Case report

MALIGNANT METASTASIZING SOLITARY FIBROUS TUMORS OF THE LIVER: A REPORT OF THREE CASES

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Solitary fibrous tumors are rare neoplasms of mesenchymal origin that have been reported in various other extrathoracic sites, including the liver. We present a case series of three malignant solitary fibrous tumors of the liver, occurring in two women 74 and 80 years old and one 65-year-old man. No clinical features were predictive of malignancy except the large sizes and synchronous presence of lung metastases in two of the three cases. Histological examinations revealed the presence of high pleomorphic cellularity with nuclear atypia, necrosis and high mitotic ratios. All patients died of disease progression.

Key words: solitary fibrous tumor, liver, malignancy, metastases.

Introduction

Solitary fibrous tumors (SFTs) are uncommon, fibroblastic neoplasms that most often arise in middle-aged adults. First described as distinctive pleura-specific tumors, SFTs are now known as anatomically ubiquitous [1, 2]. Patients are commonly asymptomatic, though large tumor size or vital structure involvement may lead to local or paraneoplastic symptoms such as dyspnea, cough, abdominal pain or hypoglycemia [3-7]. The latest edition of the World Health Organization (WHO) classification of soft tissue and bone tumors considers hemangiopericytoma as an obsolete synonym of SFT [2]. Most SFTs are benign. However, in about 10% of cases, they are aggressive and may show local or distant recurrences even many years after resection [2, 6]. The mainstream treatment for SFTs is surgery, the benefits of adjuvant radio-chemotherapy being currently controversial [3-5, 8]. We herein present a case series of malignant SFTs of the liver. Clinical and histological features of these cases are discussed.

Case histories

Case 1: A 74-year-old woman was admitted to hospital with right abdominal pain associated with abdominal distension. Computed tomography (CT) angiography showed a well-circumscribed 24 × 16 cm mass entirely involving the right lobe of the liver, characterized by peripheral enhancement in the arterial phase and dislocated hepatic vessels. Due to tumor hypervascularization, a giant hemangioma was hypothesized. The patient underwent surgical resection of the mass, which was grossly firm, grayish-white, focally myxoid and hemorrhagic, apparently capsulated. Resection margins were free. Histology revealed a lesion composed of spindle and ovoid cells arranged in a storiform pattern. Hypercellular areas with nuclear crowding, nuclear pleomorphism and cytological atypia were observed in different slides as well as necrosis. Hemorrhagic areas and increased mitotic activity (9 mitotic figures per 10 high power fields) were also noted. Immunohistochemically, the tumor was positive for vimentin, CD34, STAT6 and Bcl-2 but negative for cytokeratins, desmin, CD117,
CD99, CD10, platelet-derived growth factor receptors (PDGFR-α or PDGFR-β). The percentage of Ki-67 positive tumor cells was about 40%. Based on these results, the tumor was defined as a malignant liver SFT. Total body CT scans one, three and five months after surgery were unremarkable. However, after nine months, multiple nodules (less than 1 cm in diameter) were disclosed in the lungs and omentum as well as the mesenteric and abdominal walls. Given the suspicion of metastases from the primitive malignant SFT, multiple biopsies were performed and indeed confirmed this diagnosis histologically. The patient subsequently underwent chemotherapy, which was unsuccessful, and died six months thereafter.

Case 2: An 80-year-old female patient with dyspnea, cough, asthenia and abdominal pain was admitted to hospital for diagnostic evaluation of a large liver hypoechoic mass of the right lobe previously detected by regular surveillance ultrasound. The patient’s surgical history included a right mastectomy for a ductal infiltrating carcinoma grade 1. Subsequent CT angiography revealed a well-demarked, highly vascularized lesion measuring 19 × 15 cm in the right hepatic lobe that apparently involved the apical segment of the inferior right pulmonary lobe. The hepatic vessels, right renal vein and right kidney were displaced and compressed. An ultrasonography (US)-guided biopsy was performed. Histology revealed a highly cellular tumor composed of spindle cells with evident pleomorphism, high mitotic activity (7 or more mitotic figures per 10 high power fields), necrosis and hemorrhage. Tumor cells were positive for CD34, vimentin, STAT6 and Bcl-2 but negative for cytokeratin, desmin, CD117, CD99, CD10, PDGFR-α or PDGFR-β. The percentage of Ki-67 positive tumor cells was about 30%. The tumor was defined as a malignant liver SFT. Surgical resection was not performed due to the tumor’s extensive occupation of the right hepatic lobe. Multiples nodules were identified in the right lungs and histologically confirmed as metastatic lesions. The patient subsequently underwent palliative chemotherapy and died four months thereafter.

Case 3: A 65-year-old man was admitted to hospital with abdominal discomfort, vomiting and pain. Abdominal and chest plain radiograms showed a dislocation of the right diaphragm and bilateral lung nodular shadows. Computed tomography angiography revealed a heterogeneous solid mass of 3 × 2 cm of the right lobe of the liver with areas of irregular enhancement and multiple serpiginous vessels in the arterial phase. Vena cava and portal neoplastic thrombus were detected as well as multiple and bilateral lung metastases. A US-guided biopsy of the liver mass was histologically characterized by spindle cells in a collagenous background with areas of high cellularity. Cytological atypia, tumor necrosis and increased mitotic rate (6 or more mitotic figures per 10 high power fields [HPFs]) were noted. The percentage of Ki-67 positive tumor cells was about 30%. Immunohistochemical results included positivity for CD34, vimentin, STAT6 and Bcl-2 but not for cytokeratin, desmin, CD117, CD99, CD10, PDGFR-α or PDGFR-β. The diagnosis made was a malignant variant of SFT of the liver. Multiples nodules were identified in both lungs and histologically confirmed as metastatic lesions. The patient subsequently un-

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<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
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<tbody>
<tr>
<td>Age/gender</td>
<td>74/female</td>
<td>80/female</td>
</tr>
<tr>
<td>Tumor size</td>
<td>24 × 16 cm</td>
<td>19 × 15</td>
</tr>
<tr>
<td>Hepatic lobe</td>
<td>right</td>
<td>right</td>
</tr>
<tr>
<td>Necrosis</td>
<td>present</td>
<td>present</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>Mitotic rate</td>
<td>9 mitoses per 10 HPFs</td>
<td>≥ 7 mitoses per 10 HPFs</td>
</tr>
<tr>
<td>Immunohistochemistry</td>
<td>CD34 positive vimentin positive Bcl-2 positive</td>
<td>CD34 positive vimentin positive Bcl-2 positive</td>
</tr>
<tr>
<td>Treatment</td>
<td>surgery</td>
<td>palliative chemotherapy</td>
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<tr>
<td>Metastases</td>
<td>lungs omentum mesenteric and abdominal walls</td>
<td>right lung</td>
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<tr>
<td>Follow-up</td>
<td>died 15 months after initial surgery</td>
<td>died 4 months thereafter</td>
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HPFs – high power fields
Fig. 1. Malignant solitary fibrous tumor of the liver. Histology (hematoxylin and eosin stain): spindle and ovoid cells, hypercellular areas with nuclear crowding, nuclear pleomorphism and cytological atypia (A) intermingled with edematous areas containing spindle cells (B) with evident mitosis [Case 1 – HE stain; 20×]. The same type of cells and pattern of growth in biopsy specimens (C) [Case 3 – HE stain; 5×]. In Case 3 abdominal and chest radiograms revealed dislocation of the diaphragm and bilateral lung nodular shadows (D). CT scan revealed a heterogeneous solid mass with areas of irregular enhancement and multiple serpiginous vessels in the arterial phase (E and F).

derwent chemotherapy, which was unsuccessful, and died five months thereafter (Table I, Figs. 1, 2).

Discussion

Solitary fibrous tumors are composed of spindled to ovoid cells in a patternless architecture with prominent stromal collagen and hemangiopericytoma-like vessels. Some tumors show hypercellularity, nuclear atypia, and significant mitotic activity. The latter feature in particular often portends an aggressive clinical course [2]. Only 42 cases of primitive liver SFT have been described, and only 4 of those were classified as malignant [1]. Although there are no close correlations between morphology and malignant behavior, large size (more than 5 or 10 cm), sessile lesions, infiltrative margins, hypercellularity, nuclear pleomorphism, cytologic atypia, necrosis or hemorrhage and an increased mitotic index (more than 4 mitoses in 10 HPFs) have been described in malignant SFTs [1-17].

Histologically, the cases described herein fulfilled these criteria. The presence of synchronous, extra-hepatic metastases in two of the three cases investigated (case 2 and case 3) as well as the development of mul-
Malignant solitary fibrous tumor of the liver

Fig. 2. Immunohistochemical profile of malignant solitary fibrous tumors of the liver: the tumor was positive for vimentin [A; 20×, Case 1], Bcl-2 [B; 20×, Case 1] and CD34 [C and D; 20×, Case 1 and case 2, respectively]. Marked and diffuse Bcl-2 stain in biopsy specimens [E and F; 10×, Case 3]

Multiple metastases during the follow-up period (case 1) confirmed lesion malignancy. Another element of importance regarding the aggressive nature of malignant SFTs was demonstrated in case number 1, which, despite surgery, had a fatal outcome. Indeed, surgery alone proved insufficient therapy even though it is often considered the treatment of choice for these lesions with the aim of obtaining margin-negative specimens.

Computed tomography angiography features were similar in all cases studied: large, well-circumscribed solid tumors with mixed densities located in the upper edge of the right lobe of the liver with peripheral enhancement in the arterial phase and multiple small serpiginous vessels. No distinctive radiological parameters useful in differentiating benign from malignant liver SFTs are currently known, beyond the concomitant presence of extra-hepatic metastasis [17, 18]. Positron emission tomography–computed tomography using fluorodeoxyglucose (FDG) might be potentially useful in differentiating benign from malignant SFTs. Song et al. recently demonstrated multifocal hepatic lesions with avid FDG uptake in a 49-year-old male patient [19].

Postoperative histological examinations encompassing complete immunohistochemical panels are therefore required for a correct diagnosis of SFT to be made. The most characteristic, albeit nonspecific, immunohistochemical finding in SFT is CD34 expression, and more than 90% of SFTs are immunoreactive
to CD34 [2, 9]. Nevertheless, characteristic CD34 reactivity may be absent or only focally present in some cases. SFTs may also occasionally express epithelial membrane antigen and smooth muscle actin and may rarely label for S100, cytokeratin or desmin [2]. Recent molecular analyses have demonstrated that almost 100% of SFTs harbor an NAB2-STAT6 fusion gene, which is considered specific to this tumor type. Recent studies have therefore suggested that STAT6 immunohistochemistry is a reliable surrogate for detection of the fusion gene [2, 9]. Doyle et al. [2] and Yoshida et al. [9] have demonstrated that STAT6 is a highly sensitive and almost perfectly specific immunohistochemical marker for SFT and can be helpful to distinguish this tumor type from histologic mimics.

In conclusion, we presented a case series of malignant SFTs of the liver, focusing on their clinical and histological features. Due to the lack of specific radiological criteria for the diagnosis of malignant SFTs in the liver at present, the importance of histological examinations is highly recognized, especially in the absence of clear evidence of metastases.

Although extremely rare, malignant SFTs should be considered in the differential diagnosis of unique, isolated hepatic lesions with rich vascular serpiginous patterns in radiological imaging. In our opinion, when a unique, isolated lesion of the liver is found, multiple biopsies should be performed in order to have enough material for histological and molecular investigations and more thoroughly investigate the eventuality of this type of tumor.

The authors declare no conflict of interest.

References


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