

Ewing's Sarcoma with Metastasis to Duodenum - Rare Case

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ABSTRACT

Ewing's sarcoma is the second most common primary tumor of bone in childhood and it also arises in soft tissues. Metastasis of Ewing's sarcoma most commonly occurs in lungs, bone and bone marrow. But metastasis to small bowel is rare. Here is a case report of a 18 year old male patient of Ewing's sarcoma of left tibia after receiving radiation therapy and chemotherapy developed metastasis in first part of duodenum with no other site of metastasis which is rare.

KEYWORDS: Duodenum, Ewing's sarcoma, Metastasis.

INTRODUCTION

Ewing's sarcoma refers to tumor which is poorly differentiated and consists of small round cells. Ewing's sarcoma family tumors are not common before 8 years of age and after 25 years of age. The cell of origin of Ewing's sarcoma is unknown but is presumed to arise from mesenchymal stem cells. Approximately 95% of them have chromosomal translocations between the EWS gene on chromosome 22 and FLI1 gene on chromosome 11 or ERG gene on chromosome 21.^{1,2} Every part of the human body could be affected such as the small bowel, esophagus, vagina, pancreas or kidney. In large cooperative group study, approximately 20% of patients presented with metastatic disease. Of these patients, 44% had lung metastasis only, 51% had bone or bone marrow involvement (with or without lung metastasis) and 5% with metastasis in other organs.¹ Metastasis to small bowel (duodenum) is very rare. Metastatic disease is present in approximately 20% of patients at initial diagnosis.¹ The prognosis of metastatic disease is poor. Poor response to chemotherapy, not using surgery as part of treatment of the primary lesion, poor response to radiation therapy have all been proposed as poor prognostic factors.^{1,3-11}

CASE REPORT

18 year old male patient came with complaints of swelling over left lower limb since 7-8 months with pain over swelling on walking since 2-3 months with progressive increase in the size of swelling since 15 days. Patient was then evaluated clinically and then MRI of left lower limb was performed which showed e/o cortical thickening and destruction involving the mid shaft of tibia with involved length of tibia measured 11cms and soft tissue involvement of approximately 5.3x6.6cms. Neurovascular bundle was

displaced by the soft tissue. He then underwent biopsy from the lesion. Histologically the features were consistent with Ewing's sarcoma.

Patient was then started on chemotherapy Vincristine, Adriamycin, Cyclophosphamide alternating with Ifosphamide and Etoposide. He received 3 cycles of chemotherapy then was planned for local radiation therapy. He received 46 Gy in 23 # with boost upto 60 Gy from Oct 2014 to Dec 2014. After Radiotherapy patient still had residual disease so was continued on chemotherapy VAC alternating with IE. Then he received 4 more cycles of chemotherapy. Patient was due for next cycle of chemotherapy that time he developed complaints of nausea, vomiting, pain in abdomen, yellowness of eyes and fever. Patient was then evaluated by hematological investigations. His total bilirubin was 4mg/dl, direct bilirubin 2.3mg/dl, indirect bilirubin 1.7mg/dl. Patient was negative for HBsAg and HCV and he developed complaints of black colored stools.

Patient was then evaluated by CECT abdomen Fig (1) which revealed short segment circumferential asymmetrical enhancing bowel wall thickening noted involving pyloric antrum, first and second part of duodenum with average thickness 3.1cm. causing compression over ampulla of Vater with resultant dilatation of MPD and biliary system. Multiple pre para aortic, aortocaval, precaval, retroperitoneal, mesenteric lymph nodes. Patient then underwent oesophago-gastro-duodenoscopy which was suggestive of polypoidal necrotic ulcerated lumen occluding growth seen in D1, growth seen extending distally upto proximal jejunum with biopsy taken from the growth was suggestive of metastatic deposits of Ewing's sarcoma in duodenum. Fig. (2) and (3)



Fig 1: Contrast Enhanced CT image of abdomen with arrow showing thickening in the wall of duodenum with multiple hypodense areas within suggestive of internal areas of necrosis.

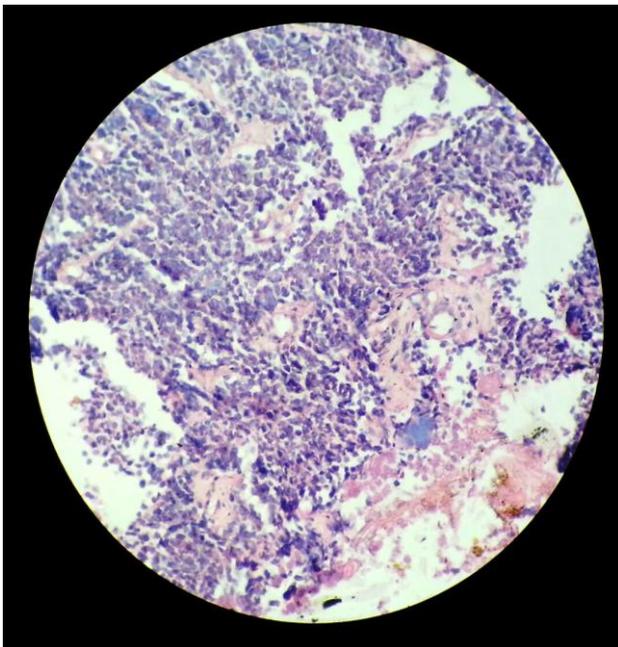


Fig 2: 10X Histopathology slide view of biopsy from duodenum showing scanty stroma with large numbers of malignant round cells.

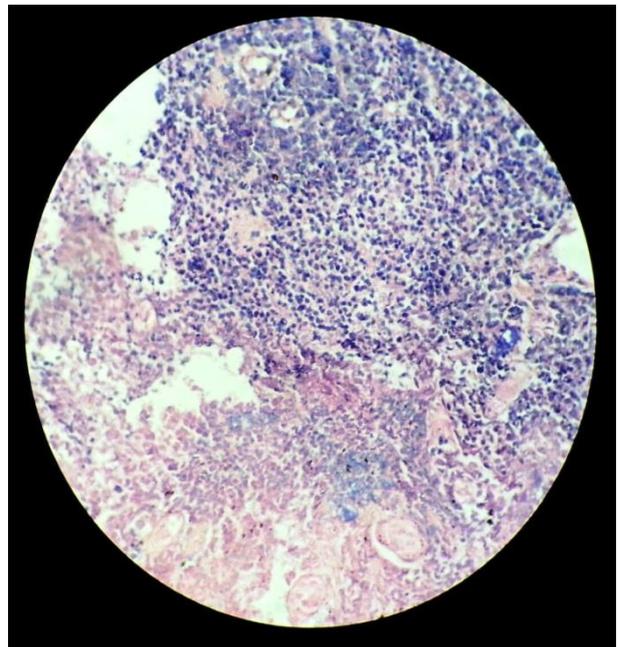


Fig 3: 40X Biopsy from duodenum showing stroma with glandular tissue with interspersed malignant poorly differentiated round cells.

DISCUSSION

Ewing's sarcoma that has spread from the initially affected bone to one or more sites in the body, distant from the site of origin, is called metastatic. The most common site to which Ewing's sarcoma spreads, or metastasizes, is the lungs. Metastatic Ewing's is typically difficult to control, though patients with lung metastases have a better prognosis than patients with other distant metastases. ES is a neoplasm of

undifferentiated small round cells, which generally affects the bone and deep soft tissue of children and adolescents. The most commonly affected site is skeletal tissue. Isolated metastasis to duodenum is rare.

ES histologically is a small round cell tumor and it is CD99 positive by immunohistochemistry. It has a genetic mutation $t(11;22)(q24;q12)$ translocation (EWS/FLI-1 fusion) that can be seen by fluorescence in

situ hybridization (FISH) or reverse transcription polymerase chain reaction (RT-PCR). These traits may be essential criteria for diagnosis in most cases of ES. But there is a small chance to be negative for the t(11;22)(q2;q12) translocation by FISH or RT-PCR because both of them have chance to be negative in ES, about 3% of time in FISH and 19% in RT-PCR.^{12,13}

Due to development of multidisciplinary approach now a days various modalities can be used to treat Ewing's sarcoma like surgery, radiotherapy and chemotherapy with a cure rate of 50% or more¹⁴⁻²⁷. For metastatic disease chemotherapy is the modality of choice along with radiation therapy and surgery. The current standard chemotherapy regimen is a combination of drugs which includes: Adriamycin® (doxorubicin), Vincristine, Cyclophosphamide and Actinomycin D® (dactinomycin). On the basis of non-randomized trials (trials which provide less conclusive evidence than randomized trials), many physicians use a regimen of VAC, alternating with ifosfamide and etoposide for the treatment of Ewing's sarcoma. Dactinomycin has been dropped from this regimen because it has not been seen as a crucial component when Ifosfamide and etoposide are added.²⁸

The presence of metastatic disease is the most unfavorable prognostic feature. Patients with isolated lung metastases have been shown to have a better prognosis than those with extrapulmonary metastases; however, survival is still disappointing^{29,30}.

In order to control Ewing's sarcomas, a radiation dose above 40 Gy is necessary. In the St. Jude's Children's Research Hospital experience with the use of lower radiation doses, a high rate of local recurrence was observed³¹. A clear dose-response correlation at doses above 40 Gy has not yet been established. For definitive radiotherapy, doses between 55 Gy and 60 Gy, most frequently not exceeding 55.8 Gy, are usually given. When surgery precedes or follows radiotherapy, the doses range between 45 Gy and 55 Gy depending on the individual risk factors (i.e., resection margins and response). It is uncertain whether irradiation of the site of completely resected lesions that demonstrate a poor histologic response is of benefit. European investigators recommend such irradiation, whereas it is not incorporated into North American protocols. There has been no controlled trial addressing this issue.

Local treatment should be individually adapted depending upon the site and size of the tumor, the anatomical structures near the tumor, the patient's age, and individual preference. In Children's Oncology Group protocols, negative margins are defined as bony margins of at least 1 cm, with a 2- to 5-cm margin recommended. In soft tissue, at least 5 mm in fat or muscle is required, with 2 mm through fascial planes, with the margin being through noninflammatory tissue. The main reconstructive options include autogenous

bone grafts, structural bone allografts (intercalary or osteoarticular), and metallic endoprosthetics. Allografts and endoprosthetics may also be used as part of a composite reconstruction.

Surgery with reconstruction should be done in patients with resectable tumor with adjuvant chemotherapy and radiation therapy. Our patient had received standard chemotherapy and radiotherapy, but patient did not undergo surgery with reconstruction, he developed metastasis to duodenum which is a rare presentation and also developed obstructive jaundice. Despite various symptomatic treatment given but he developed active bleeding from the lesion in duodenum and eventually succumbed to death.

CONCLUSION

Ewing's sarcoma with extrapulmonary metastasis has very poor prognosis. Our patient was treated with only radiotherapy and chemotherapy without surgery, maybe that's why he developed metastasis to duodenum which itself is a rare occurrence and eventually resulted in death. Multimodality treatment should be practiced in order to improve the disease free and progression free survival of the patient.

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