International Journal of Orthopaedics Sciences

ISSN: 2395-1958
IJOS 2017; 3(3): 912-915

www.orthopaper.com
Received: 04-05-2017
Accepted: 05-06-2017

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Management of pathological femoral fracture secondary to Ewing sarcoma in pregnancy: A case report

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DOI: https://doi.org/10.22271/ortho.2017.v3.i3m.134

Abstract
Ewing's sarcoma is an ultra-orphan disease (2/1,000,000/year) which requires a multimodal therapy approach in high-volume centers. Treatment consists of pre-operative therapy followed by surgery and post-operative combination of chemo-radiotherapy. Experience with diagnosis and therapy of Ewing's sarcoma in pregnancy is very limited. We herein report the case of an atypical Ewing's sarcoma detected in the second trimester of gestation. The present study reports a case of a 24-week primigravida presenting with presented with chief complains of sudden onset of pain in left proximal thigh and inability to stand from bed on 28 feb.2017 in early mornig. Consult local doctor where x ray advice & some analgesic given. X-ray done at periphery which shows pathological subtrochantric fracture. From there she refer to higher centre for further management. An internal fixator was placed in the left femur for definitive treatment of the fracture. Normal delivery was performed at 32 gestational weeks. Following delivery, staging of cancer was conducted. Subsequently, adjuvant treatment started. The rare nature of this condition underlines once more the need for a multidisciplinary team to improve the quality of care for this highly special patient collective.

Keywords: Ewing's sarcoma, Pregnancy, Multidisciplinary team approach

Introduction
According to recent literature, approximately 1 in 1,000 term pregnancies is complicated with cancer. This incidence is increasingly encountered in clinical practice with the rising trend of postponing pregnancy to later in life. Breast cancer is the most common tumor treated during gestation followed by ovarian cancer, cervical cancer, leukemia, lymphoma, and lung cancer. Bone and soft tissue sarcomas, being generally rare diseases, present more infrequently during gestation. In total, 12 patients with sarcoma and 1 with a primitive neuroectodermal tumor have been treated with chemotherapy while being pregnant. However, in total, only 5 women have been described who were primarily diagnosed and treated with Ewing's sarcoma during pregnancy. Based on the prevailing literature, we herein report the 7th case of a woman diagnosed and treated with Ewing's sarcoma in the second trimester of gestation and emphasize once more the need for a multidisciplinary team approach to improve the quality of care for this highly special patient collective.

Case Report
A 22 years female from Bhadurpur, vashali, Bihar has pregnency of 24 weeks. Presented with chief complains of sudden onset of pain in left proximal thigh and inability to stand from bed on 28 feb.2017 in early morning. Consult local doctor where x ray advice & some analgesic given. From there she refer to higher centre for further management. X-ray done at periphery which shows pathological subtrochantric fracture. (Figure 1)

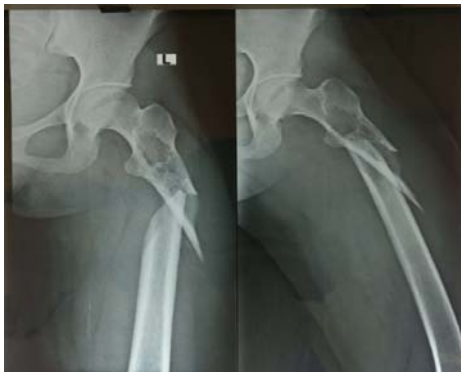

Fig 1

Through routine investigation, gynocological & RCC consultation done. USG abdomen done for fetalwell being. USG breast for secondary tomor. RCC consultation & its subequent followup show no any secondary site. After thorough evaluation, PAC fitness & informed consent. High risk consent for fetal abortion taken. Mother was cover with lead apron & thyroid shield. Approx in 4-5 exposur PFN A2 done. Post op x ray not done. Post operative period uneventful. Again gynocological consentation taken. Both mother & fetus condition well. Exposed fracture site shows cysts contain fibrous membranous lining with expansion and thinning of the overlying bone likely some bony tumor. But histopathological examination shows chronic osteomylitis. Requested pathologist to review again. On reviewing the HPE slide by pathologist shows round cell tumor. After discussion with oncologist they send again for review the slides for confirmatory of malignent round cell tumor. Immunohistochemical (IHC) Marker test that positive are Vitmentin, CD99, Fli1, Ki-67, NSE which most likely confirmatory of Ewing Sarcoma/PNET. (Figure 2)

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Regd. Dt:	23/03/2017 Acc. ID: 1016174531	Client Details:	Tara Diagnostic Center- Patna
Coll Dt. Tm:	22/03/2017 10:00:00		Besides Malti Medical Hall,East Gate of I.G.I.M
Recd Dt. Tm:	23/03/2017 10:08:56	Refd. By:	Dr. Deepak Kumar
Age:	22 Yrs Sex: Female	Report Dt. Tm:	28/03/2017 16:45:39
Name:	Mrs. Manisha Devi	Printed Date:	28/03/2017

IHC Final Diagnosis Panel # ^

LAB. NO. : I/2571/17

CLINICAL DETAILS :
Suggestive of small round cell tumor.

SITE : Left femur

SPECIMEN DETAILS :
Received paraffin block labeled as for IHC.
IHC performed on formalin fixed paraffin embedded block number

MORPHOLOGY:
Section shows tumor composed of masses of small dark round cells surrounded by fibrocollagenous septae. Tumor cells have round to oval uniform nuclei, dark clumped chromatin, inconspicuous nucleoli and small amount of cytoplasm. No rosette formation seen.Multiple bits of fibrocollagenous and fibroadipose tissue infiltrated by dense infiltrate comprising of neutrophils, plasma cells, lymphocytes and xanthoma cells are also noted.Fragments of dead bone are seen.

IHC MARKERS :	RESULT
CK	Negative
Vimentin	Strong and uniform positive in tumor cells
Ki-67	45%
CD99	Strong and uniform positive in tumor cells
Fli1	Moderate positive in most tumor cells.
NSE	Few scattered tumor cells are positive
CD56	Negative
CD57	Negative
Desmin	Negative
CD34	Negative
EMA	Negative

IMPRESSION:
Ewing Sarcoma/PNET

-All controls show expected reactivity
-Tests performed using Polymer detection system.
-This is an opinion based on material and details provided, kindly correlate clinically to reach a confirmative diagnosis.
-False negative/weak IHC results due to poor Antigen preservation in the material sent for evaluation cannot be excluded.

Fig 2

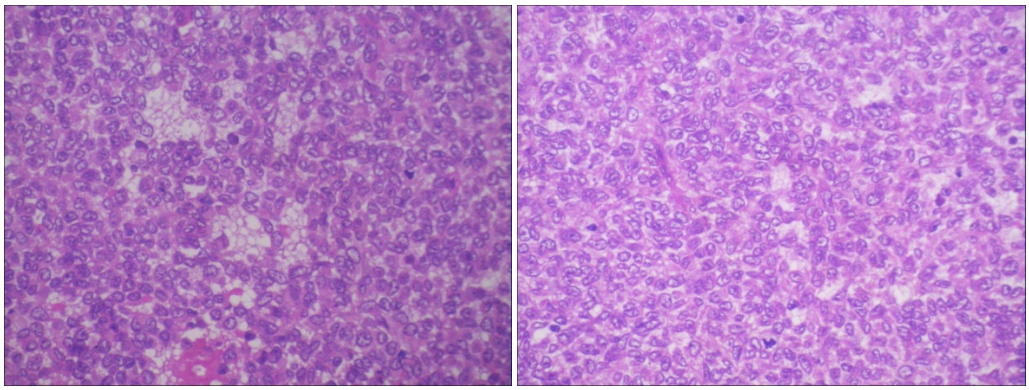

Fig 3

Biopsy of specimen shows: uniform small round cells with round nuclei (Figure 3)

Normal delivery was perform at 36 weeks of gestations. Post delivery chemotherapy for ewing scarcoma started. Post gestation x ray done shows no metastesis extension. (Figure 4)

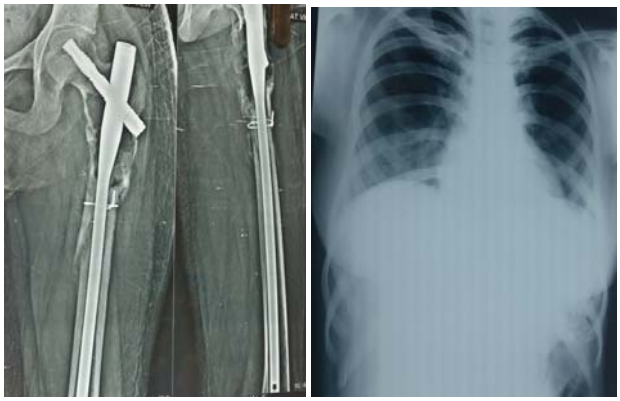

Fig 4

Three months after delivery both mother & child are in well condition (Figure 5)

Fig 5

Discussion

Lysyj and Bergquist [13] reported the first case of Ewing's sarcoma in pregnancy in 1963. Their patient presented at the 32nd week of gestation with pain in the right leg and was diagnosed with Ewing's sarcoma of the pubic ramus. Cesarean section was performed in week 36 of gestation. Neither chemotherapy nor radiation therapy was administered during gestation [13]. In the second case, a 21-year-old patient was diagnosed with Ewing's sarcoma of the left iliac wing in gestational week 25. She was treated with 1 cycle of multi-agent chemotherapy consisting of actinomycine D, cyclophosphamide, bleomycin, vincristine, and doxorubicin before she delivered a healthy baby by cesarean section in gestational week 34 [14]. The third case report by Merimsky *et al*. [10] describes the case of an Ewing's sarcoma of the right sacroiliac bone in a childbearing woman. Starting in the 27th week of pregnancy, 3 courses of 3-weekly doses of doxorubicin plus ifosfamide and mesna (ADR-IFX) were administered. Cesarean section had been pre-planned after completion of 3 cycles of chemotherapy and after achieving fetal lung maturation. The outcome was a small but normally developed baby [10]. Nakajima *et al*. [9] report the case of a 17-year-old woman with an extraskeletal Ewing's sarcoma of the left upper leg who was treated with a combination of doxorubicin and ifosfamide during the 25th to 30th week of pregnancy. After 3 cycles of chemotherapy, mild intrauterine growth retardation of the baby occurred and it was electively delivered in the 32nd week by cesarean section. The baby was small for gestational age and needed to be intubated because of irregular respiratory effort. Additionally, it received phototherapy for hyperbilirubinemia and erythropoietin because of a decrease in hemoglobin and reticulocytes. However, further on, the baby was growing adequately and had no known abnormalities at 8 months of age [9]. The 5th case report by Ateser *et al*. [17] describes the case of a primitive neuroectodermal tumor (PNET) of the ovary diagnosed in the 24th week of gestation. Starting in gestational week 30, 2 cycles of chemotherapy consisting of doxorubicin, cyclophosphamide, and vincristine were administered and a healthy baby was delivered by cesarean section in gestational week 37. After pregnancy, the mother was found to have metastatic disease and died due to progressive disease 13 months after the initial diagnosis [17].

When comparing our patient with the other case reports described above, the other women diagnosed with Ewing's sarcoma delivered safely. In this respect, it may be of interest that our patient received chemotherapy after the course of gestation that is after delivery. Comparable to our case report, most of the chemotherapy regimens were doxorubicin based. The multi-agent chemotherapy protocol administered in our patient consisted of ifosfamide, doxorubicin and vincristine and, unlike in other reported cases, etoposide. Nevertheless, the use of etoposide is documented in at least 25 sarcoma cases with a constantly favorable outcome for the offspring [18].

The care of a pregnant woman diagnosed with cancer involves evaluation of competing maternal and fetal risks and benefits. Furthermore, the diagnosis of a malignant disease during pregnancy raises serious medical as well as ethical, emotional, religious, and philosophical questions. Hence, the mother's well-being and the fetal risk by introducing early diagnosis and therapy should always be weighed against the risk to the mother's health and fetal well-being in carrying on an uninterrupted gestation. From our point of view, the curability of the mother's disease is the most important indication. Thus, in the case of a favorable prognosis or curative situation, chemotherapy should be given as early as possible.

Despite lack of robust consensus, multi-agent chemotherapy should be instituted early in the course of malignant sarcomas since the risk of metastasis occurrence is high. However, because rare scenarios like this raise major medical and ethical dilemmas, therapy should be tailored to each case and only be performed in specialized high-volume centers as the subject of a multidisciplinary consultation.

Conclusion

The diagnosis of primary bone tumours during pregnancy is rare. The very low incidence of malignant diseases during pregnancy and the confusion with pregnancy-related symptoms or complaints may cause delay in the diagnosis, as shown in this case. Clinicians should remain vigilant, certainly when complaints of the patient persist. In conclusion, diagnosis of bone and soft-tissue sarcomas in young pregnant women is rare. However, almost all types of sarcomas have been reported to coexist with pregnancy. In localized disease the goal is to treat primarily the mother and

simultaneously to try to protect and safe the life of the fetus depending on the period of gestation.

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