Giant recurrent mixed-type liposarcoma of the retroperitoneum: report of a case and review of literature

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Abstract: Retroperitoneal liposarcoma is a rare tumor with an incidence of 2.5 per million individuals, especially tumors of mixed histologic pattern. We present a case of a 63-year-old woman with a history of slowly increasing abdominal volume over 2 years. The diagnosis of giant and multiple retroperitoneal mass suspected of liposarcoma was confirmed by computed tomography. The patient underwent resection of 7 tumor masses together weighing 5 kg. The microscopic diagnosis was mixed-type liposarcoma of the retroperitoneum. 8 months after surgery, the patient suffered multiple metastases in the liver and abdominal wall, and upper digestive tract hemorrhage. Although this type of tumor is rarely seen, tumor tissue should be thoroughly gathered and analyzed on histologic examination to reach final diagnosis. Knowledge of the subtype of liposarcoma is important for proper prognosis and treatment of the patient. To the best of our knowledge, this is the first report of mixed-type retroperitoneal liposarcoma with three components described in the English literature.

Keywords: Mixed-type liposarcoma, recurrence, metastases

Introduction

Liposarcomas (LPS), accounting for about 20% of all sarcomas in adults [1], consist of 4 distinct clinicopathologic entities by the World Health Organization: well-differentiated/dedifferentiated LPS (including adipocytic, sclerosing, inflammatory, and spindle cell variants); myxoid (and round cell) LPS, and pleomorphic LPS [2]. Occasionally, some or all of these components combine and they are then called mixed-type liposarcoma, which accounts for 4% of liposarcoma [3]. LPS occurs most commonly in the extremities (52%), followed by the retroperitoneum (19%) [4]. Retroperitoneal liposarcoma is usually symptomless until the liposarcoma is large enough to compress the surrounding organs [5]. It is often misdiagnosed due to its rarity and absence of symptom. Even with complete removal of the liposarcoma, prognosis remains poor. The 5-year survival rate of well-differentiated retroperitoneal liposarcoma is 83%, while it is 20% for the dedifferentiated tumor subtype [6]. According to our best knowledge, there are no literature reports on the prognosis of mixed type liposarcoma. Here, we present a uncommon case of mixed type liposarcoma composed of WDL, MLPS and DLPS, which developed in the retroperitoneum of a 63-year-old woman, followed by review of the literature.

Presentation

A 63 year-old female was admitted to the Department of Surgery, the Affiliated Hospital, Zunyi Medical University (Guizhou, China) in December 2017, due to recurrence of abdominal liposarcoma after 19 months of presenting for operation. This time, the patient presented with abdominal distension and abdominal pain with intermittent blunt pain in the right side for ten days, accompanied by lower extremity edema and right lumbosacral pain. The physical examination indicated a 12×10 cm oval mass with a clear boundary and soft-medium texture in the right abdomen without tender-
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Figure 1. Abdominal computed tomography scan of the patient (CT). A: CT demonstrated a giant mass containing fat density in the right abdomen, pressing into the right kidney and renal capsule in the first relapse; B: CT showed the right liver was compressed by a large mass with mixed density at eight months after first relapse.

ness or rebound tenderness. The laboratory examinations, including routine blood and urine tests, gave results that were within the reference ranges and therefore normal. Computed tomography (CT; Figure 1A) demonstrated a giant mass containing fat density in the right abdomen, pressing into the right kidney and renal capsule; therefore, it was decided surgery was necessary.

During surgery, it was determined that the multiple masses originated from the right abdomen fatty tissue adjacent to the kidney, inferior vena cava, and right liver. These masses had a complete capsule. The patient received complete resection of the liposarcoma and partial resection of inferior vena cava. The diameter of the masses were from 3 centimeters to 20 centimeters in size.

Macroscopic examination of the retroperitoneal multiple masses revealed nodular, soft masses that measured 3.5 to 20 cm in the largest dimension, with complete capsule. These masses were weighed at 2.5 kg. The cut surface was soft, yellow, dark-red, with a focal gelatinous, solid portion, cystic degeneration and hemorrhage (Figure 2). Microscopic examination demonstrated three patterns: the first part had stellate or spindle cells arranged in the shape of herring bone in dedifferentiated liposarcoma (Figure 3A), the second showed “chicken-wire” like pattern on the myxoid stroma (Figure 3B), the third showed most of tumor consisting of mature fat cell-like cells with occasional multivacuolated lipoblasts in the

well-differentiated liposarcoma (Figure 3C). Immunohistochemical staining was negative for S-100 and positive for CDK4 protein in part of the spindle cells (Figure 3D), but was positive for S-100 in part of the mature fat cell-like cells. Definitive diagnosis was mixed-type liposarcoma composed of well-differentiated, dedifferentiated and myxoid areas, each of the components accounting for one third. After follow-up of 8 months, the patient experienced multiple metastases in the liver and abdominal wall, upper digestive tract hemorrhage, and hemorrhagic shock. Computed tomography showed a recurrence of right retroperitoneal fat-derived malignant tumors involving the right lobe, right kidney, left lobe of liver and right anterior abdominal wall (Figure 1B). The hemoglobin content was 34 g/L. The patient was in the hospital, and he has received therapy of tumor arterial infusion chemoembolization. After therapy, the patient was discharged without any complications, and has been well. We plan to follow up the patient every 6 months after discharge.

Discussion

Liposarcoma occurs most in the deep soft tissues of the extremities, trunk, and retroperitoneum. The most commonly diagnosed histologic types of liposarcoma are WDL and myxoid type. In addition, some liposarcomas are composed of two or more histologic types and then classified as mixed-type liposarcoma. Mixed type liposarcomas are exceedingly rare. Only 5% of liposarcomas show an admixture of different histologic subtypes in the same tumor [6]. The present study describes a case of a mixed-type retroperitoneal liposarcoma with areas of WDL, MLPS and DLPS. In order to further dissect the clinicopathologic features of mixed liposarcoma, we present 23 mixed type liposarcomas with complete data in a review of the literature (Table 1).

In our review, 23 cases of mixed liposarcoma, 12 were located in retroperitoneum or abdominal cavity (41%), and the remaining 11 cases
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Figure 2. Macroscopic findings: (A) 7 tumor masses found in retroperitoneum; (B-D) Cut surface: these were gray-white section, cystic hemorrhage, gray-yellow section respectively.

Figure 3. Histologic examination findings: (A) The spindle cells are arranged in the shape of a herring bone in dedifferentiated liposarcoma (×200). (B) The morphologic hallmark of myxoid liposarcoma is the presence of a thin-walled, capillary size vascular network, organized in a distinctive plexiform pattern (×100); (C) Most of tumor consists of mature fat cell-like cells and a few atypical spindle cells or lipoblasts, with occasional multivacuolated lipoblasts in WD (×200). (D) Tumor cells showing diffuse nuclear immunoreactivity for CDK4 in DL (×100).

In the first case reported by Wood and Morgenstern [7], tumor recurrence developed 3 years after surgery for myxoid colon liposarcoma. Some factors have been accepted as indicators of poor prognosis: age >45 years, presence of round cells, necrotic areas within the mass [8], and dissemination of the disease [9]. Our patient is 63 years old female, who after complete mass removal had a first recurrence 19 months after complete primary surgical resection. However, the patient had the second recurrence after one year. In the literature reviews of presentations, all patients were treated with complete surgical resection; however, two cases died of local disease at 29 months and 33
Table 1. Clinical data of 23 patients in the literature review

<table>
<thead>
<tr>
<th>First author</th>
<th>Gender/age</th>
<th>Size (cm)</th>
<th>Location</th>
<th>Treatment</th>
<th>Primary/recurrent</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu [15]</td>
<td>F (54)</td>
<td>&gt;15</td>
<td>Retroperitoneal</td>
<td>CR</td>
<td>Primary</td>
<td>Don’t provide</td>
</tr>
<tr>
<td>Zoran [16]</td>
<td>M (77)</td>
<td>30×15×15</td>
<td>Mesentery</td>
<td>SE</td>
<td>Primary</td>
<td>Died (8 day after the surgery)</td>
</tr>
<tr>
<td>Yoon [17]</td>
<td>M (41)</td>
<td>20×13×10</td>
<td>Ascending colon and retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>Free of disease (24 m)</td>
</tr>
<tr>
<td>Jie [18]</td>
<td>M (46)</td>
<td>No</td>
<td>Left palate</td>
<td>SE</td>
<td>Primary</td>
<td>NED</td>
</tr>
<tr>
<td>Jie [18]</td>
<td>F (28)</td>
<td>No</td>
<td>Left buccal region</td>
<td>SE+PR</td>
<td>Primary</td>
<td>NED</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (47)</td>
<td>12.2×10.8×5</td>
<td>Scrotum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (10 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>F (61)</td>
<td>25×20×20</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (32 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (65)</td>
<td>15×12.5×7</td>
<td>Buttock</td>
<td>SE+RT</td>
<td>Primary</td>
<td>NED (11 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>F (78)</td>
<td>22×17×11</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (34 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (39)</td>
<td>Fragmented Scrotum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (60 mo)</td>
<td></td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>F (35)</td>
<td>Fragmented Abdominal cavity</td>
<td>SE</td>
<td>Primary</td>
<td>Dead of local disease at 29 mo</td>
<td></td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>F (44)</td>
<td>Large</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Recurrent</td>
<td>Lung metastasis at mo; LR at 84 mo, alive with unresectable disease at last follow-up</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (84)</td>
<td>27×17.5×10</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>Died of unrelated causes at 14 mo</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (56)</td>
<td>16.5×15×14</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (11 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>M (69)</td>
<td>35×29×20.5</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (12 mo)</td>
</tr>
<tr>
<td>Jennifer [19]</td>
<td>F (73)</td>
<td>15×6.8×4</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Primary</td>
<td>NED (7 mo)</td>
</tr>
<tr>
<td>Miguel J [21]</td>
<td>M (68)</td>
<td>17.5×13×14</td>
<td>Posterior mediastinal</td>
<td>SE+adjuvant chemotherapy</td>
<td>Primary</td>
<td>Died (3 mo later)</td>
</tr>
<tr>
<td>KUC [22]</td>
<td>M (76)</td>
<td>9×5×5</td>
<td>Left upper arm</td>
<td>SE</td>
<td>Primary</td>
<td>Don’t provide</td>
</tr>
<tr>
<td>Shashikant C.U [23]</td>
<td>M (45)</td>
<td>6×5.5×5</td>
<td>Thigh</td>
<td>SE+adjuvant chemotherapy</td>
<td>Primary</td>
<td>Alive with metastatic disease</td>
</tr>
<tr>
<td>The present case</td>
<td>F (64)</td>
<td>64</td>
<td>Retroperitoneum</td>
<td>SE</td>
<td>Recurrent</td>
<td>Two relapses, liver metastasis, alive with unresectable disease at last follow-up</td>
</tr>
</tbody>
</table>
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months, 2 cases died of unrelated causes at 8 days and 14 months, and 2 cases had lung metastasis at 60 months and 15 months. The case we reported had multiple liver and abdominal wall metastases at 8 months. These data suggest that mixed liposarcoma is a highly malignant tumor, and despite the complete removal of the mass, prognosis is guarded.

CT scan and magnetic resonance imaging are the best preoperative investigations for evaluation. The histopathologic diversity of a mixed liposarcoma may cause misdiagnosis in cytology and small biopsy. The final diagnosis of liposarcoma is dependent on the pathologic and immunohistochemical analyses, and some ambiguous cases require molecular biological detection. In our case, the patient suffered upper digestive tract hemorrhage owing to multiple metastases in the liver and abdominal wall. The CT scan demonstrated a giant mass containing fat density. Microscopically, the grey-white region was dedifferentiated liposarcoma, the grey-yellow region was well-differentiated liposarcoma, and the gelatinous region was myxoid liposarcoma. Pathologic sampling from different parts are necessary to avoid misdiagnosis.

A treatment protocol has not been established because of the small number of reported cases. Surgical resection is still the main method of treatment of retroperitoneal liposarcoma; complete resection to the naked eye is the goal of surgical resection clean, encroaching upon the viscera of multi-visceral resection. The effects of chemotherapy for liposarcoma are unknown [10], but radiotherapy has been shown to affect survival rates [11]. The patient was discussed with an oncologist and no adjuvant therapy was recommended but it was suggested that regular clinical follow-up every 6 months is needed. Prognosis of patients with mixed-type liposarcoma is based on the most aggressive type found in the tumor, which, in our case, was dedifferentiated liposarcoma.

However, mixed-type liposarcoma poses conceptual problems and clinical problems when stratifying patients for treatment. Jeung [12] demonstrated multiple genes are differentially expressed in mixed-type liposarcoma and suggests that these genes are associated with differences in the morphological characteristics and pathogenesis of mixed type liposarcoma. Morphologic heterogeneity as seen in mixed-type liposarcomas is then very likely explained by different levels of maturation within a single developmental pathway from an undifferentiated stem cell [12]. The latest literature shows that the mixed-type liposarcomas are thought mostly to be unusual examples of dedifferentiated liposarcoma, based on currently available immunohistochemical and molecular studies [13]. Therefore, mixed-type liposarcomas should not be regarded as collision tumors, but as an extreme variant of the morphologic spectrum within a single biological entity, explaining the biological contradiction of mixed-type liposarcoma [12]. However, in our presentation, the case contained a component of myxoid liposarcoma and dedifferentiated liposarcoma.

One paper reported that there are different molecular changes between myxoid liposarcoma and well differentiated liposarcoma or dedifferentiated liposarcoma in mixed type liposarcomas, which should not be explained as being a collision tumor [14]. Jeung [12] demonstrated multiple genes are differentially expressed in mixed-type liposarcoma and suggests that these genes are associated with the differences in the morphologic characteristics and pathogenesis of mixed type liposarcoma. We speculate that mixed-type liposarcoma may show a worse prognosis, but there are no more data to support this prediction. More in-depth studies should be carried out to better understand this type of tumor.

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Disclosure of conflict of interest

None.

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