

Primary Ewing Sarcoma of Breast : A Rare Case Report

Dr Guddi Rani Singh, Dr Anju Singh, Dr Ravi Bhushan Raman

Abstract— Ewing's sarcoma/primitive neuroectodermal tumors (EWS/PNET) are rare malignant and aggressive tumors, usually seen in the trunk and lower limbs of children and young adults. They are uncommon in the breast. We report a case of a 20-year-old woman who developed a painless breast mass. An initial ultrasound and FNAC done outside concluded to a fibroadenoma contrasting with a rapidly growing mass. Diagnosis of primary PNET of the breast was established, based on repeat FNAC, histopathological examination of incisional biopsy and immunohistochemical findings. The patient was given 6 cycles of adjuvant chemotherapy containing cyclophosphamide, adriamycin and vincristine. Twenty months later, she is in life without recurrence or metastasis. EWS/PNET may impose a diagnostic challenge. Indeed, ultrasonographic features are non specific. The histopathological pattern is variable depending on the degree of neuroectodermal differentiation. Hence, Immuno-phenotyping is necessary to confirm the diagnosis.

Index Terms — Primitive neuroectodermal tumor, FNAC, Immunohistochemical finding, neuroectodermal differentiation, Ewing's sarcoma, breast, Diagnosis

1. INTRODUCTION

Ewing's sarcoma/primitive neuroectodermal tumors (EWS/PNET) represent a group of rare malignant tumors, probably arising from migrating embryonic cells of the neural crest and showing variable neuroectodermal differentiation. They usually arise in soft tissues or bone; commonly in children and adolescents.¹ They are extremely rare in adults, but have been reported on the chest wall and other body parts. Breast location remains exceptional. We report here a case of ewing sarcoma primarily developed in the breast.

2. Case Presentation

A 20-year-old female presented with one year history of huge right breast. Nodular swelling of about 10x10 cm and one axillary lymph node swelling of about 3x3 cm (Fig.1). On examination the swelling was freely mobile with respect to skin and underlying structure, non tender, smooth nodular surface. History taking revealed surgical excision 1 yr back and recurrence of the same. But the bad luck was that histopathological examination of that excision specimen was not done.

On laboratory investigation, Complete blood count was normal. On ultrasonography a large encapsulated lobulated solid echogenic mass noted at 3'0 clock position. Fibroadenoma ?? suspected. A chest radiograph showed an opacity in the right

hemithorax with no involvement of bony rib cage. To well document this opacity, a computed tomography (CT) scan was justified. The CT scan revealed a large expansile lytic lesion seen to involve right sided 5th anterior rib with large soft tissue component and lesion shows both intrathoracic and extra thoracic extension. Whole of the lesion measures about 18x17x16cm. (Fig.2)

On FNAC, nature of aspirate was haemorrhagic. Smear shows cluster of round cells having hyperchromatic nucleus with nil to moderate amount of vacuolated cytoplasm (Fig.3). Features suggestive of Round Cell Tumor. Differential diagnosis were Ewings sarcoma/PNET and Alveolar rhabdomyosarcoma. Biopsy.

On incisional biopsy, biopsy specimen were stained with H& E and examined under microscope. Section shows tumour cells arranged in sheets. Individual cells were round, small cells with mild pleomorphism. Background shows necrosis. Malignant round cell tumor was suggested (Fig.4). On immunohistochemical examination CD99 was focally positive (Fig. 5) and FLI 1 was diffusely positive (Fig. 6). A diagnosis of PNET of breast was made.

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Fig 1. patient with unilateral enlarged nodular breast

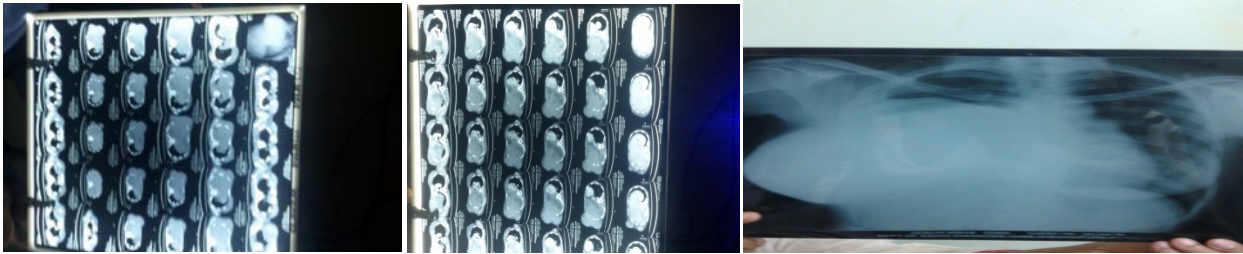


Fig. 2. X ray and CT scan finding

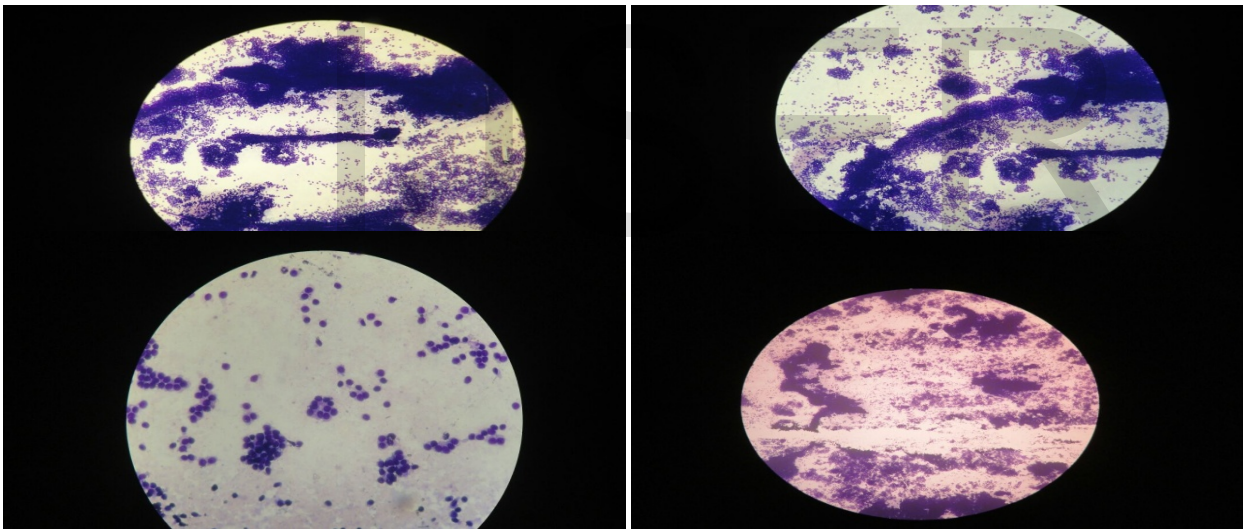


Fig. 3. FNA Findings - Small round cells in clusters and freely scattered, pseudorosettes also seen.

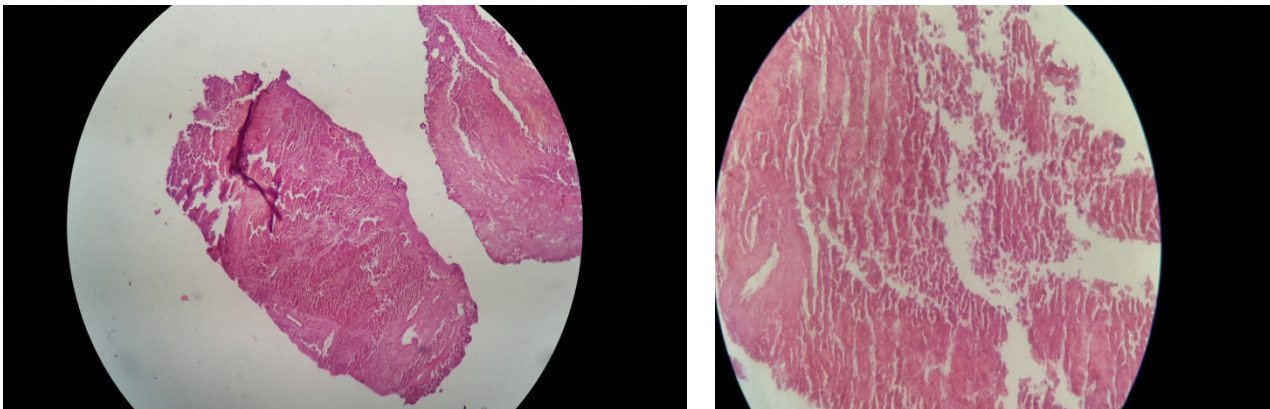


Fig.4. HPE of core biopsy from tumour

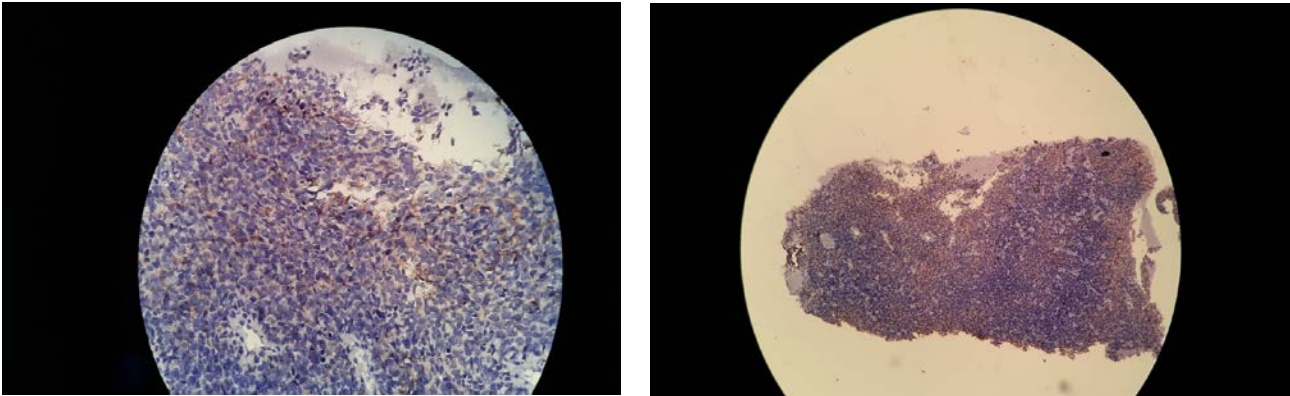


Fig. 5. CD 99 Focal positivity

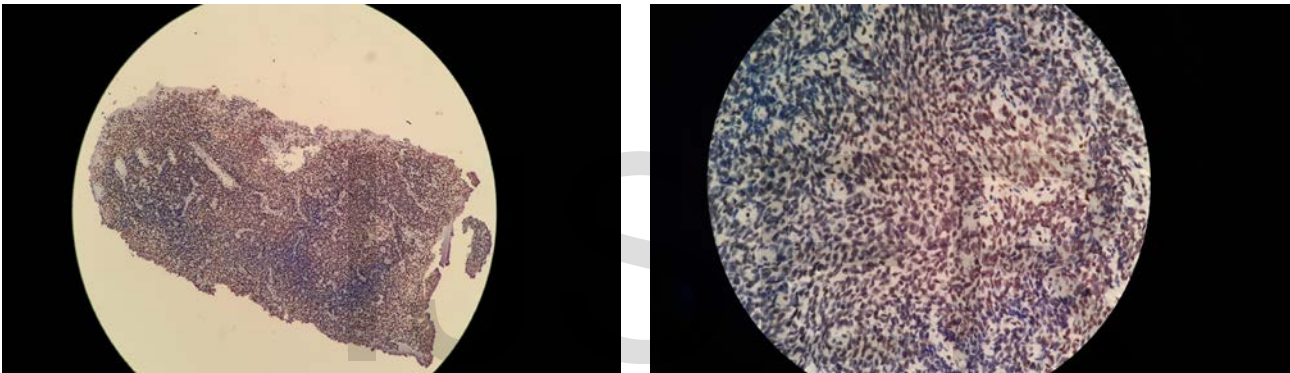


FIG.6.FLI 1 Diffuse positivity.

3. Discussion

Carcinomas are the majority of malignancies involving the breast; sarcomas represent less than 1% of breast malignancies [2]. EWS/PNET of the breast is extremely rare, with several of primary tumors previously reported in the literature. [3]. EWS and PNET form a single group of bone and soft-tissue tumors [Ewing's sarcoma family of tumors (EFT)] with typical undifferentiated Ewing's sarcoma at one end of the spectrum and PNET with clear evidence of neural differentiation at the other.[4],[5].

Several studies of adult EWS/PNET from the Royal Marsden, the Memorial Sloan-Kettering and the Dana-Faber Cancer Centers have reported a median age of 24-27 years. [6]. Our case revealed the age was 20, slightly younger than the median age.

In relation to breast presentation of EWS/PNET, the most common is unilateral palpable mass in the breast, with a median dimension of 5 cm.[6] In the present case tumor's size was initially of 3 cm, than rapidly enlarged to reach 10 cm. Majid *et al.* reported one case of bilateral primary neuroectodermal tumor of the breast.[7].

Ultrasonography features of EWS/PNET are non specific. They can vary from a hypoechoic mass with posterior enhancement to a heterogeneous mass with a necrotic area.[8] Maxwell *et al.* described sonographic findings of primary EWS/PNET of the breast as a superficial, circumscribed, hypoechoic mass with posterior acoustic enhancement and an apparent hypoechoic tract extending to the skin.[9]. These lesions were misdiagnosed as an epidermal inclusion cyst and considered therefore as benign. In the present case, sonographic findings were different, displaying a large encapsulated lobulated solid echogenic mass noted at 3'0 clock position. CT scan features of EWS/PNET are also non specific, usually showing a large, non calcified and heterogenous soft tissue mass with cystic or necrotic areas on CT.[10]. In our case the CT scan revealed a large expansile lytic lesion seen to involve right sided 5th anterior rib with large soft tissue component and lesion shows both intrathoracic and extra thoracic extension. Whole of the lesion measures about 18x17x16cm.

Ewing sarcoma shows cytomorphological diversity. But the typical pattern were characterized by many cells, both larger, light cells and smaller, dark cells with high N/C ratio, fine chromatin, and small nucleoli. In some of these cases prominent nuclear molding and crush artifact were focally seen, but necrosis was not prominent [11]. In our case , FNAC Smears shows bimodal cell population in both clusters and freely scattered.Larger, and smaller dark cells with large hyperchromatic nuclei. Neuroblastoma may be difficult to distinguish from ES, particularly because both tumors share some cytologic features, such as small cell size, high N/C ratio, and rosettes. A helpful feature is the presence of neurophil in the background of neuroblastomas and in the center of the Homer-Wright rosettes. Here we got pseudorosette.

The histopathological pattern of EFT is variable depending on the degree of neuroectodermal differentiation. The tumor is arranged in sheets, lobules or trabeculae. Pseudo-rosettes can be seen. Cells vary from small, round cells with round nuclei, fine chromatin, scant cytoplasm and indistinct cell borders to larger cells with irregular nuclear contours. Mitotic activity is high. Necrosis may be present [11]. Primary EWS/PNET of the breast might be misdiagnosed as a small cell carcinoma, medullary carcinoma, poorly differentiated ductal or lobular carcinoma or ductal carcinoma with neuroendocrine differentiation owing to its morphology and immunohistochemical characteristics. The possibility of a distant metastasis should also be raised.5 Metaplastic carcinoma with neuroectodermal differentiation should be considered, so extensive sampling and immunohistochemical investigation are compulsory to do [12],[13].

Immuno-phenotyping is necessary to confirm the diagnosis of EWS/PNET, showing positivity of tumoral cells for Fli-1 and CD99 (Mic-2) [5]. CD99 is a cell surface glycoprotein involved in cell adhesion. It shows a membranous staining and seems playing a crucial role in the diagnosis of EWS/PNET [11]. It was initially thought to be highly specific for EWS/PNET, but it is now recognized that, although its sensitivity ranges from 84% to 100% in EWS/PNET, its specificity is limited [11] and may also be expressed in metaplastic carcinoma of the breast, neuroendocrine carcinoma, lymphoma and rhabdomyosarcoma [11] EWS/PNET that are only immunoreactive to CD99, albeit rare, have been reported in the literature [5].

Thus, histological and immunohistochemical examination is contributive to propose the diagnosis of PNET in most cases. However; genotypic analysis, by DNA- and RNA-based polymerase chain reaction, Southern blotting, and fluorescent *in situ* hybridization are the only confirmatory tools.4 but in our case genotypic analysis was not done due to limitations of infrastructure.

Owing to these recent improvements in diagnostic ability, we now realize that EWS/PNET develops in diverse and previously unexpected locations and we should be able to detect more cases of EWS/PNET of the breast, some of which might have been diagnosed previously as small cell carcinomas or carcinomas with neuroendocrine differentiation.EWS/PNET is an aggressive tumor with a high incidence of local recurrence and distant metastasis. A combination of multiple treatment modalities, including surgery, chemotherapy and radiation therapy, is indicated for these patients.6 Systemic chemotherapy improves the 5-year survival rate in localized forms of PNET from 10% up to 65% which is primarily due to the elimination of micrometastases.14 Although the optimum combination chemotherapy has not yet been established, a regimen containing vincristine, adriamycin, cyclophosphamide and actinomycin D, was the standard first-line treatment for patients with localized disease.14 In patients with unresectable or metastatic disease, palliative chemotherapy may be useful [14]. The role of radiation therapy in the treatment of PNET is unclear. However, it can be combined with surgery, in order to control local disease [8].

4. Conclusion

EWS/PNET are rare tumors developed in the breast, their diagnosis need early diagnosis by FNAC, histopathological examination, and immunohistochemical examination. These ancillary techniques are necessary in order to rule out other types of malignant tumor owing poor prognosis and different way of management.

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