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Ewing's Sarcoma with Pancreatic Metastasis

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Abstract
Background :
Pancreatic metastases is a very rare presentation. The primary neoplasms which can cause pancreatic metastasis include melanoma, lung, gastrointestinal tract, breast and renal carcinomas, and lymphomas. Ewing's Sarcoma most commonly metastasizes to lung, pleura and bone. Ewings sarcoma with pancreatic metastasis is a rare entity.
Case description
20 year old female presented to hospital with pain in the right inguinal region for 2 months and was diagnosed as a case of ewings sarcoma. Patient was given External beam radiotherapy(EBRT) 50 Gy in 25 fractions and chemotherapy. After 5 years of follow up patient presented with pain in hip region. Patient was started on ifosfamide ,carboplatin and etoposide based chemotherapy. After 3 years of follow up she presented with pain abdomen. On ultrasound abdomen there was 25x11 mm lesion seen in the body of pancreas. On further investigating with CECT Chest , abdomen and Pelvis, there was soft tissue deposits were seen in pancreas, multiple bilateral lung nodule and hypodense lesion in right kidney.
Conclusion
In this case report we highlighted the rare case of Ewing Sarcoma of pubis bone with pancreatic metastasis at third relapse treated with 3 lines of chemotherapy.
Keywords*: Ewing's Sarcoma; Metastasis; Chemotherapy*
Ewing's sarcoma with pancreatic metastasis

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I. Introduction

Pancreatic metastases is a very rare presentation. The primary neoplasms which can cause pancreatic metastasis include melanoma, lung, gastrointestinal tract, breast and renal carcinomas, and lymphomas[1] . The incidence ranges from 6% to 39% in autopsies of cancer patients depending on the site of primary tumour and mostly presents with widespread disease with multiple other metastatic sites. Because of the rarity, it is crucial to distinguish between primary pancreatic carcinoma and metastatic lesion.

Ewings sarcoma, rhabdomyosarcoma and osteosarcomas are commonest tumours of musculoskeletal system in children, adolscents and young adults .The Ewing sarcoma family of tumors is a collection of small round blue cell neoplasms of neuroectodermal origin, which includes classical Ewing sarcoma, primitive neuroectodermal tumors, and Askin tumors of the chest wall [2]. Lung, pleura, and other bones are the common metastatic sites. Due to increased survival with multidisciplinary treatment, there have been increase in the unusual metastatic sites[3]. But pancreatic metastasis is extremely rare with very few cases reported in the literature. Here, we present a case of Ewing sarcoma pubis bone with pancreatic metastases.

II. Case presentation

20 year old female presented to hospital with pain in the right inguinal region for 2 months. On examination, tenderness along superior pubic ramus was present without any obvious swelling. Contrast enhanced computed tomography(CECT) of the abdomen and pelvis revealed expansile destruction involving right pubic ramus, anterior column of acetabulum and symphysis pubis. There was associated soft tissue component involving right obturator internus muscle measuring 5x3 cm. FNAC from right pubic ramus revealed Ewing's Sarcoma. Bone scan revealed increased osteoblastic activity in the right pubic bones and right acetabulum. Complete metastatic work up was done and no metastasis was found in chest , bone marrow or elsewhere. Patient was given External beam radiotherapy(EBRT) 50 Gy in 25 fractions and chemotherapy based on vincristine, Adriamycin and cyclophosphamide. After 5 years of follow up patient presented with pain in hip region, on further investigating with contrast enhanced computed tomography of chest abdomen and pelvis showed bone

destruction and erosive non enhancing necrotic soft tissue mass in right pubic ramus with bilateral lung metastasis. Patient was started on ifosfamide ,carboplatin and etoposide based chemotherapy. After 6 cycles of chemotherapy , CECT revealed stable disease. Patient was given palliative EBRT 25 Gy in 10 fractions to pubic ramus and acetabulum. After which patient denied further treatment and was kept on follow up. After 3 years of follow up she presented with pain abdomen. On ultrasound abdomen there was 25x11 mm lesion seen in the body of pancreas. Another lesion was seen in 47x33 mm in paraaortic region. On further investigating with CECT Chest , abdomen and Pelvis, there was lytic lesion seen in right pubic ramus and right acetabulum. Soft tissue deposits were seen in pancreas, gastrohepatic ligament, multiple bilateral lung nodule and hypodense lesion in right kidney(figure 1). Ultrasound guided FNAC from pancreas was done which revealed Ewing sarcoma metastasis with Immunocytochemistry positive for MIC2 and vimentin(figure 2). Patient was explained the prognosis and was started on 3rd line chemotherapy based on gemcitabine and docetaxel. After 6 cycle , assessment was done which revealed progressive disease. Patient is alive and is on best supportive care.

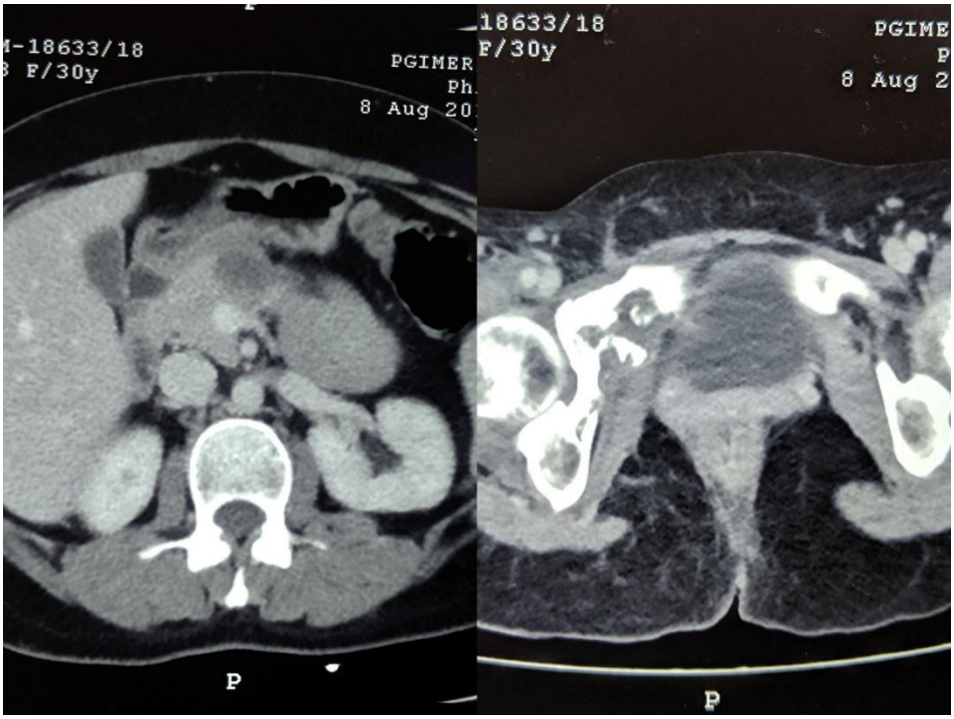

Figure 1: CECT axial section: Lytic lesion seen in right pubic ramus and right acetabulum and soft tissue deposits seen in pancreas.

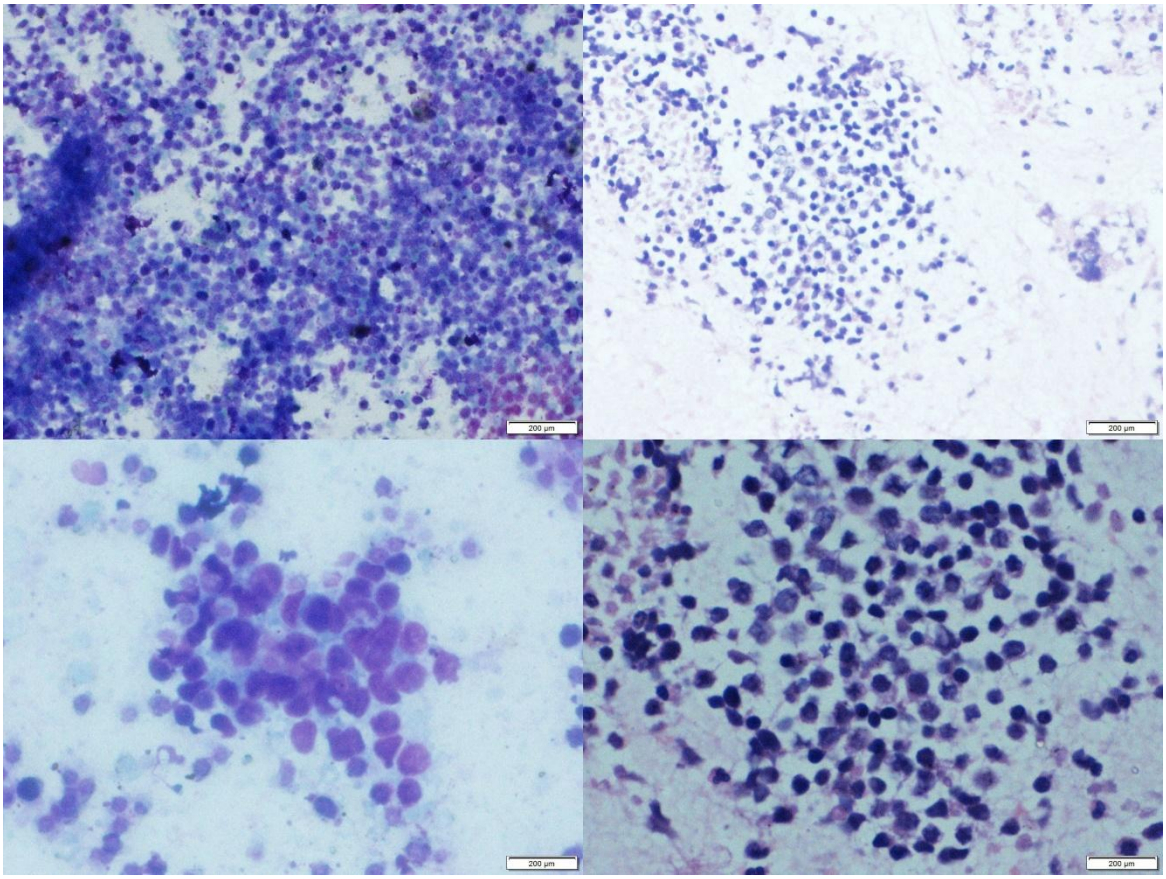

Figure 2: Degenerated cells and few clusters of small blue round cells with high N:C ratio and inconspicuous nucleoli. On Immunocytochemistry, these cells are positive for MIC2 and Vimentin.

III. Discussion

Ewing sarcoma is a rare malignancy that most often arises as an undifferentiated primary bone tumor or from soft tissue (extraosseous Ewing sarcoma). Both are part of a spectrum of diseases known as the Ewing sarcoma family of tumors (EFT). Around 25 percent of patients have overt metastases at the time of diagnosis and most common site of metastasis is lung , bone and pleura. Due to advancement in the management of these tumours and increase in survival , there have been unusual site metastasis reported with ewings sarcoma. And Ewing sarcoma with pancreatic metastases is a very rare presentation. On searching literature , there were 3 case reports reported of Ewing sarcoma with pancreatic metastasis. Details of these case reports are given in table 1.

Refrence no	Diagnosis	Age/sex	Clinical symptoms	Years after diagnosis	Relapse number	Associated metastasis	Treatment	Outcome
[4]	Femur ewings sarcoma	26/M	No	0(synchronous)	0	Bone	RT+CT	Died due to disease
[8]	Pubis Ewings Sarcoma	28/M	No	3	second	Local relapse	RT	Dead of other cause (exudative pancreatitis) 8 months
[9]	Hemithrax extraosseus ewings sarcoma	15/F	Jaundice		second	No	NA	NA
Present case	Pubis ewings sarcoma	20/F	Pain abdomen	8	Third	Lung, kidney, retroperitoneal	RT+CT	Alive withProgressive disease

As it is a rare presentation, so it is crucial to differentiate between a primary pancreatic metastasis and primary lesion and this may be very difficult based merely on clinical and radiological features[4]. The clinical symptoms are non-constant and non-specific, mostly related to compressive effect. If a patient has a history of sarcoma, the diagnosis of pancreatic metastasis may be suggested by imaging if multiple pancreatic lesions are present. However, if the pancreatic lesion is solitary, it should be distinguished from primary pancreatic carcinoma. Thus, histological diagnosis is must with IHC[5]. For primary pancreatic cancers usually CK7 and CK20 are positive and in addition to this Maspin, S100P, MUC5AC can be positive[6]. IHC marker for Ewing sarcoma are CD99 (membranous staining), FLI1, PAS+ diastase sensitive (glycogen), vimentin, neuron specific enolase and MIC2[7]. In our patient , FNAC from pancreas was done which showed Ewing sarcoma metastasis with IHC positive for MIC2 and vimentin.

The prognosis of pancreatic metastasis is poor. There is no clearly defined management guidelines available. Although role of surgery is not clearly defined, but there are reports of prolonged survival after removal of isolated pancreatic metastasis for different cancers including carcinomas [10-12] and soft tissue sarcomas [13]. As isolated pancreatic metastasis is a very rare presentation and generally patients presents with other systemic disease also, so systemic chemotherapy is a better option. Options in Ewing sarcoma with metastasis include ifosfamide and etoposide with or without carboplatin, gemcitabine -docetaxel, topotecan/irinotecan with cyclophosphamide and temozolomide. Palliative radiotherapy to the metastatic site can provide with the symptomatic relief[14].

In our patient , gemcitabine and docetaxel was given as this was the third relapse and patient had already received VAC based chemotherapy and ifosfamide ,etoposide and carboplatin based chemotherapy. After 6 cycles of chemotherapy disease progressed.

Around 30-40% of Ewing sarcoma patients present with relapses and have poor prognosis. Late relapses (more than 2 years) with lungs only metastasis have better prognosis than early relapses and non-pulmonary metastasis. Other poor prognostic markers at relapse are poor response to therapy and raised LDH at initial diagnosis and at the time of relapse. In a retrospective analysis, it was seen that site of first relapse and time of first relapse are the most significant prognostic markers [15].Our patient is still under follow up since 5 months of completing chemotherapy with best supportive care and palliative management.

IV. Conclusion

In this case report we highlighted the rare case of Ewing Sarcoma of pubis bone with pancreatic metastasis at third relapse treated with 3 lines of chemotherapy. As pancreatic metastasis is a rare presentation, primary pancreatic carcinoma should be ruled out. Diagnosis should be confirmed with immunohistochemical markers. Systemic chemotherapy plays an important role in the management with or without palliative radiotherapy.

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