

## CASE REPORT

**A Case Report of Aggressive Primary Ewing Sarcoma***Pramod Chinder<sup>1\*</sup>, Shwetha Rupendu<sup>2</sup>, Shruthi Shivashankar<sup>2</sup>*<sup>1</sup>*HCG Cancer Care Centre, Sampangiramnagar, Bangalore-27 (Karnataka) India,*<sup>2</sup>*Kempegowda Institute of Medical Sciences, Bangalore-560070 (Karnataka) India***Abstract:**

Ewing's sarcoma (EWS) is the second most common malignant bone tumour in children. We present a case report of a 21 year old male who presented with pain and swelling of his left leg since three months. At the time of diagnosis he had non-metastatic Ewing sarcoma of left tibia with a variant chromosomal translocation. He underwent six cycles of chemotherapy and one and a half months later he underwent limb salvage surgery with wide resection of tumour. Within four weeks after surgery he developed metastatic relapse. He expired four months after first presentation due to advanced disease with pulmonary metastasis with sepsis and respiratory failure. We conclude that not all cases of non-metastatic disease have similar clinical outcome and should not be treated with similar treatment strategies, instead have to be divided as standard risk and high risk and treated accordingly.

**Keywords:** Ewing's sarcoma, Left tibia

**Introduction:**

Ewing's sarcoma (EWS) is the second most common malignant bone tumour in children following osteosarcoma. It is a small round cell tumour commonly located in the metaphysis of long bones [1,2].

Non metastatic disease is associated with long term survival of 69% to 75%. Metastatic disease has a long term survival of 20% [1].

The standard treatment approach involves classifying patients according to disease-stage as non metastatic, metastatic and recurrent and patients within each group receiving the same treatment. However this classification is not

always related to clinical outcome, because 30% of the patients who present with non metastatic disease die much before expected [3].

In this article we discuss the adequacy of standard treatment approach in a high risk patient with Ewing sarcoma.

**Case Report:**

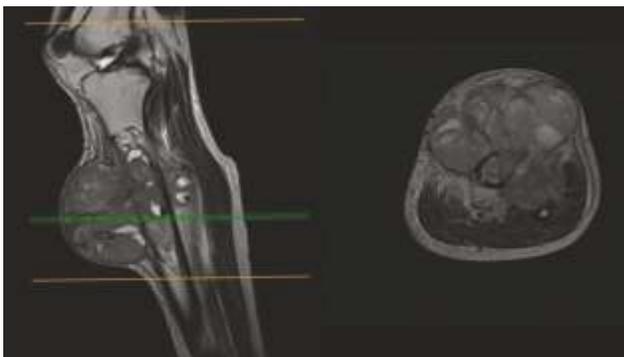
A 21 year old male presented with complaints of pain and swelling in the left leg since three months. On clinical examination there was a bony swelling of the left leg in Fig. 1 with no distal neurological or vascular deficit. Plain radiograph of the left leg with knee, taken at the time of presenting showed ill defined permeative osteolytic lesion in the proximal shaft of tibia. Magnetic resonance imaging (MRI) showed a lobulated mass in the left proximal leg with irregular cortical destruction of proximal shaft of left tibia with local extension, encasing the anterior tibial artery (Fig. 2). Whole body Positron Emission Tomography (PET) showed no metastatic deposits. Biopsy was performed and histopathology revealed the diagnosis of Ewing's sarcoma. Immunohistochemistry of the neoplastic cells expressed CD (cluster of differentiation) 99, Vimentin and were negative for Pan-cytokeratin (Pan- CK), Leucocyte Common Antigen (LCA). He underwent six cycles of chemotherapy with vincristin, adriamycin, cyclophosphamide + ifosfamide, etoposide (VAC + IE) and intraarterial chemotherapy with injection cisplatin. However tumour response to chemotherapy was poor (Picci grade 1)[4]. One and a half months later he

underwent wide resection of tumour and 'tibialisation of fibula', gastrosoleus flap and Split Thickness Skin Graft (SSG) (Fig. 3). Post operatively on day four he developed infection of the operated site for which he was treated. On week four he developed a small swelling just below the operated site. Due to increasing size of the swelling a PET scan was performed which revealed recurrent disease with subcutaneous and intramuscular metabolically active lesion in proximal mid left leg and distal thigh and popliteal

and left inguinal metastatic lymphadenopathy with pulmonary metastasis and mediastinal lymphadenopathy (Fig. 4). He failed to respond to standard line of treatment and was further investigated with a cytogenetics study which revealed variant translocation and additional changes 48-53,XY,5, ins(6;17)(p21;q11q25), +8, +8, +9, +9, +9, t(12;22)(q24;q12), del(17)(q11), +20 (Fig. 5). Oncoprint® revealed that the tumour was not responsive to Cetuximab, Temozolamide, Melphalan and Irinotecan (Fig. 6). As the tumour



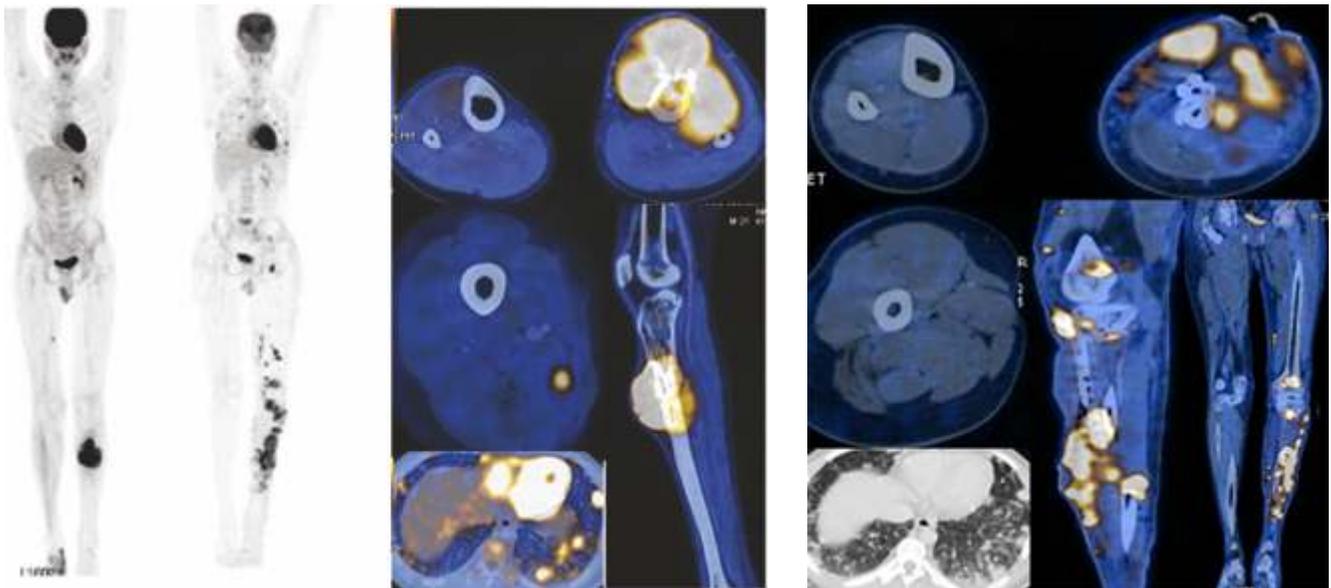
**Fig 1: Patient Presenting with a Bony Swelling of the Left Leg**



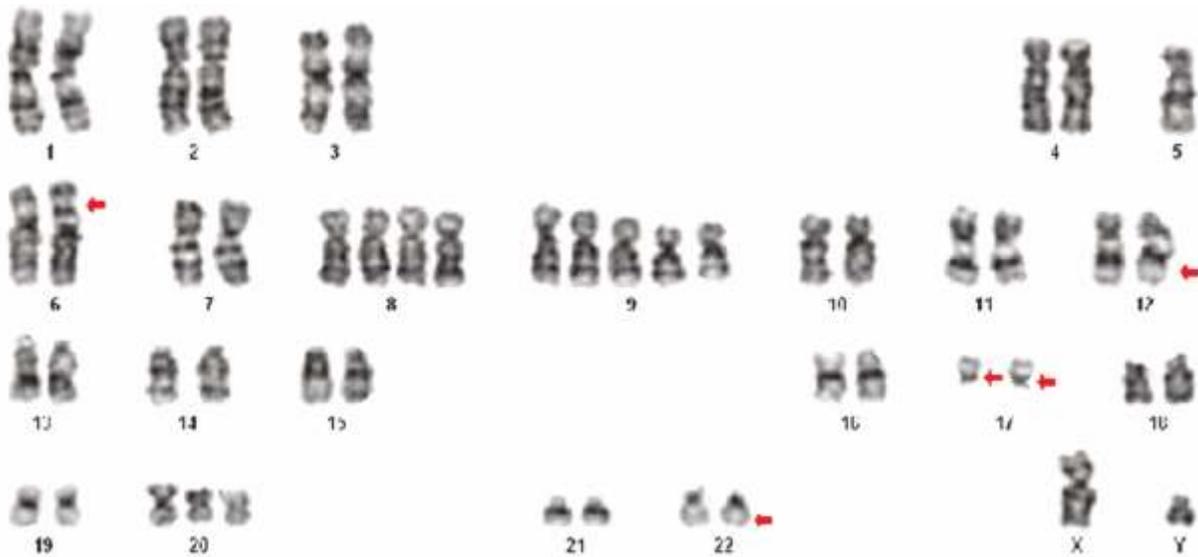
**Fig 2: MRI showing a Lobulated Mass Arising from the Left Proximal Tibia Encasing the Anterior Tibial Artery at the Time of Presentation**



**Fig 3: Wide Surgical Resection of the Tumour**



**Fig. 4: Whole Body PET Scan Showing (A) Localized Tumour at the Time of Presentation (B) Metastases to the Thigh, Lungs and Mediastinum**



**Fig. 5: Cytogenetic Study Revealing A Variable Translocation 48-53, XY, 5, ins(6;17) (p21;q11q25), +8, +8, +9, +9, +9, t(12;22)(q24;q12), del(17)(q11), +20**

was a neuroectodermal tumour, LV Dotanate therapy was tried but was not beneficial. He was admitted to intensive care unit seven weeks later with complaints of breathlessness and foul smelling discharge from the wound. His CT lung

showed significant increase in pulmonary metastases and mediastinal lymph nodes. He expired on 17/10/2011, four months after first presentation due to advanced disease with pulmonary metastasis with sepsis and respiratory failure

**Table 1: Oncoprint Sensitivity Report**

<b>Sample received on</b>	<b>14<sup>th</sup> Aug 2011</b>	<b>Report generated on</b>	<b>19<sup>th</sup> Aug 2011</b>
<b>MBT #</b>	338	<b>Hospital Name</b>	HCG
<b>Trial I Id</b>	MBB-0006	<b>Patient Initial</b>	M-S
<b>Age/Sex</b>	21/M	<b>Type of Cancer</b>	Bone Tumour
<b>Tumour Site</b>	Tibia	<b>Tumour stage</b>	Unkonwn
<b>Collection procedure</b>	Biopsy	<b>Sample type</b>	Primary

<b>Drug Combined Tests</b>	<b>Results</b>
<b>Cetuximab</b>	Non-Responsive
<b>Temozolamide</b>	Non-Responsive
<b>Melphalan</b>	Non-Responsive
<b>Irinotecan</b>	Non-Responsive

**Discussion:**

Ewing sarcoma is second most common bone tumour following osteosarcoma in patients younger than 30 years. It has an incidence of less than 1 per 1 million per year and has a higher incidence in males [1]. In the Indian population it has been reported to be relatively common among malignant primary bone tumours [5]. The Indian patients also present at a more advanced stage and the compliance of treatment is suboptimal [6].

Currently patients are classified by disease stage, as non metastatic, metastatic and recurrent and patients within each group are treated the same. But apparently this subdivision is not always related to clinical outcome, because 30% of the patients who present with non metastatic disease, die within five years. It is therefore important to identify prognostic factors to separate high risk patients from low risk and identify chemotherapy resistance and metastasis early and design separate therapeutic approaches for patients in each risk group [3].

The worst prognostic factor is the presence of distant metastasis. Even with aggressive treatment patients have only a 20% chance of long term

survival [7,1] . The size of primary lesion has been consistently shown to have some prognostic significance but specific parameters have not been firmly established [1]. Tumours located in the axial skeleton have shown to have poor prognosis compared to tumours placed in the extremity [8]. Histological grade is of no prognostic significance all Ewing sarcoma are considered to be high grade. Fever, anaemia, and elevation of white blood cell count, erythrocyte sedimentation rate and lactate dehydrogenase have reported to indicate more extensive disease and a worse prognosis [1]. Older age at presentation >12years and male sex is associated with poor prognosis [1,7]. Specific translocation versus a variant translocation does not affect clinical outcome , however, presence of secondary genetic alterations such as aberrant TP53 expression is associated with poor prognosis [1,7]. Greater than 90% necrosis after preoperative chemotherapy indicates good prognosis [1]. Recurrent disease is associated with poor prognosis. 40% of patients with initially localised disease develop recurrence. Recurrence within one year of treatment of primary tumour is a strong indicator of poor prognosis [8,9].

Our patient is a 21 year old male who presented with pain and swelling of his left leg since three months. At the time of diagnosis he had non-metastatic Ewing sarcoma of left tibia, a tumour volume of 700ml with a poor response to preoperative chemotherapy (Picci grade 1) [4]. Within four weeks after surgery, he developed metastatic relapse. He had a variant chromosomal translocation. His age at presentation, sex, the time of interval of only three months between onset of symptoms and diagnosis, a high tumour volume and a poor response to preoperative chemotherapy, are indicators of a high risk case. He was treated with the standard treatment protocol of a non metastatic Ewing sarcoma which included neoadjuvant or adjuvant chemotherapy and wide surgical resection. Our patient failed to respond to the standard line of treatment.

Thus concluding that our patient had very poor prognosis inspite of having non metastatic disease posing as an example to the fact that all cases of non-metastatic disease do not have similar clinical outcome and should not be treated with similar treatment strategies .

Patients with non metastatic disease should be divided as standard risk and high risk [3]. Chemotherapy resistance and metastasis should be suspected early in a high risk patient and these patients should be treated more aggressively than standard risk patients.

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\*Author for Correspondence: Dr. Pramod Chinder, HCG Cancer Care Centre, Sampangiramnagar, Bangalore-27 (Karnataka) India Cell: 09945106676 Email: drpramods@gmail.com