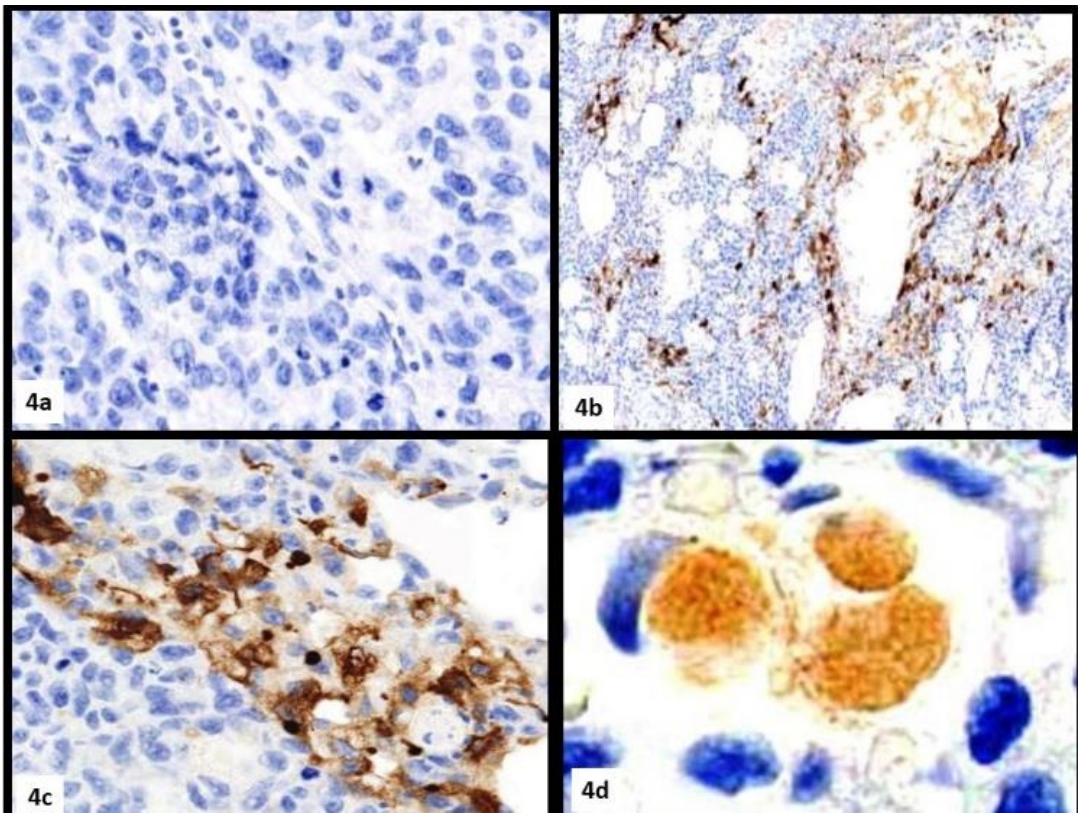

Fig 4–a) *AFP in solid area. Totally negative (175X);* **b-c-)** *Expression of AFP in reticulo cystic pattern; Hyaline globule expressing AFP (250X)s*

Postpubertal Yolk sac tumor, as in the case in question, unlike the prepubertal one, presents itself predominantly in the mixed form, that is, associated, in various combinations, with other Germ Cell Tumors (Embryonal Carcinoma, Teratoma, Choriocarcinoma). The association between YST and Seminoma is the rarest: only 3% of mixed germ cell tumors [1]. Pure (non-mixed) post-pubertal YST sac tumor is an extremely rare neoplasm that accounts for <1% of the adult testicular tumors.

A miniseries of 4 of these cases has recently appeared in the literature [2] From the examination of these cases it emerge that in all of them there is a commistion of the various YST patterns, the solid one was present focally in two. In a study on 52 post pubertal cases (17 -54 years), dedicated to the solid pattern of YST, it is reported that the a purely solid pattern is found only in 4% of cases. In the remaining it is associated with others with a prevalence for the microcystic/reticular one (75% of cases) [3]

Differential Diagnosis

Seminoma: The main differential diagnosis. However, seminomas show more uniformity in cell morphology, with clear cytoplasm and absent hyaline globules. Embryonal carcinoma and other germ cell tumors could also present with solid patterns, but the absence of PLAP and the presence of hyaline globules ruled this out.

5. Conclusion

This case highlights a rare pure postpubertal YST with a predominant solid pattern, which mimicked a seminoma. However, upon closer examination of the morphology and immunohistochemical staining, the tumor was distinguishable as a YST due to the presence of hyaline globules, microcysts, and AFP expression in certain areas. The correct diagnosis is critical as YST and seminomas have distinct prognostic implications and treatment strategies. The report underscores the importance of critical evaluation of both morphological and

immunophenotypic features to differentiate between seminoma and YST, as they require very different therapeutic approaches.

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