Virilizing ovarian fibrothecoma with minor sex cord elements in a 13 year old girl: a rare case

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Abstract

Fibrothecoma accounts for 3-4% of all ovarian neoplasms; it is usually hormonally inac-
tive, but can be estrogenic or sometimes androgenic (11%); it is rare under 30 years. In a very few cases, minor sex cord elements (less than 10% of the tumor area) are present; therefore, it is considered as a separate sub-
group of stromal tumors. The importance of immunohistochemistry in recognizing this kind of tumor has been fully documented, with variable results on inhibin staining, but specific
positivity for calretinin in such cases. We report here the rare case of a 13-year-old child
with ovarian fibrothecoma and minor sex cord stromal elements, who showed negativity
for inhibin and positivity for calretinin.

Introduction

Sex cord stromal tumors represent approxi-
mately only 8% of all ovarian neoplasms, and are composed of granulosa, theca, Sertoli and
leydig cells, together with fibrolasts, singly or in combination. Fibromas and thecomas may
show a significant morphologic overlap, which has led to the use of the term fibrothecoma.
This kind of tumor accounts for 3-4% of all ovarian neoplasms. Another subgroup, which was first described by Young and Scully, comprises fibroma/fibrothecomatosus with minor (<10%) sex cord elements; it is designated as
stromal tumor with minor sex cord elements. On examination, it contains discrete tubules
or small nests of cells resembling granulosa cells, Sertoli cells, or indifferent cells of sex
cord type with or without steroid hormone-cell

type in the spindled stroma. This group is usually hormonally inactive, but functional
differentiation in producing hormones by
luteinized theca cells or leydig cells deter-
mines its course. To the best of our knowledge, only 14 cases
of ovarian stromal tumor with minor sex cord elements have been documented till date, with only 3 cases of fibrothecoma with minor sex cord elements. Even though 11% of fibroth-
ecoma can be androgenic, no case of virilizing fibrothecoma with minor sex cord elements
has been found in the previous literature.

The immunohistochemistry using cal-
retinin, inhibin, vimentin, smooth muscle
actin, CD10, EMA and CK has been found to be
useful in ruling out differential diagnosis of
adenofibromas, Brenner’s tumor and other sex
cord neoplasms. This report enlarge the exist-
ing list of similar uncommon tumors, and

demonstrates superiority of calretinin over inhibin in such cases.

Case Report

A 13-year-old, unmarried, female patient presented with complaints of oligomenor-
rohea, masculinizing features of enlarged clitoris, facial hair, deep voice and rapidly
growing abdominal lump in left side since one
month. Magnetic resonance imaging revealed normal right ovary and a 10-cm neoplastic
isointense to hypointense capsulated mass in the left ovary. Uterus and cervix were unremarkable. Hormonal study showed CA 125-37.5 IU/mL, AFP 8.6 ng/mL, HCG-4 IU/L and testos
teron 1196 ng/mL. Unilateral salpingo-
oophorectomy was done and specimen was
sent for histological examination. Histologically, these cases usually show pre-
dominant luteinized/stereoid cells with less
than 5% area of sertoliform cells

Gross

Received ovarian mass measuring 10 cm in diameter with attached tube. Outer surface
was nodular. Cut surface was solid with focal
cystic and hemorrhagic areas (Figure 1a).

Histology

Sections examined from ovary showed a well-encapsulated mass with proliferation of
plumped, ovoid to spindle cells arranged in
cords, micro and macrotubules (sertoliform
cells of intermediate differentiation) were
seen at the periphery (Figure 1b-d). Reticulin
fibers showed pericellular pattern in spindle
cell area with grouping around sertoliform

cells.

Discussion

Young and Scully were the first to describe
ovarian stromal neoplasms, predominantly
fibromatous or thecomatous tumors, containing
scattered minor sex cord elements (as above) in
less than 10% of the tumor area, with the
age of presentation ranging from 16 to 65
years, with a mean age of 39 years. These
patients generally present with abdominal
pain, bleeding per vagina and adrenal mass-
es, rarely with androgenic features.

However, in the present case, the patient
was only 13 years old, much younger than
usual, and she presented with oligohypomen-
orrohea, masculinizing features and abdomi-
nal lump. These tumors are usually hormonal-

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ly inactive, but have been occasionally associated with estrogenic features, e.g. endometrial hyperplasia or diffuse complex atypical hyperplasia or even adenocarcinoma. In the present case, tumor was hormonally active, but with masculinizing features and without operative correction.

Out of seven reported cases of fibromatous tumors of the ovary by Young et al., five cases were ovarian fibroma with minor sex cord elements. Two of them were luteinized thecomas with steroid-hormone cell types without reinke’s crystalloids, as in this case, and stromal-lyedig cell tumor with steroid-hormone-cell type with reinke’s crystalloids, but sertoliform areas were not described in these two cases unlike this case.

Zhang et al. reported fifty cases of ovarian stromal tumors and found steroid hormone secreting cells in a background of predominant pattern of fibroma/thecoma. He also reported the cases of steroid cells without reinke’s crystalloids, as found in the present case. However, combination of sertoliform cells and steroid cells/theca cells, as in our case, have not been described by them, but only recently by Sherwani et al. (without virilization).

This tumor was highly cellular composed of uniform spindle cells, arranged in sheets and intersecting fascicles, with scant to moderate amount of eosinophilic cytoplasm, elongated nuclei without nuclear atypia or significant mitosis and focal thin collagen with a minor component of sertoliform cells as observed by Sherwani et al. Sex cord elements can vary from fully differentiated granulosa cells to indifferent tubular structure resembling immature Sertoli cells, and form less than 10% of the tumor area as per diagnostic criteria. On immunohistochemistry, the sertolized cells in these tumors show diffusely positivity for smooth muscle actin (SMA), weak expression of vimentin and are negative for epithelial membrane antigen (EMA) and cytokeratin (CK) as also noted by us. Minor sex cord elements have also been reported to be positive for calretinin, CD 56, CD 99, antikeratin antibody KL1 and MIC and negative for Vimentin, SMA and EMA, as in this case. However, inhibin positivity was seen in luteinized cells and not in sertoliform areas and spindle cells, unlike positivity reported by majority. Calretinin has been found to be more specific in sex cord elements and detected even in inhibin negative cells as in this case. The differential diagnosis includes ovarian fibromatosis, adenofibromas, Brenner’s tumor.

Ovarian fibromatosis may closely resemble as they envelopes follicles and their derivatives unlike fibrothecomas where the normal follicles cannot be identified. Ovarian adenofibroma has variable sized, larger and well described glandular elements within the proliferation of fibroblastic cells. Both these entities are inhibin and calretinin negative. Brenner tumor may show an abundant fibrothecomatous or luteinized thecomatous stroma with rounded to elongated, sharply demarcated, and small nests of epithelial cells of transitional cells, mucinous cells or both with a solid pattern or a central lumen, EMA and CK positive. These tumors, like fibromas, are thought to behave in a benign fashion and have a good prognosis.

Alpha inhibin cannot be used alone to identify sex cord stromal cells as found in this case, as calretinin was found to be more superior and specific for these elements. Andra et al. described that bilaterality of ovarian fibrothecoma with bilateral pleurisy is also associated with a particular high elevated serum CA-125, but in the present case there was no contralateral ovary involvement in our case.

The awareness about this entity along with judicious use of immunohistochemistry helps in avoiding misdiagnosis. Incidental presence of sex cord elements in the ovarian stromal tumor needs to be confirmation both by inhibin and calretinin to categories this distinct entity. Rare occurrence of this lesion in younger age group needs to work up properly.

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