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# High cellularity and mitotic activity in a primary ovarian fibro-thecomatous tumor of a young patient: a diagnostic and clinical challenge

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**Summary**

*Purpose of Investigation:* Solid ovarian tumors represent a clinical challenge, in particular in case of young patients who require a fertility sparing treatment. The authors report a case of hypercellular mitotically active ovarian fibrothecoma in a very young woman, successfully treated with a fertility sparing surgery. *Materials and Methods:* A 21-year-old nulliparous woman presented at the present hospital with a 14-cm right ovarian mass, consisting of solid and pseudo-cystic components. There was neither an elevation of tumor markers nor evidence of metastatic disease. A laparotomic right salpingo-oophorectomy was performed. Uterus and left adnexa were preserved. *Results:* The neoplasm consisted of a prevalent population of spindle-shaped elements and of a minor component of cells with wider cytoplasms, attributable to a thecomatous differentiation. The mitotic activity was focally elevated. Cytological atypia was mild to focally moderate. Clear areas of coagulative necrosis were not observed. At present 48 months after surgery, the patient is alive with no evidence of recurrence. *Conclusions:* The authors reported the lesion as a hypercellular and mitotically active fibrothecoma. The uneventful follow-up confirms the low malignant potential of the lesion. Caution is required reporting hypercellular stromal ovarian tumors, in order to avoid overdiagnosis and overtreatment, particularly in young patients.

*Key words:* Gynaecological oncology; General gynaecology; Gynaecological surgery.

## Introduction

There are no certain criteria to predict preoperatively the malignant potential of solid ovarian tumors, so surgical excision and histological diagnosis are mandatory. These tumors represent a challenge for the Gynecologist, in particular in case of young patients who require a fertility-sparing treatment. Also, the pathological diagnosis may be extremely insidious, especially in terms of assessment of the degree of biological aggressiveness, with a relevant impact on clinical management and prognosis.

The authors report a case of hypercellular mitotically active ovarian fibrothecoma in a very young Caucasian woman, successfully treated with a fertility-sparing surgery. The differential diagnosis and the clinical management are discussed, reviewing the most recent literature, with a particular emphasis in prognostic factors influencing treatment decisions and prognosis.

## Case Report

A 21-year-old nulliparous woman with a prior history of cerebellar neuroblastoma successfully treated by craniospinal radiotherapy in infancy and complicated ten years later by a post-actinic intracranial meningioma, that was radically excised, presented at the authors' hospital with persistent pelvic pain and abdominal enlargement. Abdominal ultrasound and pelvic magnetic resonance imaging detected a 14-cm right ovarian mass, consisting of solid and pseudo-cystic components. The serological dosages showed no elevation of tumor markers CA125, CA15.3, CA19.9, CEA or AFP. A laparotomic right salpingo-oophorectomy with peritoneal washing was performed. Intraoperative examination of the frozen sections showed an ovarian stromal neoplasm of uncertain malignant potential. Uterus and left adnexa were preserved.

At scanning magnification, the tumor showed an alternation of hypocellular and hypercellular areas, where mitotic activity was focally elevated, up to nine mitotic figures per ten high-power fields (MFs/10 HPF), with a moderately high proliferation cell index (Ki-67 protein expression in 20% of the cells). Atypical mitoses were not observed. Although submassive thrombosis were focally present in intratumoral vessels, clear areas of coagulative necrosis were not detected (Figure 1a).

The neoplasm consisted of a prevalent population of spindle-shaped elements and of a minor but significant component of cells with wider cytoplasms and prominent nucleoli, attributable to a thecomatous differentiation. Cytological atypia was mild to focally moderate (Figure 1b).

Immunohistochemistry (IHC) was consistent with an ovarian stromal tumor. Peritoneal washing cytology was negative for the presence of malignant tumor cells. Considering the lack of severe cytological atypia or coagulative necrosis, a diagnosis of hypercellular and mitotically active fibrothecoma was formulated.

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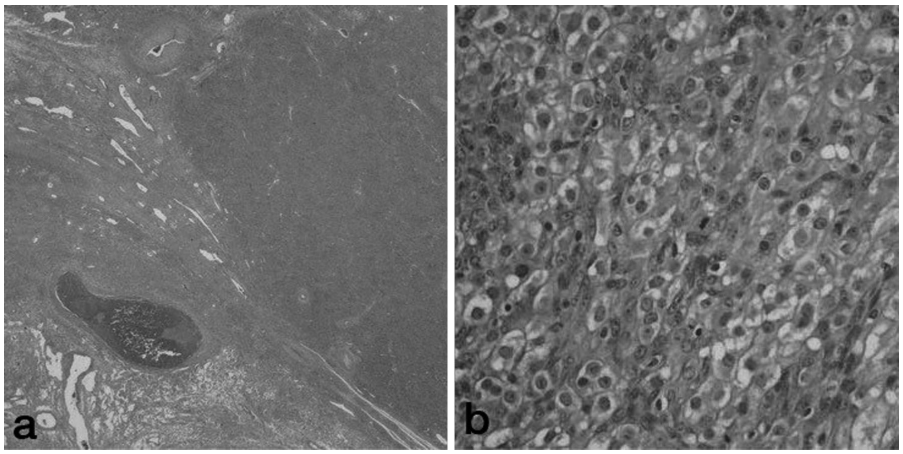


Figure 1. — a) Hematoxylin & Eosin, ×40: pseudonodular pattern of the neoplasm with areas of high cellularity (right side) next to more edematous areas (left side). b) Hematoxylin & Eosin, ×200: area of thecomatous differentiation with nuclear pleomorphism and high mitotic activity.

The present authors set a biannual follow-up consisting of a gynecological examination with transabdominal and transvaginal ultrasound. At present, 48 months after surgery, the patient is alive with no evidence of relapsing disease.

## Discussion

In the present case, laparotomy was preferred to laparoscopy because of the large volume of the tumor. In fact, the laparoscopic morcellation of a tumor with unknown malignant potential could result in the spread of disease and so it should not be performed. Considering the absence of metastatic disease, the young age of the patient, and the impossibility to assess the degree of biological aggressiveness on frozen sections, the lesion was removed preserving the patient's fertility and the diagnosis was deferred to the definitive pathology.

The pathological diagnosis of ovarian stromal tumors presents concerns regarding the correct definition of histotype and the assessment of the degree of malignancy, with a relevant impact on clinical management and prognosis. In 1981, Prat and Scully proposed the diagnostic criteria to assess the malignant potential of these tumors, emphasizing the importance of the mitotic count to diagnose ovarian fibrosarcoma [1]. More recently, Irving reported a series of 75 ovarian stromal tumors with high mitotic count, but lacking severe atypia, better identified as hypercellular and mitotically active fibromas (HMAF), rather than fibrosarcomas [2]. The diagnosis of ovarian fibrosarcoma requires both an increased mitotic activity (>4-10 MFs/10 HPF) and a diffuse cytological atypia. Accordingly, most of the previous reported cases with long-term survival would be more appropriately labeled as HMAF instead of fibrosarcomas, thus explaining their uneventful outcome [3-5].

Mellembakken *et al.* described a thecoma with increased mitotic activity and uneventful outcome, reporting the term "hypercellular and mitotically active thecoma", thus extending to thecomas the same concept applied by Irving *et al.* to HMAFs [6].

Considering the coexistence of fibroma and thecoma features, the high mitotic count and the lack of severe atypia, the present authors reported this lesion as a "hypercellular and mitotically active fibrothecoma". In this case, the evaluation of cellular atypia was even more difficult, because of the presence of the usual cytological pleomorphism in the thecomatous areas [7, 8]. The uneventful follow-up of the patient confirms the low malignant potential of the lesion.

In conclusion, the authors remark the need of caution reporting hypercellular stromal ovarian tumors, especially in presence of a thecomatous component, in order to avoid overdiagnosis and overtreatment, particularly in young patients.

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