Sertoli-Leydig cell tumor of the ovary – morphological and immunohistochemical analysis

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Abstract

Sertoli-Leydig cell tumor is a rare and usually unilateral tumor of the ovary occurring in women's reproductive age. Only about 10% of these patients are over 50 years of age. One third of these patients are suffering from signs of virilisation. This work summarizes the morphological and immunohistochemical characteristics of this tumor in a 56-year old woman with clinical signs of virilisation.

INTRODUCTION

Sertoli-Leydig cell tumor belongs to the broad range of tumors, previously classified by WHO (2003) as tumors from specific mesoderm and stroma (sex cord stromal tumors). Sertoli-Leydig cell tumor is a rare tumor that accounts for 0.5–1% of all ovary tumors (Young 2011). These tumors are in literature stated as androblastomas or arrhenoblastomas. Tumor may occur at any age with a peak incidence around 30 years of age, rarely occurring in women above 50 years of age. It is usually unilateral but bilateral localizations has been already described (Kiran *et al.* 2009). The current histopathological WHO classification (Tavassoli *et al.* 2003) is:

- well-differentiated type,
- moderately-differentiated type with heterologous elements,
- undifferentiated type with heterologous elements,
- retiform type with heterologous elements,
- Sertoli cell tumor.

CASE REPORT

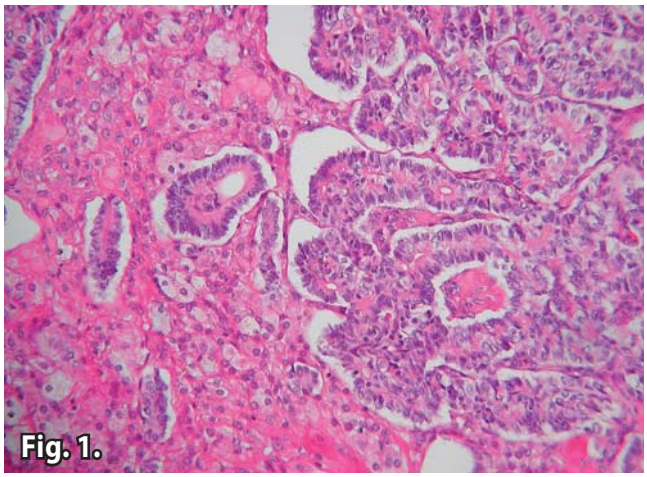
A 56-year-old woman treated 15 years for hypertension, during last 3 years she suffered from an excessive hair loss, weight gain and signs of virilization. Menopause occured at the age of 51 years. Laboratory results showed higher values of testosterone and normal values of androgens. On CT has been proved a tumor of right ovary (tumor size was 2.5 cm in diameter).

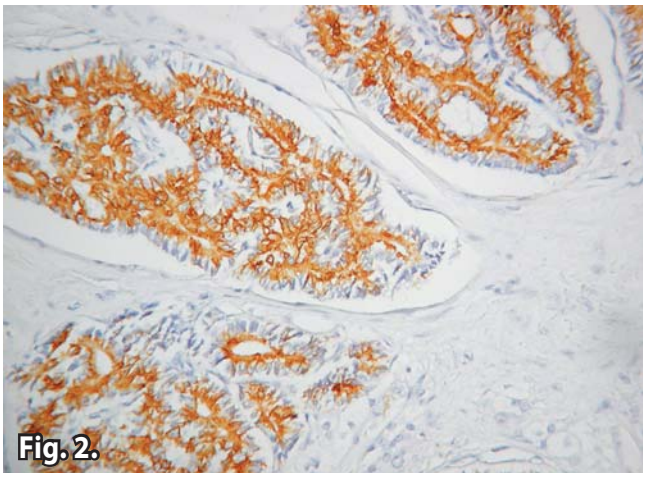
MATERIAL AND METHODS

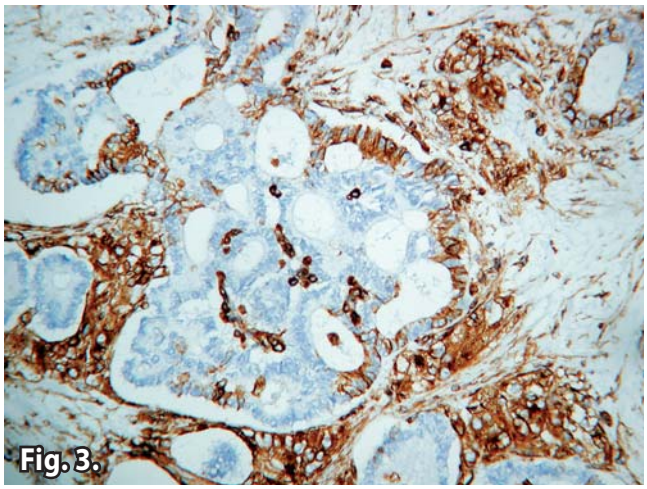
Adnexotomy has identified a tumor of the right ovary (25×22×20 mm) of yellow-whitish color with small foci of hemorrhage.

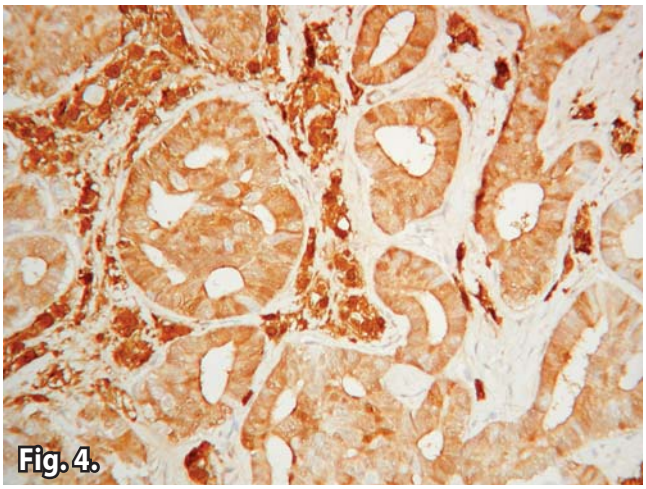
Immunohistochemical examinations were performed on formalin-fixed, paraffin embedded sections from tumor tissue of the right ovary. Microtome sections of 5 nm thickness were cut and deparaffinized in xylene a rehydrated in graded alcohols. Immunohistochemical staining was performed using Dual Link System – HRP (Dako En Vision).

CASE REPORT









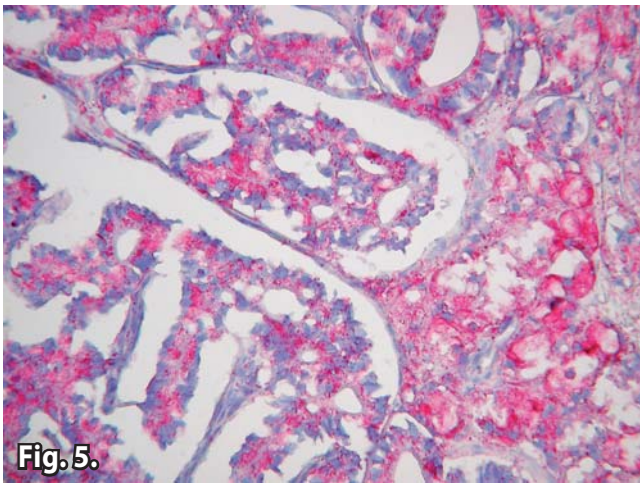


Fig. 1. Sertoli-Leydig tumor of ovary. HE (200×).
Fig. 2. Immunostaining for Cytokeratins AE1/3. Intense positivity in Sertoli cells (200×).
Fig. 3. Immunostaining for Vimentin. Focal positivity of Sertoli cells, intense stainig of Leydig cells (400×).
Fig. 4. Immunostaining for Calretinin. Intense positivity on both Sertoli and Leydig cells (400×).
Fig. 5. Presence of lipids in Sertoli and Leydig cells. Frozen section. Oil Red (400×).

To improve staining efficiency, antigen retrieval method was used. Deparaffinized secions were heated 3 times for 5 min. in 10 mM citrate buffer, pH 6.0, or the sections were revitalized with EnVision Flex Target Retrival Sol (Dako). Sections were washed with phosphate-buffered saline (PBS), pH 7.2, and were immersed in 0.3% H_2O_2 in PBS for 30 min. to inhibit endogenous peroxidase activity. The sections were incubated with primary antibodies for 60 min. at room temperature (EMA, AE1/3, calretinin, alfa inhibin, vimentin, CD 10, CD 99, chromogranin, synaptophysin) – Dako,). After 3 rinses with PBS sections were incubated with secondary antibodies EnVision Dual Link System – HRP for 30 min. Peroxidase activity was visualized with Liquid DAB + Substrate Chromogen System (Dako, North America, USA). Sections were counterstained with EnVision Flex Hematoxylin (Dako, Denmark). The immunohistochemical staining was performed in Autostainer Plus, Dako.

RESULTS

Microscopic examination of the tumor masses revealed that the tumor consists of mainly adenous tubular structures that were elongated or oval. These tubular structures were lined by Sertoli cells of cubic to cylindric shape. The nuclei were mostly oval without prominent nucleolus. The stromal component consisted of fibrous tissue and various number of Leydig cells (Figure 1) that separated the tubular structures. Larger parts of the tumor, formed by tubular structures, were well-differentiated, only in one place the tumor cells formed an intermediate differentiation pattern. No heterologous structures were present. Staining for fat was positive on both cell components. Immunohistochemistry revealed EMA negative tumor cells, cytokeratines (AE1/3) were positive in Sertoli cells of tubular tumor structures (Figure 2). Immunohistochemical examination using antibodies against vimentin was highly positive in intersticial Leydig cells and focally also in Sertoli cells. (Figure 3). Tumor cells were also positive for antibodies against calretinine (Figure 4) and moreover positive reaction with antibodies against alfa-inhibine. Focal positivity in Sertoli cells was observed using staining for antibodies against CD 99 and CD 10. Histological staining using oil red was positive in both cell components (Figure 5). Crystals of Reinke were present in Leydig cells. Mitotic activity was very low – 3 mitosis/10 HPF.

DISCUSSION

Sertoli-Leydig tumor belongs to a group of rare and mostly unilateral ovary tumors. It occurs at young age (mean age of patients is 25 years). Only 10% of these tumors occur in menopause women (Russel *et al.* 2002; Young 2011). Clinical symptoms include virilisation, also amenorhea, hirsutism, breast atrophy as a result of androgen production from this tumor. About half of patients are without endocrine paraneoplastic signs.

In differencial diagnostics it is very important to distinguish this tumor from epithelial tumors (e.g. serous papillary adenomas and carcinomas, endometrioid tumors and mucinous tumors of the ovary). Remarkable positivity of calretinin and alfa inhibin proves the histogenetical origin of this tumor from specific mesoderm. Negativity of epithelial membrane antigen (EMA) in Sertoli-Leydig tumor cells is typical for these tumors (Russell *et al.* 2002; Soslow *et al.* 2006: Young 2011).

It is important to distinguish the tumor from prognostically worse yolk sac tumor, because the microscopic appearance can be similar to Sertoli-Leydig tumors. Immunohistochemical negativity using antibodies against alfa fetoprotein can help exclude this very malignant tumor (Deavers *et al.* 2009).

Negative reaction using antibodies against chromogranin and synaptophysin can help in differential diagnosis against carcinoid.

Intermediary type of Sertoli-Leydig tumor may be distinguished from granulosa cell tumor of the ovary based on microscopic cell appearance of both tumors as well as on endocrine behavior of these tumors (Young 2011).

In general well differentiated Sertoli-Leydig ovary tumors have a very good prognosis. Moderately-differentiated types and undifferentiated types have worse prediction. Presence of heterologous structures in this tumor often leads to metastasis (Deavers *et al.* 2009).

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