Case Report:

Unusual Presentation of Peripheral Primitive Neuroectodermal Tumor: A Rare Case Report

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Abstract:

A primitive neuroectodermal tumor (PNET) is a rare entity occurring most commonly in the 2nd and 3rd decade and is very rare in patients over 40 years of age. PNET is a round cell malignancy of presumably primitive neuroectodermal tissue or migratory neural crest cells arising from soft tissue or bone. PNET occurring outside the central nervous system is called peripheral PNET (p PNET) and most commonly involves the trunk and extremities Here we present a case of PNET diagnosed in an elderly male who presented with a soft tissue mass in the gluteal region. The histopathology with ancillary techniques including immunohistochemistry and molecular studies helped in establishing the diagnosis of PNET. They are characterized by translocation leading to the fusion of Ewing's Sarcoma (EWS) gene on 22q12 with any of the member of the ETS (E 26 transformation specific or E -twenty – six) family of transcription factors with the most frequent being t (11;22) (q24;12). Intensive multiagent chemotherapy is the mainstay of treatment as it has great potential for metastatic spread. The prognosis of adults with Ewing's sarcoma (ES)/PNET is not well known, however, some reports suggested that adults with ES/PNET have a poorer prognosis than children. Cytology is the first line of diagnosis for RCT. However, the type-specific diagnosis or final diagnosis of p PNET is based on histopathology aided with IHC and other ancillary techniques.

Keywords: Round cell tumor, p PNET, CD99, FLI1.

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Introduction:

Extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor is a rare entity and most commonly involves the trunk and extremities. The PNET occurring outside the central nervous system is called the peripheral PNET (p PNET).[1] These tumors are "small blue round cell tumors" and the recent clinicopathological studies suggest that they belong to the Ewing's sarcoma family of tumors(ESFTs).[2,3] More than 90% of ESFT have specific chromosomal rearrangements between the EWS gene on chromosome 22 and different members belonging to the ETS gene family of transcription factors.[4] PNET can be seen in every age, with most of the cases in the 2nd and 3rd decade but it is rarely found in patients over the age of 40 years.[3] It is extremely rare in patients over 50 years. The differentiation of ES/PNET from other small round cell neoplasms is possible with the aid of ancillary techniques which include immunohistochemistry, cytogenetic analysis, reverse transcriptase polymerase chain reaction (RT-PCR), and fluorescent in-situ hybridization (FISH).[5]

Here we report a case of a round cell tumor in an elderly male who was diagnosed as p PNET with the help of immunohistochemistry and molecular studies for EWS-FLI1 (friend leukemia integration 1transcription factor) gene translocation which was positive.

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Case Report:

A 66-year-old elderly male presented with a right gluteal mass measuring 10cm x 6cm which was rapidly increasing in size for the past two months. On examination, there were no inguinal nodes. The rest of the clinical examination was unremarkable. Magnetic resonance imaging (MRI) revealed a large well defined T1w/Trim hyperintense lesion in the right gluteal region extending through the greater sciatic foramen and infiltrating into the right gluteus medius, gluteus minimus, and part of right pyriformis. No bony involvement or metastasis was identified (Figure 1). A PETCT was also done and no abnormal uptake at any other sites or metastasis was noted.

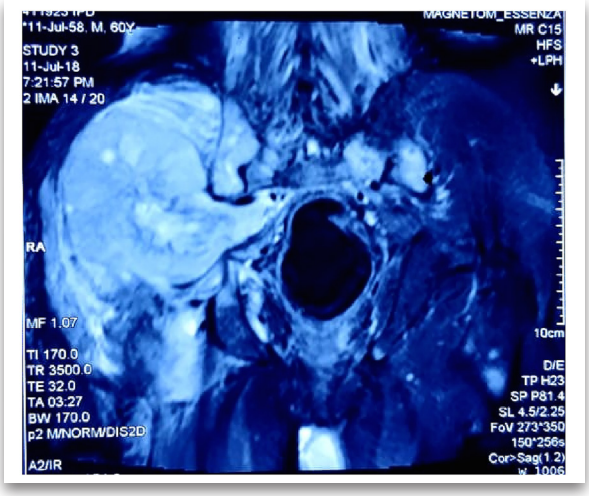

Figure 1: Magnetic resonance imaging (MRI) shows a mass in the right gluteal region extending through the greater sciatic foramen and infiltrating into the right gluteus medius, gluteus minimus, and part of right pyriformis.

Fine needle aspiration cytology (FNAC) was advised as the first line of investigation as it is simple, easy, and cost-effective, however, histopathology remains the gold standard for the diagnosis of round cell tumors. FNAC yielded a blood mixed aspirate. The cytology smears were cellular showing the presence of tumor cells present singly and in clusters along with the formation of rosettes at few places. The cells were pleomorphic, round to oval with scant cytoplasm, having hyperchromatic nuclei and inconspicuous nucleoli (Figure 2). The presumptive diagnosis on FNAC was Round cell tumor and histopathology with Immunohistochemistry (IHC) was advised for type-specific diagnosis.

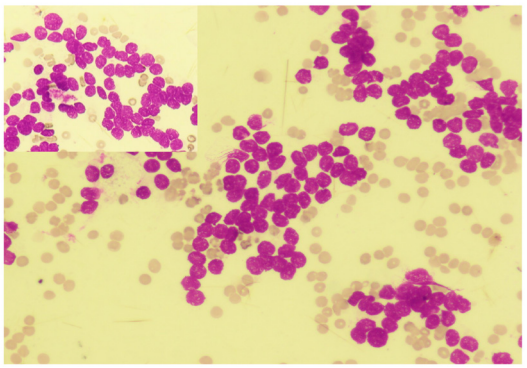

Figure 2: Giemsa-stained smears show round to oval cells in clusters having hyperchromatic nuclei and inconspicuous nucleoli. Few areas show rosette formation (200X).

The histopathological examination revealed cells arranged in sheets and clusters which were round to oval with hyperchromatic nuclei and scant cytoplasm forming rosettes at places (Figure 3). Immunohistochemistry (IHC) for CD-99 showed diffuse membranous positivity (Figure 4). However, IHC for Non-Specific Esterase (NSE), Leukocyte common antigen (LCA), Desmin, S-100, and pan- Cytokeratin (pan-CK) were negative. Based on the histopathological and IHC findings a provisional diagnosis of extra skeletal soft tissue Ewing's sarcoma/PNET (primitive neuroectodermal tumor) was made. Molecular analysis for EWS-FLI-1 was also positive thus confirming the diagnosis.

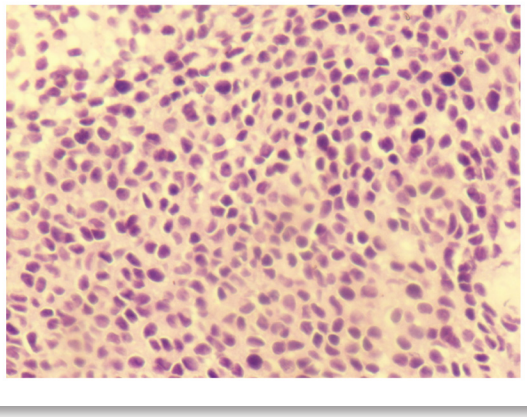

Figure 3: Sections show small round to oval in sheets and few forming rosettes at places. The tumor cells have hyperchromatic nuclei, scant cytoplasm and inconspicous nucleoli.

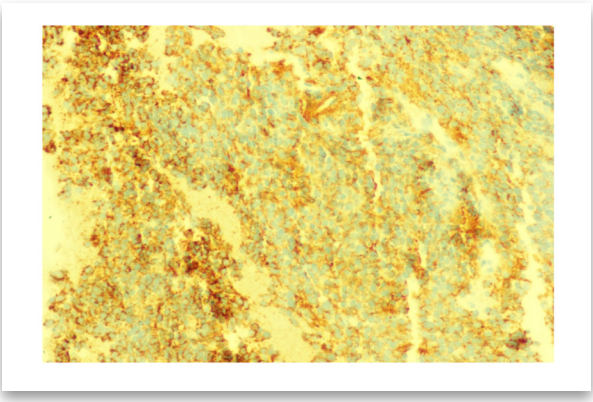

Figure 4: The tumor cells show membranous positivity for CD 99.

Wide local resection of the tumor was done, and the patient was kept on close clinical follow up. No new lesion or recurrence of the tumor was noted.

Discussion:

Malignant small round cell tumors (MSRCT) include Ewing's sarcoma (EWS), peripheral neuroectodermal tumor, rhabdomyosarcoma, synovial sarcoma, non-Hodgkin's lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma.[6] PNET arises from presumably primitive neuroectodermal tissue or migratory neural crest cells from soft tissue or bone. It is seen in older children and adults and includes round cell tumor of thoraco-pulmonary region (Askin's tumor), extra skeletal Ewing's sarcoma, peripheral neuroblastoma, and peripheral neuroepithelioma.[7] The pelvis and the femur are the most commonly involved and a majority of cases are reported in the second decade of life.[8]

Our case was extremely rare as the patient was an elderly male of 66 years with a tumor primarily involving the extra skeletal soft tissue in the buttock region. According to the literature, there are only a few handfuls of case reports of PNET seen in the elderly and the sites reported by various authors include the maxilla and pelvis.[1,3]

PNET, Askin's tumor, and skeletal-extra skeletal ES are considered to belong to the ES/PNET family of tumors based on recent advancements of immunohistochemical, cytogenetic, and genetic techniques. These tumors have random translocations leading to the fusion of the EWS gene on 22q12 with any of the members of the ETS family of transcription factors. Of the various translocations, the most common translocation reported is t (11;22) (q24;12).[1]

ES-PNET are on the two ends where PNET shows a definite neuroectodermal differentiation whereas, ES on the other hand is poorly differentiated, however, they are considered together for treatment and prognostication.[2]

Fine needle aspiration cytology has the advantage of being a less invasive procedure in aiding the tissue diagnosis before starting the treatment. However, in the case of small round cell tumors, it may pose a difficulty in arriving at a definitive diagnosis due to morphological similarities between the various types of round cell tumors.[9] Histopathology along with the ancillary technique is of great diagnostic significance in such cases.[1]

The cytology smears show tumor cells in clusters with few cells arranged compactly. The tumor cells have a high nuclear-cytoplasmic ratio with round or irregular nuclei and inconspicuous nucleoli. Ewing's sarcoma consists of two types of cells, larger chief cells, and smaller darker cells. The cytoplasm is vacuolated due to glycogen showing positive staining by periodic acid Schiff stain (PAS). The other findings include pseudo rosettes, Homer Wright rosettes, and fibrillary matrix.[6]

The tumor cells are positive for CD99 showing membranous expression which is highly sensitive and thus helpful in distinguishing it from other malignant small round cell tumors.[7] In the present case, morphology pointed towards a round cell tumor and the membranous positivity of CD99 supported the diagnosis of ES/ PNET. Since CD99 can be positive in other tumors like mesenchymal chondrosarcoma, poorly differentiated synovial sarcoma, and lymphoma, therefore it should be used along with a panel of other immune stains.[7] In our study, the tumor cells were negative for the immunomarkers like LCA, NSE, S100, Desmin, myoD1, and pan-cytokeratin and vimentin. The molecular studies give a definitive diagnosis with FLI1 protein which is a gene product of FLI1, t (11:22) positive in 80% of cases.[7] The molecular study for translocation for EWS-FLI1 translocation was positive in the present case.

Ewing's sarcoma/PNET has a great potential for systemic spread and therefore intensive multiagent

chemotherapy is the mainstay of treatment. The other options include surgery, combined surgery, and radiation therapy or radiation therapy alone.[2] In the present case, a mass was resected with wide local excision and the patient was kept on close clinical follow-up, but no new lesion or recurrence of the tumor was noted to date.

The prognosis of adults with Ewing's sarcoma/ PNET is not well known due to a handful of cases reported in the literature as mostly the patients with this tumor are found in the 10-20 years age group.[2]

Conflict of interest: None.

Ethical Approval Issue: Ethical clearance was taken from the Institutional Ethical Committee.

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Authors' Contribution: Each of the authors has contributed to, read and approved this manuscript.

References:

1. Kulkarni MM, Khandeparkar SG, Joshi AR, Barpande C. A rare case of extraskeletal Ewing's sarcoma/ primitive neuroectodermal tumor developing in maxillary sinus of an old patient. J Oral Maxillofac Pathol. 2016;20(2):330.
2. Baldini EH, Demetri GD, Fletcher CD, Foran J, Marcus KC, Singer S. Adults with Ewing's sarcoma/ primitive neuroectodermal tumor: adverse effect of older age and primary extraosseous disease on outcome. Ann Surg. 1999;230(1):79-86.
3. Saada E, Thariat J, Follana P, Birtwisle-Peyrottes I, Haudebourg J, Trojani C, Bacque P, Thyss A. Primitive neuroectodermal tumor of the pelvis in an elderly patient. Onkologie. 2009;32(8-9):499-502.
4. Lopez-Guerrero JA, Machado I, Scotlandi K, Noguera R, Pellin A, et al. (2011) Clinicopathological significance of cell cycle regulation markers in a large series of genetically confirmed Ewing's sarcoma family of tumors. Int J Cancer.2010;128(5):1139–50.
5. Manduch M, Dexter DF, Ellis PM, Reid K, Isotalo PA. Extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor of the posterior mediastinum with t(11;22)(q24;q12). Tumori. 2008;94(6):888-91.
6. Rajwanshi A, Srinivas R, Upasana G. Malignant small round cell tumors. J Cytol. 2009;26(1):1-10
7. Silverman JF, Berns LA, Holbrook CT, Neil JSA, Joshi W. Fine needle aspiration cytology of primitive neuroectodermal tumors: A report of these cases. Acta Cytol. 1992;36:541–50.
8. Variend S. Small cell tumors in childhood: A review. J Pathol. 1985;145:25.
9. Das DK.Fine-needle aspiration (FNA) cytology diagnosis of small round cell tumors: value and limitations.Indian J Pathol Microbiol. 2004;47(3):309-18.