Ewing Sarcoma of the Jejunum: A Case Report and Literature Review.

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Case Report

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Abstract

**Background:** Ewing sarcomas (ES) are highly aggressive malignancy and are predominant in the long bones of extremities of children and young adults with a slight male predilection and rarely presents at extra skeletal locations.

**Case Summary:** A 55 year-old lady came to our hospital after finding out her elevated tumour biomarkers during her physical examination. Her enhanced CT scan showed a jejunal mass. The patient underwent laparoscopic enterectomy. The mass was later diagnosed as Ewing sarcoma, evidenced by Fluorescence In Situ Hybridization (FISH) whereby the GLP EWSR1 probe was used, showing that more than 10% of the cells showed a red-green-yellow signal proving the breakpoint rearrangement of the EWSR1 gene in chromosome 22.

**Conclusion:** We described a case of localised ES at the jejunum, in China, based on literatures.

Introduction

Ewing sarcoma (ES) is a small round cell tumour with simple sarcoma specific genetic alterations resulting in TET/FET family member and ETS family member fusion proteins[1]. Ewing sarcomas are rare small round cell tumours that arise predominantly in children and young adults with a slight male predilection [2–4]. Ewing sarcoma most often arises in the mid-shaft or diaphysis of the long bones of the extremities with the spine making up 8% of primary sites[5]. Extra osseous ES occur in the soft tissue of the extremities, paravertebral region, and pelvic cavity[6] and have also been discovered in most organs including the pancreas, liver, adrenal gland, oesophagus and uterus[7–13]. Extra skeletal cases are rare, and these patients generally present at an older age and demonstrate a greater overall 5-year survival than skeletal Ewing sarcoma tumours [14, 15]. Reports of primary liver involvement have been noted, as well as gastrointestinal sites of origin, including the stomach, small intestine, and colorectal [16–19]. Nevertheless, ES is extremely rare in the small bowel. Here we report a case of primary ES in the jejunum with EWS rearrangement.

Case Presentation

A 55 year-old, otherwise healthy, female patient came to our hospital after finding out that she had elevated tumor biomarkers during her annual physical examination. Abdominal examination revealed no mass or distension. Bowel sounds were active. Her CA-153 level was 38.04 u/mL, CA-199 109.5 u/mL and CA-125 47 u/mL. Her abdominal CT scan showed a contrast-enhanced mass in the small intestine at the left lower quadrant of abdomen (Fig. 1). The white blood cell count was low at 3.39 × 10^9/L (normal range 3.50–9.50 × 10^9/L) and lymphocytes were low at 0.79 × 10^9/L (normal range 1.10–3.20 × 10^9/L). The patient underwent minimally invasive exploratory laparotomy. During the exploration, the tumor was located in the distal jejunum. It was well-circumscribed and had a fleshy pink surface similar to that of gastrointestinal stromal tumor. A segment of the jejunum was resected 5 cm away from the
edges of the tumor on both sides and an anastomosis was made using mechanical staple. The patient recovered uneventfully after surgery. The pathological examination showed that the tumor, of size 3.5 cm x 3.0 cm x 2.3 cm, was malignant whereby there is invasion of the entire wall of the intestine. The resected sample has negative margins (R0) (Fig. 2). Fluorescence in situ hybridisation (FISH) for an EWSR1 gene rearrangement (22q11) was performed using GLP EWSR1 probe, showed more than 10% of the cells showed a red-green-yellow signal, proving the breakpoint rearrangement of the EWSR1 gene in chromosome 22 (Fig. 3). Post-operatively, bone X-rays were done to rule out any primary lesion from her skeletal system (Fig. 4). The patient was discharged on POD 8 and referred to oncology department for further treatment. The regimen included vincristine, adriamycin, cyclophosphamide, doxorubicin, and addition of ifosfamide and etoposide (VACD-IE), given every 2 weeks for 12 cycles. It started one month post-operatively. However, after 4 cycles the patient stopped the adjuvant therapy because of fear of side effects. So far there is no sign of relapse and the patient recently showed interest in continuing the adjuvant therapy after thorough thought.

**Discussion**

Ewing sarcoma is known to harbour 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 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%) [20]. It most commonly arises from bone but can develop in extra skeletal sites[21]. Ewing sarcoma of the small intestine is extremely rare based on literature [22–24].

Among the 37 cases found, 3 cases were derived from the oesophagus, 9 from the stomach, 5 were of colorectal origin and 20 arouse from small intestines. 22 cases were found to be among males and 15 among females. The age range is from 9 years old to 68 years old. FISH break-apart EWSR1 was positive in 19 cases, negative in one case and was not carried out in 17 cases[9, 18, 22, 23, 25–49]. Our patient characteristics fall within these demographic data. Till date demographic research has shown that the frequency of Ewing sarcoma is higher in United States Caucasian population than China[50].

Ewing sarcoma predominantly affects children and young adults with a peak incidence between 10 and 20 years of age. About 30% occur in adults over the age of 20 and fewer than 5% occur in adults over the age of 40 [51].

So far, the outcome of 5-year survival rate of metastatic patients is usually poor (< 30%) compared to localised ES (65%-75%), despite the use of chemotherapy[52]. Several studies have indicated that localised extra skeletal ES has a more favourable outcome than skeletal tumours[53, 54].
According to NCCN guidelines, postoperative radiation therapy should begin within 60 days of surgery and is given concurrently with consolidation chemotherapy[55]. This explains why our patient was referred to oncology department shortly after surgery for further treatments.

Intergroup Ewing’s Sarcoma Study-I and Intergroup Ewing’s Sarcoma Study-II showed that radiation therapy and chemotherapy with VACD (vincristine, adriamycin, cyclophosphamide, doxorubicin) was superior to VAC (vincristine, adriamycin, cyclophosphamide)[56]. The 5-year relapse-free survival rate was 60% and 24% for VACD and VAC, respectively (p < 0.001). The corresponding overall survival rate was 65% and 28% (p < 0.001). Womer et al[57]. reported that VACD-IE given on every 2 weeks schedule was found to be more effective and no increase in toxicity.

**Conclusion**

Ewing sarcoma is a highly aggressive small round cell tumour that arises in adults. We have described a patient with Ewing sarcoma occurring in the jejunum. This case report helps solidify jejunum as a potential site for Ewing sarcoma origin and surgical approach with adjuvant chemotherapy does prove beneficial. However, this is a single case study and conclusion be made only based on our experience.

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Written informed consent was obtained from the participants for publication of this article and any accompanying tables/images. A copy of the written consent is available for review by the Editor of this journal.

**Availability of data and materials**

Not applicable

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**
KS, DR and XP all have made substantial contributions to conception, acquisition of data, analysis, and interpretation of data. All of them have been involved in drafting the manuscript and revising it critically for important intellectual content. All authors read and approved the final manuscript and take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of work.

The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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Abbreviations

CT: Computer tomography, ES: Ewing sarcoma, FISH: Fluorescence in situ hybridization, EWSR1: Ewing sarcoma breakpoint region 1, ETS: E26 transformation-specific, POD: post-operative day

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**Figures**

**Figure 1**

Transverse spiral computed tomography scan of the abdomen, with intravenous contrast enhancement showing dilation of jejunal wall at the left lower quadrant.
Figure 2

Low magnification of the resected sample using formalin-fixed, paraffin-embedded sections of tumour stained with hematoxylin-eosin demonstrating sheets of small, round-to-spindle, uniform tumor cells with clear cytoplasm.

Figure 3
Fluorescence in situ hybridisation of the tumour showing more than 10% of the cells showed a red-green-yellow signal, proving the breakpoint rearrangement of the EWSR1 gene.

Figure 4

Post-operative bone X-ray which shows no lesion in skeletal system thereby excluding metastasis.