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Peripheral Primitive Neuroectodermal Tumor of the Chest Wall

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A thirty-one-year-old Bangladeshi male presented to the surgical outpatient clinic with a painless lump. Histopathology revealed peripheral primitive neuroectodermal tumor (PNET) arising from the chest wall. The tumor was characterized by two populations of cells, predominantly small round cells and invading nearby tissue. The histological examination was complemented by immunohistochemistry; the tumor cells were positive for CD99, BCL2, NSE, EMA and Vimentin.

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Ewing Sarcoma (EWS) or primitive neuroectodermal tumor (PNET) is an aggressive soft tissue tumor that carries EWS translocation, most commonly t(11:22)(q24;q12) which results in EWS-FL1 fusion protein (1=25,26)[1,2]. Soft tissue tumors other than Ewing sarcoma/peripheral primitive neuroectodermal tumor carrying EWS translocations could present differently in terms of clinical features and prognosis, such as Angiomatoid Fibrous Histiocytoma t(12;22)(q13;q12), Clear Cell Sarcoma t(12;22)(q13;q12) and Desmoplastic Round Cell Tumor t(11;22)(p13;q12)[1]. This rare malignant tumor has a predilection in children, adolescents, and young adults.

The aim of this presentation is to report a case of PNET presenting as a painless mass in an adult male.

THE CASE

A thirty-one-year-old Bangladeshi male presented with a painless mass on the lateral chest wall. The lump was present since childhood and recently started to increase in size. He denied any history of weight loss, anorexia or trauma to the region.

On examination, a 7x10 cm well-defined firm to hard in consistency mass was located on the lateral chest wall with limited mobility. The mass was non-tender, and the overlying skin was unremarkable. The provisional diagnosis was benign lesion; therefore, neither biopsy nor radiological imaging were requested.

Intraoperatively, there was a solid adherent mass with many finger-like projections into the surrounding soft tissue. The surgeon was unable to enucleate the whole lump.

The mass was suspicious of malignancy. Grossly, it was 35x30x24 mm round, firm tan lump, weighing 21 g. The cut surface is solid and grayish-tan in color with areas of hemorrhage and necrosis.

Microscopically, the lump was formed by two populations of tumor cells that showed lobular growth patterns associated with ramifying fibrovascular septa. The first population showed cells that have scanty, pale cytoplasm and round open nuclei with a very finely distributed chromatin. The other cell population showed dark elongated nuclei, suggestive of neuroendocrine origin, see figure 1. The tumor cells showed apoptosis with infrequent mitosis (2/10 HPF). Focal areas of necrosis were also noted. The tumor infiltrated through adjacent skeletal and adipose tissues and appeared to be incompletely excised, see figure 2.

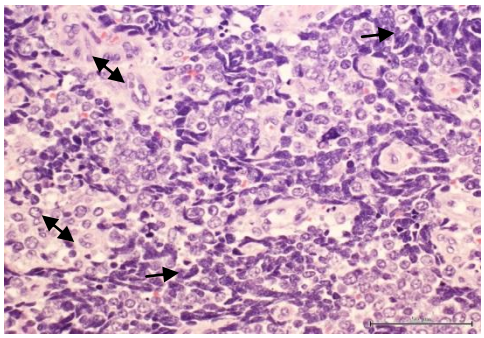

Figure 1: PNET: Two Populations of Cells; Round Open Nuclei with Pale Cytoplasm (Double Headed arrow) and Dark Elongated Nuclei (Arrow) (H&E, HPF)

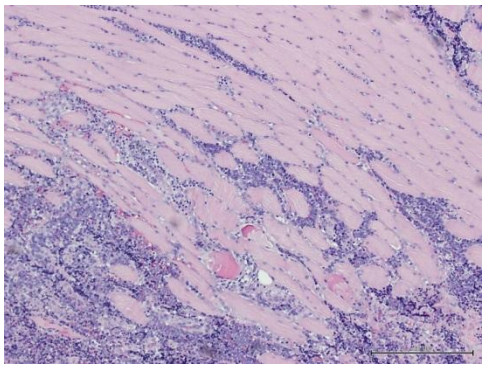

Figure 2: PNET: Infiltrative Borders with Extension into Skeletal Muscle Tissue (H&E, LPF)

CD99, BCL2 and Vimentin showed strong positivity, see figure 3. While NSE shows weak positivity and EMA reveals spot positivity, see figure 4.

Synaptophysin, CK AE1/AE3, S-100, Chromogranin A, SMA, CD20, CD45, LCA, CD3, CK20, WT-1 and Desmin showed no expression (negative).

The combination of morphology and immunohistochemistry is suggestive of peripheral primitive neuroectodermal tumor (PNET).

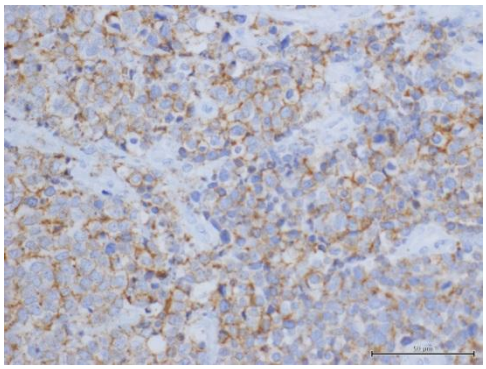

Figure 3: PNET: CD99 Membranous Positivity within the Tumor Cells (CD99, MPF)

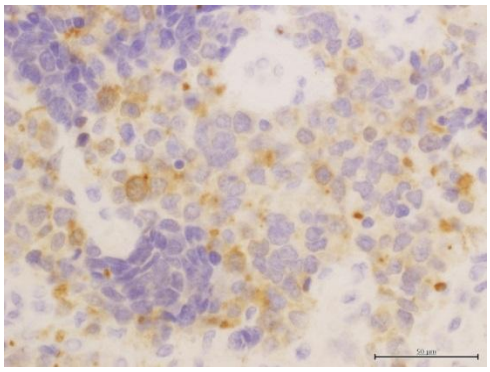

Figure 4: PNET: Tumor Cells Cytoplasm were Positive for NSE (NSE, HPF)

Postoperative PET-CT scan showed 5.9x1.03 cm elliptical area of residual disease with active tracer uptake (SUV max of 9.8).

The tumor board recommended that the patient should receive systemic chemotherapy and local radiotherapy. However, he has been delayed due to personal and financial reasons. At that time, he had a regrowth of the residual tumor with clinical evidence of subcutaneous nodules around the operative scar.

Systemic treatment was started from April 2013 to July 2013 by induction of 4 cycles of chemotherapy (VAC alternating with IE: vincristine, actinomycin-D, cyclophosphamide, ifosfamide, etoposide). PET-CT scan on 15 August 2013 showed remarkable regression of the previously noted operative bed with decreased 18 F-FDG uptakes. He received radiotherapy to the left lateral chest wall, a dose of 60 Gy in 30 fractions from 1 September to 10 October 2013. Adjuvant chemotherapy was given; the patient received another ten cycles of VAC-IE, the last dose was in April 2014.

Regular follow-up revealed no evidence of local or distant metastasis. The last PET-CT on 15 September 2014 showed no residual or recurrence of the primary disease.

DISCUSSION

Historically, the first osseous EWS case was reported 90 years ago by James Ewing, and hence the name. Other similar cases followed, and the initial impression of osseous Ewing sarcoma has expanded to include extra-osseous cases and PNET. The World Health Organization have included EWS and PNET under the same entity and termed it as Ewing family of tumors[1,3].

EWS/PNET arises from primitive mesenchymal cells and sometimes showing neural differentiation[4]. PNET is a rare tumor and is considered the second most common sarcoma in children and young adults. This tumor affects males more than females and often occurs in children, adolescents, and young adults[5].

Twenty to forty percent of all EWS/PNET are extra-skeletal and mainly found in the soft tissues of the trunk, extremities, head and neck, retroperitoneum and kidney[1,6,7]. In our case, the tumor was arising from the chest wall, and, in that case, this tumor could also be called ASKIN tumor[8].

Clinically, the majority present with pain; but paresthesia, weakness or loss of function indicating nerve involvement are not uncommon. Mass formation, fever, weight loss and other constitutional symptoms have also been reported[1,5].

Radiologic features are non-specific; they appear as large heterogeneous masses with intratumoral, multiple, patchy, unenhanced areas suggesting cystic and necrotic degeneration. Calcification is a rare feature[5].

EWS/PNET are variable, they could be well-circumscribed, nodular, lobulated or infiltrative with areas of hemorrhage, cysts and/or necrosis. Gross and microscopic examination of the margins is very important, as any positive margins should be treated with radiotherapy[1].

Microscopically, the classical variant, as in our case, constitutes about 60%-70% of the cases and shows small, round to oval cells arranged in nests or lobules with finely dispersed nuclear chromatin and nucleoli. The cytoplasm is clear to vacuolated (PAS-D positive). The tumor is usually surrounded by fibrosis, spindle cells as well as aggregates of rosettes (Homer-Wright) and pseudorosettes, which represent neural differentiation. Mitosis can be variable; in our case, only 2/10 HPF mitotic figures were seen[1,9].

Other uncommon microscopic variants include large cell, medulloepithelioma, adamantinoma-like, vascular and sclerosing pattern[1].

Diagnosis of EWS/PNET is rather difficult and should be differentiated from other small round cell tumors by the use of immunohistochemistry and molecular genetics (FISH and reverse transcription polymerase chain reaction)[1].

EWS/PNET is positive for CD99 (membranous), Fli1 (nuclear) and Cavolin-1 (membranous) with negative desmin and myogenin. CD56, NSE, synaptophysin are used for neuronal differentiation[1].

The treatment of EWS/PNET is chemotherapy followed by definitive surgery, radiation or both, depending on the size, location, resctability of the tumor and initial chemotherapy response. The five-year survival rate ranges from 60%-75% for non-metastatic tumors and 20% for metastatic counterparts[8,10].

Adverse prognostic features include any tumor more than 8 cm with an axial location, metastasis, and recurrence of EWS/PNET after therapy. Younger age of onset and cutaneous/superficial EWS/PNET are good prognostic factors[10,11]. Due to lack of evidence, it is now debatable that neural differentiation carries poorer prognosis as was believed in the past[12].

CONCLUSION

A rare case of ASKIN tumor occurring in a 31-year-old male was presented. Diagnosis of EWS/PNET is challenging and should be considered in the differential diagnosis of other small round cell tumors.

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