Primary Monophasic Synovial Sarcoma of the Duodenum Confirmed by Cytogenetic Analysis with Demonstration of t(X;18): A Case Report

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Abstract

Synovial sarcoma (SS) is an uncommon malignant neoplasm of the soft tissues. It mainly affects the periarticular tissues of the extremities in young adults, but has been described at nearly all sites; nevertheless, the gastrointestinal tract is an exceptional location. We report a case of a primary synovial sarcoma of the duodenum in a 69-year-old woman. Histological study showed a monophasic pattern. The tumor cells demonstrated diffuse vimentin and Bcl-2 expression, partial EMA expression and focal AE1/3 positivity. The differential diagnosis includes gastrointestinal stromal tumors. Cytogenetic analysis confirmed the diagnosis, with detection of the X;18 translocation. The patient presented postoperative complications and died one month following the intervention.

Key words

Duodenum – synovial sarcoma - fluorescence in situ hybridization.

Introduction

Synovial sarcomas (SS) are malignant mesenchymal tumors of uncertain histogenesis. They mainly affect the soft tissues of the extremities in close proximity to the joints, and less often other sites lacking synovial and periarticular structures, including the head and neck, abdominal wall, intra-abdominal cavity, intracranial cavity, mediastinum, bones, vessels, nerves and visceral organs, such as the lung, heart, kidney and prostate [1-3]. The gastrointestinal tract is an unusual location of SS, with 12 cases described in the literature to date [1, 4-14].

We present the first case of a primary monophasic SS in the first portion of the duodenum.

Case report

A 69-year-old woman with a history of squamous cell carcinoma of the cervix diagnosed 13 years before and treated with surgery and adjuvant chemotherapy and radiotherapy, chronic diarrhea due to radiotherapy enteritis, and chronic renal failure was seen in our service. For the last 3-4 months she had experienced a weight loss of 5 kg, asthenia and mild anorexia, epigastric discomfort, nausea and postprandial fullness. The physical examination provided no relevant data. Laboratory analyses and intestinal transit results were normal. Duodenoscopy disclosed an ulcerated pyloric tumor that circumferentially affected a segment of the duodenum, causing stenosis. Abdominal computed tomography (CT) study (Fig.1) confirmed the endoscopy findings, demonstrating concentric thickening of the walls of the first portion of the duodenum, approximately 4-5 cm in length and with considerable lumen stenosis, consistent with an intramural duodenal neoplasm. First histologic examination made of the endoscopic biopsy of the duodenal mucosa showed infiltration of the tissue by a proliferation of mesenchymal spindle cells whose morphology and immunophenotype suggested monophasic SS.

The patient underwent cephalic duodenopancreatectomy. During the postoperative period, she presented a biliary fistula caused by dehiscence of the hepatico-jejunal anastomosis, and massive hematuria due to radiation cystitis. This condition, which could not be controlled by conservative or transurethral treatment, led to progressive dysfunction with irreversible multiorgan failure and death at one month after the intervention.

The surgical specimen included a subtotal gastrectomy of 22.5 cm at the largest curvature and 13 cm of proximal perimeter, a 23-cm segment of the small intestine (duodenum) and 7 cm of distal perimeter, as well as the pancreatic head, which was 6.5x5x3.5 cm in size. At 1.5 cm from the pylorus, a grayish, 8x7x3 cm intramural mass was seen, which extended concentrically along the entire first portion of the
Microscopic examination disclosed a spindle-cell neoplasm that had infiltrated the intestinal wall to the subserous layer and mesenteric fat, with focal invasion of the pancreatic head. The cells were arranged in sheets with irregularly interlacing fascicles and had small superimposed ovoid nuclei, inconspicuous nucleoli, and scant cytoplasm with poorly delimited borders (Figs. 2-3). There were 7 to 11 mitoses in 10 high-power fields. No glandular or epithelioid differentiation was observed in any of the sections. The surgical margins were free of disease, and metastasis was not detected in any of the 37 lymph nodes isolated.

Immunohistochemistry study of the neoplastic cells showed diffuse expression of vimentin, CD56 and Bel-2, partial expression of EMA, and isolated focal expression of AE1/3 (Fig. 4). No immunoreactivity was found for S-100, smooth muscle actin, desmin, CD34 or chromogranin. The ki-67 cell proliferation index was elevated (50-60%).

Fluorescence in situ hybridization (FISH) in interphase and metaphase cells was performed on formalin-fixed paraffin-embedded tissue with the LSI SYT (18q11) Break Apart probe. This is a mixture of two probes, the LSI 5´SYT, which labels in orange and extends from the 5´ end of the SYT gene to the centromere, and the LSI 3´SYT probe, which labels in green and extends from the 3´ end to the

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**Fig 1.** Abdominal computed tomography (CT) showing concentric thickening of the walls of the first portion of the duodenum with intestinal lumen stenosis. Gross appearance of the duodenal tumor.

**Fig 2.** Low power view of the duodenal tumor demonstrating extension of the tumor into the superficial subepithelial stroma.

**Fig 3.** The cells tumor have oval nuclei with fine chromatin and inconspicuous nucleoli.

**Fig 4.** The neoplastic cells show positivity for vimentin, Bel-2, CD56 and EMA.
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centromere. Normal cells, which have an intact SYT locus in both copies of chromosome 18, show two fusion signals (orange-green-red-yellow). Cells with t(X;18) present one yellow fusion signal corresponding to the intact copy of chromosome 18, and a separate red signal and green signal corresponding to the translocation (Fig 5). Demonstration of the t(X;18) (p11.2;q11.2) chromosome rearrangement confirmed the morphological diagnosis of SS.

Discussion

Synovial sarcoma represents 5-10% [2, 3, 15] of soft tissue sarcomas. It preferentially affects young adults between 15 and 35 years of age, with a predilection for men [3, 5]. Approximately 90% are located in the soft tissues of the extremities [1-3, 16] mainly around the knee (30%), but they have been described in nearly all parts of the organism [17]. The gastrointestinal tract is an unusual location, with 12 cases described in the literature; the majority occurred in the esophagus [8] and the remaining in the gastroesophageal junction, gastric antrum, distal duodenum, jejunum, and colon. Our case is the first reported case of SS occurring in the proximal duodenum. The clinical and pathological characteristics of these cases and the case presented herein are summarized in Table I [1, 4-14]. The age of the affected patients ranged from 14 to 75 years, with a slight predominance of males. The symptoms varied according to the location: in SS of the esophagus, the most frequent symptom was dysphagia, whereas those occurring at other sites evidenced a variety of gastrointestinal symptoms, such as epigastric pain, rectal bleeding, nausea, and vomiting. The tumors varied in size from 4.5 to 21 cm and appeared macroscopically as polypoid masses; two intramural cases were described, one of them being ours. Histologically, the biphasic type predominates over other histological types. In our patient, glandular structures were not observed at a conventional histological study or with immunohistochemistry techniques; a diagnosis of monophasic type was established.

The etiology of SS is unknown. It was initially thought to derive from synovial cells because of its frequent relationship with periarticular areas, but its presence in sites far from the joints has led to rejection of this theory [3]. Currently it is accepted that these neoplasms can derive from mutated, pluripotential mesenchymal cells, present in various locations [18]. Although there are no known predisposing factors for the development of these tumors, individual cases have been related to a metal hip replacement implant [19] and exposure to radiotherapy in the case of a 28-year-old patient receiving this treatment for Hodgkin disease [20]. By definition, postradiation sarcoma is a disease developing in an irradiated field after a latency period of at least two years. Our patient received pelvic radiotherapy for a squamous carcinoma of the cervix, but the SS was located outside the irradiated area; hence an association could not be established.

The primary differential diagnosis for monophasic SS of the small intestine is a gastrointestinal stromal tumor (GIST). Although these two tumor types possess histological and immunohistochemical characteristics that help to differentiate them, establishment of a definite diagnosis in this location may require a cytogenetic study, as in our case. The X;18 chromosome translocation is considered specific for SS [16], being detected in 90% of cases, and is likely to be related to the genesis of the tumor [28]. Although t(X;18) has been sporadically found in other tumors such as fibrosarcoma [21], malignant fibrous histiocytoma [22], malignant peripheral nerve tumor [23], it has not yet been described in GIST. There are two known types of breakpoints on chromosome X, exactly in two chimeric genes, SYT-SSX1 and SYT-SSX2. A high correlation has been observed between these genes and the different histological subtypes [3,18]. The SYT-SSX1 fusion gene has been observed in nearly all the biphasic tumors, whereas in the majority of monophasic types, SYT-SSX2 is detected [3].

Synovial sarcoma is considered a malignant sarcoma with capacity for recurrence at two years and distant metastasis, particularly in the lung, bones and lymph nodes [2, 15, 17, 18] but apparently, not all cases evolve in the same fashion. Follow-up of gastrointestinal SS seems to indicate that these tumors have a more favorable prognosis than SS in other anatomical locations, particularly esophageal tumors and with a polypoid morphology [6]. Nonetheless, this may not be true for intramural SS, which includes the case arising in the gastric antrum and our patient, in whom the evolution was unfortunate, with the death of both patients occurring within months after surgery.

The overall survival of patients with these tumors is 36-76% at 5 years and 20-63% at 10 years [2]. The prognosis is independent of the histological type or immunophenotype and has been related to the type of translocation. SYT-SSX2, which is mainly found in the monophasic histological type of SS, has been associated with a more favorable prognosis [17]. Other predictive factors of evolution include patient age and tumor size, number of mitoses and status of the resected margins [2,3,10]. The X;18 chromosome translocation was detected in 50% of gastrointestinal tract SS, but the translocation subtype in only two of them; hence the prognostic relevance in these tumors is unknown. The
Table I. Reported cases of synovial sarcoma of the gastrointestinal tract

<table>
<thead>
<tr>
<th>Location</th>
<th>Presenting symptoms</th>
<th>Age (year)</th>
<th>Gender</th>
<th>Gross features</th>
<th>Size (cm)</th>
<th>Histologic type</th>
<th>Trans-location</th>
<th>Treatment</th>
<th>Follow-up (month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Billings et al, 2000 [6]</td>
<td>Stomach</td>
<td>55</td>
<td>F</td>
<td>Spherical, intramural</td>
<td>16</td>
<td>Biphasic and poorly differentiated</td>
<td>t(X;18)</td>
<td>SUR</td>
<td>DOD, 1</td>
</tr>
<tr>
<td>Butori et al, 2006 [9]</td>
<td>Esophagus</td>
<td>72</td>
<td>F</td>
<td>Polypoid</td>
<td>11</td>
<td>Biphasic</td>
<td>t(X;18)</td>
<td>SUR+QT (Ifosfamide)</td>
<td>6</td>
</tr>
<tr>
<td>Parfitt et al, 2007 [12]</td>
<td>Colon</td>
<td>32</td>
<td>M</td>
<td>Polypoid</td>
<td>2</td>
<td>Monophasic</td>
<td>t(X;18)</td>
<td>SUR</td>
<td>5</td>
</tr>
<tr>
<td>Schreiber-Facklam et al, 2007 [14]</td>
<td>Distal duodenum</td>
<td>39</td>
<td>F</td>
<td>Polypoid</td>
<td>5</td>
<td>Monophasic</td>
<td>t(X;18)-SSX2</td>
<td>SUR+CHT (gemcitabine+taxotere)</td>
<td>Recurrence, 8 mo after surgery</td>
</tr>
<tr>
<td>Company et al, 2009</td>
<td>Proximal duodenum</td>
<td>69</td>
<td>F</td>
<td>Spherical, intramural</td>
<td>8</td>
<td>Monophasic</td>
<td>t(X;18)</td>
<td>SUR</td>
<td>Died due to complications, 1 mo</td>
</tr>
</tbody>
</table>

Abbreviations
- M: Male, F: Female; DOD: died of disease; AWOD: alive without evidence of disease; AWD: alive with residual disease; SUR: surgery; RAD: radiation; CHT: chemotherapy; mo: month

The treatment of choice is surgical resection with wide margins, complemented with radiotherapy, chemotherapy or both [18].

In conclusion, synovial sarcoma of the gastrointestinal tract is unusual, and may be an underdiagnosed or erroneously diagnosed condition. Cytogenetic study plays a key role in the diagnosis of monophasic types arising in exceptional locations such as the small intestine. It is important to consider synovial sarcoma in the differential diagnosis of any malignant spindle cell tumor of the gastrointestinal tract.

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References