A Unique Fibrous Tumor of the Ovary: Fibrosarcoma or Mitotically Active Cellular Fibroma?

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Abstract. A unique fibrous tumor of the ovary is reported. A 32-year-old nulliparous woman was diagnosed with a left ovarian tumor and underwent left salpingo-oophorectomy. Macroscopically, the cut surface of the tumor showed yellowish multilobular areas. There was no sign of necrosis or hemorrhage within the tumor. Microscopically, the tumor consisted of two well-circumscribed components. One corresponded to the yellowish lobular areas; there were more than 10 mitotic figures per 10 high-power fields and strong staining for Ki-67, suggesting fibrosarcoma, but nuclear atypia was not severe. In the other component, there were few if any mitotic figures; there was no nuclear atypia and marked cellularity. Pathologically, the tumor was considered a variant fibrosarcoma or a mitotically active cellular fibroma. In light of these pathological findings along with the patient’s age and obstetrical history, no further treatment was performed. There has been no evidence of recurrence after 1-year follow-up.

Ovarian fibrosarcoma is a very rare tumor that originates from the ovary (1). Mitotic activity is reported to be the most important factor in diagnosing fibrosarcoma; the nuclear grade together with cellular pleomorphism is not particularly reliable (2). However, a recent study (3) has indicated that a considerable percentage of patients with ovarian fibrous tumors showing a large number of mitotic figures have favorable clinical outcomes. Herein, we report a patient with a rare ovarian fibrous tumor with a large number of mitotic figures but without severe nuclear atypia. Interestingly, the tumor consisted of two components, one of which was mitotically active and the other was mitotically inactive.

Case Report

A 32-year-old nulliparous woman was admitted to our hospital with a complaint of lower abdominal pain. Upon abdominopelvic examination, a solid, movable mass with accompanying tenderness was noted in the left lower quadrant. Serum tumor marker levels (CA125, CEA) were within the normal range. A 6.6x6.0x4.4 cm solid mass was detected in the pelvis by magnetic resonance imaging (MRI) (Figure 1). The tumor had no continuity with the uterus or the digestive tract. Computed tomography (CT) examination revealed no lymph node swelling or sign of distant metastasis.

Upon laparotomy, a left ovarian tumor was found and standard left salpingo-oophorectomy was performed subsequently. The right ovary and the uterus appeared normal and no peritoneal dissemination was observed.

Macroscopically, the left ovary was 6.6x6.0x4.4 cm and firm. The capsule was intact, showing no infiltration. Incision of the tumor revealed multiple yellowish lobular areas of various sizes. The lobules were well demarcated from the surrounding whitish areas (Figure 2). Demarcation of the two components was clear on a hematoxylin and eosin (H&E)-stained specimen (Figure 3). There was no sign of necrosis or hemorrhage on the cut surface.

Microscopically, the tumor consisted of two well-circumscribed components. In the yellowish lobular component, there were 17 mitotic figures per 10 high-power fields (HPFs) (Figure 4A, B). The other components, the surrounding whitish areas, had higher cellularity, but the mitotic count averaged less than 3 per 10 HPFs and there was very little nuclear atypia (Figure 4A, C). Demarcation of the two components was very clear. No necrosis or hemorrhage was observed in the background, and nuclear atypia was mild. There was no capsular invasion or capillary space involvement.

Immunohistochemical analysis results of the two components of the tumor are shown in Table I. Interestingly, Ki-67 staining was strongly positive in the areas where...
mitotic figures were numerous, but was completely absent in the areas where mitotic figures averaged fewer than 3 per 10 HPFs (Figure 5A-C).

In light of these pathology findings and the patient’s age and obstetrical history, no further treatment was performed. There has been no evidence of the disease for one year after surgery.

**Discussion**

The most noteworthy finding in our case is the fact that the tumor consisted of two well-circumscribed components. In one component, mitotic figures numbered more than 10 and staining for Ki-67 was strongly positive, suggesting fibrosarcoma, but nuclear atypia in this component was not severe. In the other component, pathology findings were entirely different. There were few, if any, mitotic figures and there was no nuclear atypia. However, prominent cellularity was observed.

In 1981, Prat and Scully (2) found mitotic activity to be the most important factor in diagnosing ovarian fibrosarcoma; nuclear grade together with cellular pleomorphism was not particularly reliable. They suggested that a tumor containing fewer than 3 mitotic figures per 10 HPFs should be diagnosed as a cellular fibroma; a tumor containing more than 4 mitotic

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**Table 1. Results of immunohistochemical analysis of the two components of the tumor.**

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<tr>
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<th>Mitotically active area</th>
<th>Mitotically inactive area</th>
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<tbody>
<tr>
<td>Ki-67</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>SMA</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>HHF35</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>Vimentin</td>
<td>+</td>
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<tr>
<td>PR</td>
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<td>Desmin</td>
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+, positive; ±, slightly positive; –, negative. SMA: smooth muscle actin; PR: progesterone receptor; ER: estrogen receptor; HHF35: anti-muscle-specific actin (clone; HHF35).
figures per 10 HPFs should be diagnosed as a fibrosarcoma (2). However, subsequent case reports (4-9) have suggested that such tumors with a high number of mitotic figures often have favorable outcomes. In the majority of these cases, the diagnosis was based on a mitotic count of 4 or more mitotic figures per 10 HPFs, but importantly, nuclear atypia was reported as mild to moderate.

Immunohistochemical staining for Ki-67 antigen is used to assess the proliferative activity of various tumors and the Ki-67 labeling index is reported to be related to other prognostic factors in case of soft tissue sarcoma (10). In 1997, Tsuji et al. (10) reported that the MIB-1 (Ki-67) labeling index and proliferative index by DNA flow cytometry, which were higher in fibrosarcomas, could also be used in the differential diagnosis of ovarian tumors especially in cases with 3-4 mitotic figures per HPF. This finding has been confirmed by others (5, 9, 11). In our case, Ki-67 staining was strongly positive: positivity for Ki-67 was observed in 50% of tumor cells in the areas with large numbers of mitotic figures, but it was completely absent in the other areas, and the demarcations were clear.

A recent large study (3) has suggested that cellular fibromatous neoplasms of the ovary with weak nuclear atypia should not be classified as fibrosarcomas, even though they show more than 10 mitotic figures per 10 HPF. Such tumors with weak nuclear atypia are to be subclassified as either cellular fibromas or mitotically active cellular fibromas, depending on the number of mitotic figures. This is based on the fact that there was no recurrence in 18 patients with mitotically active cellular fibroma, including 3 with ovarian surface adhesions or extraovarian involvement.
In summary, ours may be a case of mitotically active cellular fibroma. Therefore, we have not performed any further treatment. However, there have been no previous reports of a tumor such as this patient’s with clear demarcation between the two components, one with a large number of mitotic figures and strongly positive staining for Ki-67, and the other with only a few mitotic figures and no staining for Ki-67. These findings raise the question whether the tumor in our case is a fibrosarcoma. Like the subtyping required for uterine smooth muscle tumors (12), more detailed classification may be necessary for fibrous tumors of the ovary.

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References


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