Extraskeletal Ewing Sarcoma of the Jejunum: A Case Report

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ABSTRACT
Introduction: Ewing sarcoma most commonly arises in bones but rarely presents in extraskeletal locations. We report one such case arising from the jejunum.

Case Presentation: A 67-year-old woman presented with acute-onset, right lower quadrant pain. Computed tomography results showed a large mass within the midjejunum with pneumoperitoneum. Surgical excision was performed, and an extraskeletal Ewing sarcoma of the jejunum was suspected histologically. The diagnosis was confirmed with fluorescence in situ hybridization studies.

Conclusion: This case emphasizes the importance of recognizing this rare presentation in the small intestine to broaden the differential diagnosis of adult intraabdominal tumors.

INTRODUCTION
Ewing sarcoma most commonly affects the bony skeleton of patients younger than 20 years of age and is the second-most common pediatric sarcoma of the bone. Extraskeletal cases are rare, and these patients generally present at an older age and demonstrate a greater overall 5-year survival than skeletal Ewing sarcoma tumors.1-3 The most common sites of extraskeletal presentation are the chest wall, paravertebral region, lower extremities, and gluteal region.

Reports of primary liver involvement have been noted, as well as gastrointestinal sites of origin, including the stomach, small intestine, and colorectum.4-6 Extraskeletal Ewing sarcoma of the small intestine is extremely rare, with only 16 reports found in the literature.7-24 Exhaustive unsuccessful attempts were made to contact this patient. An effort has been made to anonymize patient information so as to not cause harm to the patient.

CASE PRESENTATION
Presenting Concerns
A 67-year-old woman presented with a 1-day history of acute-onset, right lower quadrant pain that radiated to the back. She reported never experiencing pain like this before. She reported recent constipation, but denied having nausea, emesis, fevers, night sweats, unintentional weight loss, and blood in the stool. She reported no personal or family history of malignancy. Results of spiral computed tomography scans of the abdomen and pelvis with intravenous contrast enhancement demonstrated a heterogeneous mass in the midjejunum with multiple foci of extraluminal free air adjacent to the mass.

She was taken to the operating room for an exploratory laparotomy, which revealed a solitary midjejunal mass perforating extraluminally. The mass was excised.

Pathologic Findings
Gross findings showed a 5.7 x 4.5 x 4.4-cm, pink-tan, soft, and polypoid tumor. Formalin-fixed, paraffin-embedded sections of tumor stained with hematoxylin-eosin demonstrated sheets of densely packed primitive blue cells separated by broad fibrous septae, with areas of necrosis and focal rosette-like formations. The tumor transmurally involved the small bowel with mucosal ulceration. The individual tumor cells showed oval-to-angulated nuclei with frequent nuclear grooves, indistinct nucleoli, and minimal, clear cytoplasm (Figures 1 and 2). Scattered mitotic figures were also noted.

On immunohistochemical analysis, the tumor was positive for vimentin, CD99 (Figure 3), CD117, and cyclin D1. The tumor was focally positive for S100 (Figure 4) but negative for SOX10. It was also negative for pancytokeratin, CAM5.2, synaptophysin, CD56, CD45, SF-1, FOXL2, DOG1, STAT6, CD110, CD21, CD35, CD43, TdT, CD163, MDM2, ER, calretinin, inhibin, muramidase, pan-melanoma, smooth muscle actin, desmin, and CD34.

Figure 1. Low magnification demonstrates sheets of small, round-to-spindle, uniform tumor cells with clear cytoplasm (hematoxylin-eosin stain, 20 × magnification).

Figure 2. High magnification demonstrates tumor cells showing oval-to-angulated nuclei, frequent nuclear grooves, indistinct nucleoli, and minimal, clear cytoplasm (hematoxylin-eosin stain, 60 × magnification).

Figure 3. Tumor cells showing strong, positive membranous immunoreactivity (CD99 immunostain, 40 × magnification).

Keywords: case report, Ewing sarcoma, fluorescence in situ hybridization, immunohistochemistry, oncology, pathology

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Therapeutic Intervention and Treatment

The final pathologic diagnosis for the jejunal mass was extraskeletal Ewing sarcoma with associated EWSR1–FLI1 fusion. All operative margins and evaluated lymph nodes were negative for disease. The patient’s postoperative course was complicated by slow wound healing and wound infection. The poor performance status excluded multiagent adjuvant chemotherapy, so she was instead prescribed serial imaging surveillance.

Follow-up and Outcomes

However, the patient ultimately did not return for follow-up. Her outcome is unknown. Table 1 shows a timeline of the case.

DISCUSSION

Ewing sarcoma is known to harbor multiple balanced translocations, and fusions involving the EWSR1 gene on chromosome 22 exist. The most common translocation is t(11;22), EWSR1–FLI1 fusion (85% of cases), causing overexpression of the FLI–1 protein. The second most common translocation is t(21;22), EWSR1–ERG fusion (5%–10% of cases). Numerous other, less common variant translocations exist. Lack of reverse transcription-polymerase chain reaction for Ewing sarcoma fusion transcripts for EWSR1-FLI1 and EWSR1-ERG does not exclude the possibility of Ewing sarcoma because it does not rule out fusion transcripts that may be present below the limit of detection for the given assay (5%).

For differentiation of small-intestine Ewing sarcoma from other diagnostic entities such as malignant GNET, malignant gastrointestinal stromal tumor, clear cell sarcoma, synovial sarcoma, rhabdomyosarcoma, desmoplastic small round cell tumor, and lymphoma, an exhaustive panel of immunohistochemical stains and fluorescence in situ hybridization tests are recommended. Malignant GNET is an extremely rare and recently recognized entity that was first described in 2003 and demonstrates overlapping features with Ewing sarcoma. It is histologically characterized by a sheet-like or nested population of primitive-appearing epithelioid or oval-to-spindle cells with small nucleoli and occasional mitoses. Occasionally, cytoplasmic clearing and osteoclast-type multinucleated giant cells may be evident. There is strong expression for neural markers (S100, SOX10, and vimentin) without expression for melanocytic markers. Rare reports of FLI1 expression have been reported. Similar to Ewing sarcoma, GNET shows EWSR1 gene rearrangements. The EWSR1 fusion partners in GNET are most commonly ATF1 or CREB1. These findings raise the issue of whether Ewing sarcoma may be related to GNET.

CONCLUSION

We have described a patient with Ewing sarcoma occurring in the small intestine. This case report helps solidify the small intestine as a potential site for Ewing sarcoma.

Table 1. Timeline of the case

<table>
<thead>
<tr>
<th>Date</th>
<th>Diagnostic tests</th>
<th>Diagnostic findings</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2017</td>
<td>CT scan</td>
<td>Small bowel mass with perforation through the bowel wall</td>
<td>NA</td>
</tr>
<tr>
<td>May 2017</td>
<td>Exploratory laparotomy</td>
<td>5.7-cm mass of the jejunum</td>
<td>Complete tumor resection with negative surgical margins</td>
</tr>
<tr>
<td>June 2017</td>
<td>Pathology evaluation</td>
<td>Extraskeletal Ewing sarcoma of the jejunum</td>
<td>Serial imaging surveillance</td>
</tr>
<tr>
<td>October 2017</td>
<td>CT scan of the abdomen and pelvis</td>
<td>No evidence of disease</td>
<td>3-month radiology follow-up</td>
</tr>
<tr>
<td>January 2018</td>
<td>CT scan of the abdomen and pelvis</td>
<td>Patient lost to follow-up</td>
<td>NA</td>
</tr>
</tbody>
</table>

CT = computed tomography; NA = not applicable.
sarcoma origin, and helps highlight the need for robust immunohistochemical and molecular cytogenetic analysis for accurate diagnosis.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

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References

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