Case report

Cellular fibroma in the Douglas cavity, mimicking a malignant neoplasia: fibroma, fibrosarcoma or mitotically active cellular fibroma?

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Key words

Cellular fibroma • Fibrosarcoma • Mitotically active cellular fibroma

Summary

Introduction. Ovarian fibroma is a benign stromal tumour composed of spindle/ovoid fibroblastic cells producing collagen. Approximately 10% of fibromas are densely cellular with small amount of collagen. In these cases, if mild nuclear atypia is present, they are best addressed as cellular fibroma. However cellular fibroma may show a greater mitotic activity and therefore they should be referred as mitotically active cellular fibromas. Mostly benign, it is necessary to differentiate them from malignant tumours such as fibrosarcomas.

Methods. We report a case of an unusual presentation of mitotically active cellular fibroma, detected in the Douglas cavity of a young woman, with normal appearing ovaries and uterus, mimicking a malignant neoplasia clinically and on imaging. In fact abdominal mass may be associated with acute pain, resulting in clinical emergency, really difficult to distinguish from a frank malignancy, before surgical procedure.

Results. We described the clinical, radiological and pathological characteristics of our case and we make a comparison of what previously described in literature.

Discussion. The differential diagnosis among those entities is based on the microscopic features such as atypia and the number of mitoses. However, according to their dimensions, it may be necessary to generously sample these tumours and sometimes, to perform a panel of immunohistochemical markers, in order to make a correct diagnosis, establish the best treatment and the right follow-up. In fact, the prognosis is not certain, due to the possible recurrence, especially if not completely excised.

Introduction

Ovarian fibroma is a benign sex cord-stromal tumor, accounting for 4-5% of all ovarian neoplasms 1. Mostly occurring during peri and postmenopause, the median age is about 52 years, very rare in children. Lesions tend to be asymptomatic. If symptoms are present, the most common is abdominal pain 1-3. Clinically, acute pain due to an abdomino-pelvic mass, is a common clinical emergency and difficult to differentiate from malignant lesion 4. Diagnosis is usually made by ultrasonography showing a solid ovarian lesion, or, on some occasions, mixed tumors with solid and cystic components 1. On gross pathology, they are firm and white or dark in color. On microscopic examination, ovarian stromal tumors composed of a pure proliferation of fibroblastic cells are fibromas, cellular fibromas (CFs), and rarely, fibrosarcomas 5. CFs are characterized by higher cellularity however, increased mitotic activity and sometimes nuclear atypia may be present raising the necessity to differentiate it from fibrosarcomas.

To better classify these lesions in 1981 Prat proposed histologic criteria for the distinction of CFs from fibrosarcomas 2. According to Prat, CFs were characterized by cellular proliferation of fibroblasts with mild to moderate nuclear atypia and mitotic count of ≤ 3 mitosis/10 HPF 2, and a low malignant potential. In contrast, fibrosarcomas were usually associated with severe nuclear atypia, ≥ 4 MFs/10 HPFs, and an aggressive clinical course 3.
Nevertheless, recent studies demonstrated that patients with ovarian fibroma with high mitotic rate had a good clinical outcome and therefore cellular fibromatous neoplasms with weak nuclear atypia should be subclassified in CFs or mitotically active cellular fibroma (MACFs), based on the number of mitotic figures. We report a challenging case of a pelvic mass detected in a young woman with normal appearing ovaries and uterus, mimicking a malignant neoplasia.

Case presentation

A 40 years old nulliparous woman came to clinic for menstrual irregularities, abdominal distention and acute pelvic pain. Clinical examination raised the suspicion for a large mass mainly solid, with minimal mobility. Ultrasonography revealed the presence of a voluminous solid pelvic mass, with some cystic areas and magnetic resonance imaging (MRI) confirmed the finding of a large lesion measuring 20 cm in maximum diameter. No obvious connections between the lesion, the uterus or the gastrointestinal tract were identified. No lymph node swelling or distant metastases were found. Tumor marker levels in the serum were within the normal range. Upon laparotomy, a solid mass was found in the Douglas cavity, minimally connected to the right ovary. However, both ovaries and the uterus were normal and there was no sign of peritoneal implants. Gross pathology revealed a tumor weighing 550 gr and measuring 23 x 11.7 x 5.8 cm. The external surface was yellow and the tumor was partially covered by a serosal surface and surrounded by a thin capsule, without any sign of rupture. Serially sliced, the tumor has a variegated appearance with solid and cystic areas, filled with a gelatinous and mucinous material. There was no clear evidence of necrosis.

Frozen sections was performed showing non-atypical spindle cells, arranged in storiform pattern with no evidence of high mitotic rate or atypical mitotic figures. The diagnosis was of fibrothecoma and, in agreement with surgeons, uterus and ovaries were not removed to preserve patient fertility.

The remaining material was fixed in formalin, processed and stained with hematoxylin-eosin. To adequately sample the lesion 30 blocks were obtained (approximately one block for every cm of maximum dimension). Microscopic examination showed a spindle cell tumor within which focal highly cellular areas, with mild nuclear atypia, were identified (Fig. 1). Cystic degeneration was present, 4 mitosis in 10 HPFs were counted but there was no evidence of necrosis (Fig. 2). Immunohistochemical analysis were performed to further characterize the lesion. The tumor cells show positive staining for vimentin, CD34, CD56 and PR (Fig. 3). They were negative for pankeratins, calretinin, S100, smooth muscle actin (AML), CD 10, synaptophysin and chromogranin (Fig. 4). MIB-1 was positive in 5% of the cells (Fig. 5).

Discussion

Abdominal pain with an associated pelvic mass is a common emergency. Ovarian tumours and uterine myomas are the most common lesions found in the female pelvis. However, only with clinical evaluation, it may be really difficult, to establish if the tumor is benign or malignant. In certain cases, cystic degeneration of fibromas has been reported to lead pre-operative misdiagnosis of malignant ovarian tumors. In a previous paper, Adad et al. described a similar case of a woman with a final diagnosis of cellular fibromas who came to clinicians for gastrointestinal disease. Our patient was admitted to the accident and emergency department for the acute abdominal pain. After radiologic evaluation, she was referred to gynecologic department for a suspicious volu-
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minous pelvic mass detected on imaging. However onco-
logic markers (CEA, Ca 19,9 and Ca 15,3) were negative
and there was no evidence of serous effusions.
In contrast to our case, Adad et coll. described a cellular
fibroma with a prominent multicystic component filled
with mucinous-content. The tumor that we describe,
instead, is mainly solid with only small cystic components
filled with gelatinous material. However, in both cases
the radiological suspect was of an ovarian, mucinous tumor 6.

On frozen section the diagnosis was of fibrothecoma,
but of course only some sections of the solid compo-
nent were examined. The patient was treated according
to her age, clinical and surgical evaluation, gross pathol-
ogy and frozen section result. Therefore to preserve her
fertility, only the mass was removed and adjacent organs
left in situ.

Regarding the prognosis, cellular fibroma has an uncer-
tain malignant potential, capable of aggressive growth,
especially if incompletely excised. The mitotic count is
considered the most useful predictive marker, but in oth-
er studies, the completeness of excision has been con-
sidered important as well as the mitotic activity 2,3,5,6.
The main differential diagnosis is fibrosarcoma, a ma-
lignant mesenchymal tumor derived from connective
tissue. It is characterized by the presence of spindle cells
in a storiform pattern with different degree of differenti-
ation: low, intermediate and high grade. Depending on
the grade of differentiation, tumor cells may resemble
fibroblast or being anaplastic cells with severe atypia 7.
According to literature data, the mitotic activities, the
presence of necrosis and the grade of cellular atypia are
considered the main criteria for a diagnosis of malign-
nancy 5. In our case, we did not find any necrosis, mild
nuclear atypia was detected only in focal highly cellular
areas and we counted 4 mitoses in 10 HPF. However,
we also performed the Ki67 (MIB-1) immunostaining,
in order to evaluate the proliferation index. Usually, cel-

cular fibroma shows less than 3% of MIB-1 positivity.
In our case, 5% of the tumor cells were positive. Some
authors described that mitotic activity and MIB-1 posi-
tivity were considered important prognostic factors 8.
In particular, Haung et al. in a retrospective study, con-
cluded that cellular fibromas are characterized by low
rate of mitosis (maximum 3 mitoses/10 HPF) and MIB-
1 (2-3%) as well as the presence of cellularity and no
evidence of rupture or aggressive clinical behavior 8,9,10.
In this case, we found 4 mitosis in 10 HPF, but the MIB-
1 staining was strong and higher than 3%. We did not
have sign of rupture of the tumor or adhesions and we
found no more than mildly cellular atypia, in focal high-
ly cellular areas.

In a large retrospective study, Irving et al. reviewed the
characteristics of fibroma and fibrosarcoma, describ-
ing also another entity: “mitotically active fibroma”
(MACF). In their series, cellular fibromatous neoplasms
with bland cytology and elevated mitotic count (more
than 4 mitoses in 10 HPF) are associated with good out-
come. This entity should be referred as MACF. How-
ever, they suggested a long-term follow-up for these
patients in order to exclude recurrences 5. In the present
case, 30 months after surgery, patient is still alive with-
out any recurrences.
A panel of immunohistochemical markers have been
performed to better characterise the lesion. The tumor
cells stained positive for vimentin, CD34, CD56 and PR.
They were negative for the following markers: panker-
tins, calretinin, S100, smooth muscle actin, CD 10, sin-
aptothsin and cromogranin. So that, we could exclude
mesothelial, neural, smooth muscle, neuroendocrine and
endometrial stromal differentialiations. The positivity for
CD56 and PR suggested the probably ovarian origin of
the mass 11, in fact it was removed from the Douglas
cavity and it did not show any connection with the sur-
rounding structures.
According to the morphology, the mitotic rate and the
immuno profile, we concluded that it was a MACF and a prolonged follow-up advised. In conclusion, it is difficult to make a right diagnosis of a pelvic mass with clinical evaluation only. In particular, in young women, the nature of the tumor is important to choose the type of surgery (ie. ovary-preserving surgery). However, sometimes, only after generously sampling of the tumor, and a wide immunohistochemical profile, it is possible to assess the best treatment and follow-up for each patient.

References


