Malignant fibrous histiocytoma of the ovary: a case report

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Summary

Malignant fibrous histiocytoma (MFH) is the most common soft-tissue sarcoma of late adult life occurring predominantly in the extremities and the retroperitoneum. MFH of the ovary is very rare, with only six cases previously reported. A 67-year-old woman with a right pelvic tumor highly suspicious of ovarian carcinoma was submitted to exploratory laparotomy. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, pelvic and paraaortic lymphadenectomy with right hemicolectomy along with permanent cutaneous ileostomy were performed. Since a storiform-pleomorphic type of MHF was diagnosed from histopathological and immunohistochemical findings, chemotherapy was proposed as the postoperative treatment. Despite extensive surgery with negative surgical margins, the patient had recurrence of the tumor within four months, and was submitted to secondary surgery. A combination of chemo- and radiotherapy was performed postoperatively, but the patient developed respiratory problems and died one year later from the primary diagnosis.

Key words: Malignant fibrous histiocytoma; Ovary; Storiform-pleomorphic type; Prognosis.

Introduction

Malignant fibrous histiocytoma (MFH) is the most common type of soft tissue sarcoma (about 20-25%) in adults and tends to occur in the deep soft tissue of the extremities and retroperitoneum [1].

Malignant fibrous histiocytoma was first described as a separate entity in the category of soft tissue sarcomas by O'Brien and Stout as "malignant fibrous xanthoma" in 1964 [2]. The origin of the tumor cells is still unclear and a matter of ongoing debate, but the term is reserved for a small number of undifferentiated high-grade pleomorphic sarcomas. MFH is very diverse with five distinct subtypes: storiform-pleomorphic, myxoid, inflammatory, giant cell and angyomatoid [3].

Primary MFH of the ovary is extremely rare, with only six previously reported cases [4].

The management of MFH is controversial because of the heterogeneous nature of the disease. Surgical resection of all macroscopic disease is independently associated with improved disease-specific survival, and adjuvant chemotherapy and radiation could be acceptable alternatives if the surgical margins are tumor-free [4].

The prognosis is usually poor in the cases of intraabdominal and ovarian localization because the tumor is usually diagnosed in advanced stage, with a high percentage of local recurrences and systematic metastatic disease with surgical therapy as the only reliable method [5].

We report an usual case of a woman with a right ovarian tumor infiltrating the ileum and cecum, diagnosed after exploratory laparotomy as MFH.

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Case Report

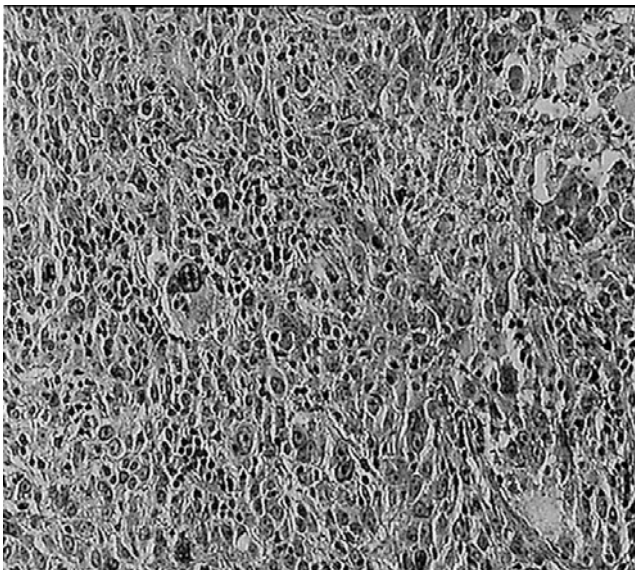
A 67-year-old, gravida 4, para 1, abortus 3 woman presented with abdominal distention and pain, and mild anemia together with a suspicious right adnexal and iliac mass. She was referred to our Oncology Unit in November 2005. The complaints had started two months before and had aggravated gradually, especially the abdominal pain and distention. Her personal medical history revealed arterial hypertension and chronic compensatory myocardiopathy. Her past surgical history included operative resection of an uterine leiomyoma 30 years before.

A 11.5 x 5.5 x 6.5 cm, solid, heterogeneous mass with irregular margins was discovered in the right adnexal region with a small amount of ascites using sonography. A 12 x 5.5 x 6.8 cm, lobulated heterogeneous mass in the right adnexa was found infiltrating the ileum, cecum and ascending colon with suspected breakthrough into the cecal lumen, but no tumoral implantation on the peritoneum and omentum was detected by computed tomography (CT) scan.

The serum level of CA 125 was 77.2 IU/ml (0-35 IU/ml), while other markers - CEA, CA 19-9, CA 15-3, and alpha feto protein were within reference range. Laboratory tests revealed moderate anemea a with a normal platelet count (361000/mm^3) and white blood cell count of 113000/mm^3; all the other parameters were normal. The RTG scan of the thorax showed no pathological findings, whereas abdominal ultrasound (US) plus pelvic pathology detected a cystic formation with a diameter of 10 mm in the right hepatic section.

The initial diagnosis was suspicious for advanced right ovarian carcinoma. The patient underwent exploratory laparotomy due to a right adnexal and retrouterine mass highly suspicious of malignancy. Exploratory laparotomy was performed and a large, solid, lobulated, necrotic, grey-yellowish tumor about 120 mm in the largest diameter was found occupying the right adnexal and iliac space infiltrating the cecum and ascending colon, approximately 160 mm in length, and the uterine surface with a small amount of ascites. The left ovary and the left uterine tube were normal and all seemed completely independent of the mass. On the uterine surface the infiltration of the tumor was evident in the right half and anterior uterine wall. On gross examination the surface of the liver, spleen, and peri-

Fig. 1



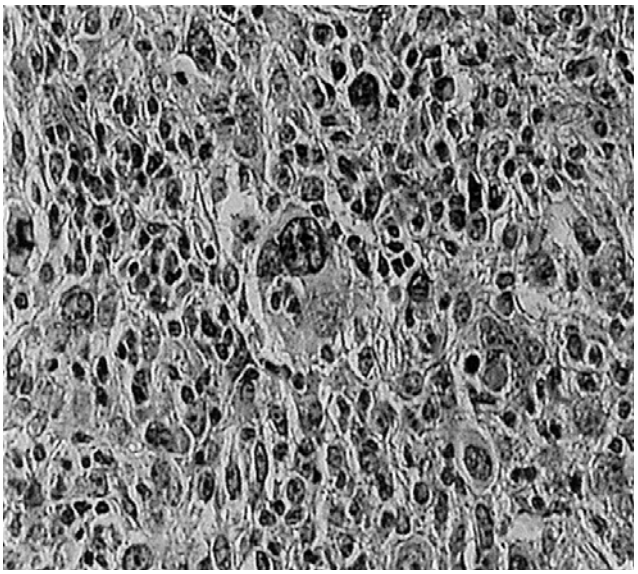


Fig. 2

Figure 1. — Malignant pleomorphic cells proliferating in an epitheloid arrangement and atyical spindle shape cells in storiform pattern admixed with giant cells (hematoxylin and eosin, 200 x).
Figure 2. — Giant, multinuclear, multilobulated tumor cells with bizarre appearance are scattered throughout storiform pattern of pleomorphic cells (hematoxylin and eosin, 200 x).

toneal surface was without implants or deposits. There was about 100 ml of serous ascetic fluid, and specimens of peritoneal washings for cytology were also taken.

Total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, pelvic and paraaortic lymphadenectomy with right hemicolectomy along with permanent cutaneous ileostomy were performed.

The histopathological examination of the specimen revealed highly undifferentiated sarcoma or carcinoma sarcoma of the right ovary highly resembling MFH. In part of the ileum, the tumor was infiltrating the whole diameter of the bowel wall, with subsequent penetration into the lumen (from the serosa layer to mucosal layer). All 11/11 iliae lymphatic nodes were negative.

The histopathological report showed a poorly differentiated almost anaplastic solid tumor, with high mitotic activity (63/10 HPF) and atypical mitoses, together with increased cellularity and cytological pleomorphism. A heterogeneous growth pattern consisted predominantly of an epitheloid arrangement of large pleomorphic cells with eosinophilic cytoplasm and multilobulated, hyperchromatic nuclei, together with areas of atypical spindle shaped cells in a storiform growth pattern admixed with the giant cells (Figure 1).

Nuclear pleomorhism was evident, and giant multinuclear tumor cells with a bizarre appearance were scattered through the tumor (Figure 2). An inflammatory component was evident around the tumor, with persistent lymphovascular space invasion in perineural spaces. Tumor necrosis was a common finding in the specimen.

Additional immunohistological staining was warranted to obtain a definitive histopathological diagnosis. Positive staining was recorded for EMA (+), vimentin (+), CD 68 (+), S-100 (+) only in intertriginous cells, CD 3 (+), inflammatory component, while other markers were negative (AE 1/AE 3 (-), CK 7 (-), CK 20 (-), CD 34 (-), CD 117 (-), SMA (-), desmin 8 (-), CD10 (-), CD 20 (-), CD 21 (-), CD 30 (-), CD 35 (-) and Ki index 55%).

The definitive pathology diagnosis showed a pleomorphic undifferentiated sarcoma involving the right adnexa with no normal ovarian tissue identified. The staining pattern was consistent with a pleomorphic sarcoma (vimentin (+), S-100 (+), CD 34 (-) and suggestive of ovarian stromal origin CD 56 (+). The definitive histopathological diagnosis showed a storiform pleomorphic MFH with inflammatory component. The Coindre score was 8/9 with a G-3 degree of histological malignancy.

The postoperative course was expected to have no complications. Three months following the first laparotomy, while receiving chemotherapy (gemcitabine and docetaxel), the patient complained of bloody vaginal discharge, abdominal distention with pain predominantly in the epigastrium, and fatigue.

An 86 x 70 mm, irregular mass, predominantly cystic in the right pelvic cavity was diagnosed by US. In the right iliac region there was a hetero-dense mass 7 x 5 cm with predominantly expansive growth and close contact with the anterior wall of the rectum and posterior wall of the urinary bladder; no susceptible enlarged lymph nodes were identified by CT scans of the pelvis and abdomen. Recurrence of the tumor in the pelvis and abdomen was treated surgically.

Complete resection of the mass and small bowel (15 cm in length) and terminal end-to-end bowel anastomosis were performed. Postoperative chemotherapy with subsequent radiotherapy was administered. A year after the initial diagnosis was established the patient experienced respiratory difficulties and intermittent chest pain, and subsequently was diagnosed with widespread lung metastasis. Unfortunately, despite aggressive treatment which included two surgeries and adjuvant therapy, the patient died of progressive disease two months later.

Discussion

Today the term malignant fibrous histiocytoma is reserved for a small number of undifferentiated high-grade pleomorphic sarcomas [6]. It accounts for about 20-25% of soft tissue sarcomas, occurring most commonly in the lower extremities (70-75%), followed by the

retroperitoneum in males over 40 years of age (peaking in the 5th and 6th decades).

Histiogenesis of the tumor is still uncertain and remains controversial. It is thought to originate from undifferentiated primitive mesenchyme cells which are capable of multidirectional differentiation [7, 8].

Occurrence of the tumor has been reported in almost all parts of the body including the ovaries. These sarcomas have rarely been documented in the lung, kidney, bladder, stomach, small intestines, ovaries, liver and other soft tissues [9].

The ovary as a primary site of MFH is very rare with only six cases previously reported, including all five subtypes. Intraabdominal MFH is rare, as is MFH of the Mullerian tract, though cases involving the vagina and paravaginal space have been described [10].

The clinical manifestations are dependent on size of the tumor and are very unspecific. The lesions can grow to a large size due to their intraabdominal (retroperitoneal) location before the onset of symptoms which contributes to the delay in diagnosis of the disease.

Preoperative diagnosis of MFH is very difficult and additionally, even at laparotomy, is hardly possible. In most cases the definitive diagnosis is histopathological or immunohistohemical. MHF has no specific or characteristic finding on US or CT scans and MRI. Also, no tumor markers are useful or specific in the case of MFH. Therefore, the pathological diagnosis is a necessity [11].

Pathological diagnosis of soft tissue sarcoma is occasionally difficult as in our case and immunohistochemistry must be employed together with the clinical findings at laparotomy. The initial diagnosis of all six cases of primary ovarian MFH was ovarian carcinoma. Two of the reported cases showed arising MFH from a benign dermoid cyst and one case was associated with an appendicular carcinoid lesion [10]. Surgery was a basic treatment for all cases with additional chemotherapy in four of six cases including cisplatinum, cyclophosphamide, gemcitabine, and docetaxel.

MFH is an aggressive tumor with a high potential of demonstrating metastases to other body parts and with high rates of local recurrence. Metastatic rate varies with histologic subtype: storiform/pleomorphic (20-65%), giant cell (50%), myxoid (23-30%) and inflammatory (25-30%). The incidence of local recurrence of all soft tissue sarcomas except myxofibrosarcoma is reported to be 40% [12]. Patients with MFH have had poor outcomes because of high affinity for local recurrence and hematogenous spread [13].

The American Joint Committee on cancer staging system (in the absence of metastatic disease) uses the histologic grade to define stage, with additional contributions from tumor size and depth. High-grade histology for soft tissue sarcoma is connected with negative prognostic factors for those patients, regardless of the grading system. Patients with high-grade tumors with poor differentiation, cellular pleomorphism, coagulative necrosis, and numerous bizarre mitoses are at considerable risk for metastatic disease, and as many as 50% of these patients die from the disease [1].

Tumor grade, as in most soft tissue sarcoma subtypes, predicts the risk of developing distant metastases, but not local failure. Mortality is associated with histological tumor grade, but also to quality of surgical margins [13].

Radical surgical treatment is still the only therapy with curing possibilities. In most cases resection must be extended to the adjacent organs as well, in order to guarantee radical removal. The primary standard therapy is complete excision with a tumor-free resection margin if possible. Adjuvant treatment with radiotherapy and chemotherapy are brought into question [14].

When surgical resection was the only treating tool, 42% of 200 cases of MFH developed metastases within two years involving the lungs (82%), lymph nodes (32%), liver (15%) or bone (15%), with a 2-year survival rate of 60%. The rate of local recurrence is 44% [15]. The 5-year survival rate after undergoing surgery is 67.2% in contrast to 14% with a 5-year survival rate of patients with abdominal MFH [16].

Pezzi *et al*. in 1992 [17] reported a 5-year disease-free survival of 50.6% among a series of 227 patients who received only surgery (26%) or a combination of surgery with radiation therapy (73%). Tumor size and histological grade are the most important prognostic signs for MHF. The five-year survival rate was reported as 82% if the primary tumor was smaller than 5 cm, while if it was larger than 5 cm to 10 cm, the overall survival was 68%.

The Soft Tissue and Bone Sarcoma Group of the European Organization for Research and Treatment of Cancer has been investigating for more than two decades the role of different chemotherapy protocols for advanced and metastatic soft tissue sarcomas including MHF. The conclusion is that the most active single agent is doxorubicin with response rates of 20-25% and with no multiagent regimen yet proven superior in survival [18, 19].

Factors predictive of poor outcomes in MFH are proposed to be high-tumor grade, tumor size more than 10 cm, the presence of tissue necrosis on histological examination, identification of 19 p chromosomal aberrations and expression of proliferating cell nuclear antigen [10, 20].

Two reports stated that generally large tumor size (more than 5 cm for non-myxoid types, and more than 10 cm myxoid), high grade, deep infiltration beyond the subcutaneous layer and positive resection margins are all poor prognostic factors [5, 15].

In general, prognosis is poor with a 60% survival rate after two years and a recurrence rate of 50-82% in cases of retroperitoneal MFH. The most frequent sites of metastatic spread are the lungs, liver, bone and bone marrow [21].

The number of reported cases of MFH of the ovary is insufficient to form any therapy protocols and references regarding prognosis, thus the only available data concern MHF of other localizations in the body.

Complete surgery with negative resection margins is the treatment of choice in cases of MFH of ovarian origin. As postoperative supplementary treatment, radiation therapy and chemotherapy were involved. Since there are no sufficient reports regarding supplementary therapy for MFH of intraabdominal localization, further investigations are necessary.

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