



International Journal of Scientific Research in Dental and Medical Sciences

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Primitive Neuroectodermal Tumor of Axilla: A Rare Case Report

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ARTICLE INFO

Article history:

Received 03 August 2023

Received in revised form 01 September 2023

Accepted 05 September 2023

Available online 07 September 2023

Keywords:

Axilla

General Surgery

Neuroectodermal Tumors

ABSTRACT

Primitive neuroectodermal tumors (PNETs) are poorly differentiated small round cell neoplasms. It is commonly seen in children and is rare in adults. Superficial primitive neuroectodermal tumors are rare but have a favorable prognosis compared to conventional deep-seated tumors. PNETs are quite rare, with the incidence of PNET axilla being extremely rare, and very limited cases have been reported due to its rareness in literature. This paper reports a case of a 71-year-old male patient who presented with a right axillary swelling. He underwent wide local excision of axillary swelling, which on histopathological examination showed features consistent with primitive neuroectodermal tumor. He was treated with multimodality treatment. Further, treatment was deferred due to the poor general condition of the patient, and he was kept on the best supportive care.

1. Introduction

The Ewing's sarcoma/ Primitive neuroectodermal tumor (ES/PNET) is a member of Ewing's sarcoma family of tumors (ESFT) and belongs to a rare group of malignant neoplasms that arise from neuroectodermal elements having a small round cell morphology. [1] PNETs are rare, small, round-cell malignant tumors. Its incidence is 1% of all sarcomas, with a highly aggressive biological behavior and poor prognosis. [2] ESFT includes Ewing's Sarcoma of bone, Extrasosseous Ewing's Sarcoma (ESS), Askins tumor, and PNET. ES and PNET share similar chromosomal translocation characteristics between chromosomes 11 and 22 (11; 22), clinical appearances, cellular molecular characteristics, prognosis, and strong express Cluster of differentiation 99 (CD99), differing only in their neural differentiation degree. [3] The most common location of extra-skeletal ES/PNET is the deep soft tissues, with only a few cases published of primary cutaneous ES/PNETs. [4] Differential diagnosis includes other members of the ESFT and other small round blue cell tumors. [5] Treatment approach is multimodality consisting of surgery, chemotherapy, and radiation therapy. The standard of care for localized disease is surgery, which may or may not be followed by adjuvant chemotherapy and radiation therapy. In this paper, we report a case of a 71-year-old male patient with a primitive neuroendocrine tumor (PNET) of the right axilla who was treated with a multimodality approach.

2. Case Presentation

A 71-year-old male patient attended the Department of Radiation Oncology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur,

India, on 23/03/2022 with a painless swelling in the right armpit for the past seven months. The swelling was initially small and gradually increased over the course of 7 months to attain a size of 8.0 cm × 5.0 cm, for which he underwent incisional biopsy at a private hospital. The patient also complained of tingling pain with numbness of the fingers of the right hand and the inner aspect of the right forearm. There is no history of swelling of the right upper limb, ulceration or discharge from the right axillary swelling, or any other swelling in other body parts. There is no history of cough, chest pain, hemoptysis, or chest wall swelling. There is no history of cigarette smoking, alcohol consumption, or tobacco chewing. There is no significant history of any chronic disease. On examination, the patient had an average build with good general condition. His Body Surface Area (BSA) was 1.5 m², and he had a Karnofsky Performance Score (KPS) of 90%. On physical examination, a significant swelling of about 9.0 cm × 5.0 cm was palpated in the right axilla with a surgical scar. The swelling was firm, non-tender, fixed to the overlying skin around the scar, but free from the other neighboring structures, with smooth margins and surface. No other peripheral lymph node or swelling was clinically palpable in the body. The incisional biopsy report showed features consistent with Ewing's sarcoma family of tumors with marked epithelial differentiation. 18FDG PET CT Scan showed a hypermetabolic multiple discrete right axilla level I nodes with increased vascularity in the right anterior chest wall and axilla, mildly hypermetabolic right axillary level III and right internal mammary lymph nodes, with a SUV max of 10.58, and the largest one being 9.4 cm × 4.8 cm in size and no distant metastasis. The patient underwent wide local excision, including the scar, and the excised specimen

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showed a large malignant small round cell tumor of 10.0 cm × 5.5 cm in size with areas of necrosis on histopathological examination (HPE). The surgical margin of resection was free but was close, and the tumor had a high mitotic index (Ki67) of around 80%. Immunohistochemistry (IHC) was positive for CD99, Chromogranin, and Synaptophysin and negative for Thyroid transcription factor 1 (TTF1) and Leucocyte common antigen (LCA) (Figs. 1 and 2). All these features were consistent with diagnosing a Primitive neuroendocrine tumor of the axillary lymph node.

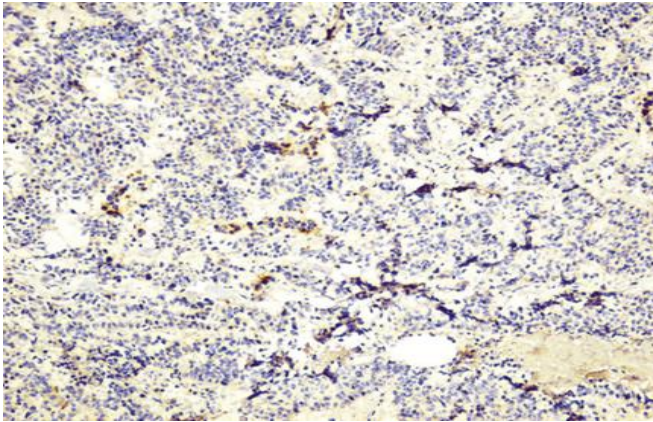


Fig. 1. IHC of the excised specimen showing Chromogranin positive.

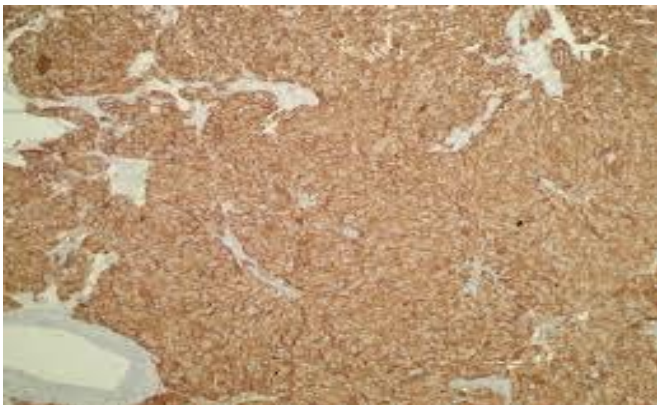


Fig. B. IHC of the excised specimen showing Synaptophysin positive.

Postoperative events were uneventful. Routine baseline investigations were found to be normal. The metastatic workup (PET-CT scan) found no other metastasis site or organ involvement. The patient was planned for adjuvant chemotherapy with Injection of Etoposide and Injection of Ifosfamide, three weekly cycles for a total of six cycles, with all the necessary pre- and post-medications due to the close surgical margin of resection, high mitotic index, and large tumor size. One month after the completion of adjuvant chemotherapy, the patient complained of numbness in the right hand along with occasional tingling pain. On physical examination, the left supraclavicular node was about 2.0 cm X 2.0 cm, the right supraclavicular node about 3.0 cm X 3.0 cm, and the right axillary lymph node about 4.5 cm × 4.0 cm in size was palpated. Contrast Enhanced Computed Tomography (CECT) scan of the neck showed multiple enlarged moderately heterogeneously enhancing right axillary and bilateral supraclavicular lymph nodes, causing complete 360° encasement of right axillary arteries and probably causing compression on right brachial plexus. CECT Thorax showed ground glass opacity in the dependent region of both lungs, with few fibrotic bands in both lungs (Figs. 3 and 4). A repeat biopsy of the axillary

swelling was done, and it showed features consistent with PNETs. Fine needle aspiration cytology (FNAC) of supraclavicular swellings showed metastatic PNET.

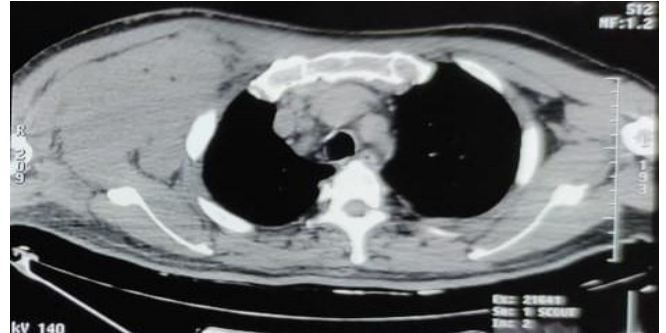


Fig. 3. CECT of the upper thorax (axial view) showing a heterogeneously enhancing mass in the right axillary region.

The patient was planned for salvage chemotherapy with a VAC regime (Vincristine, Adriamycin, and Cyclophosphamide). The patient showed no response to salvage chemotherapy and was scheduled for palliative local radiation therapy.

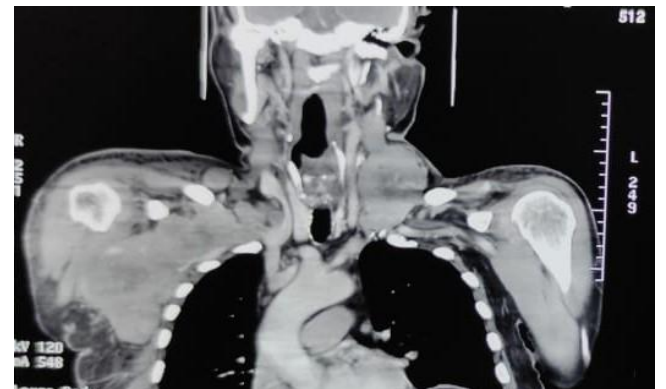


Fig. 4. CECT of neck and thorax (coronal view) showing a large mass in the right axillary region with encasement of the right axillary arteries and probably right brachial plexus.

The patient was treated with External Beam Radiotherapy (EBRT) by Cobalt-60 teletherapy machine to the right axilla, by two parallel opposed fields (AP & PA) and to a total tumoricidal dose of 5000cGy in 25#, in conventional fractionation. Following the completion of radiation treatment, there was a good local response with more than a 30% reduction in the tumor size [as evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1]. However, the patient's general condition deteriorated due to widespread disease. Hence, further treatment was deferred, and the patient was kept on best supportive care.

3. Discussion

ES/PNETs are small round cell tumors seen mainly in children, affecting bones and soft tissues of the limbs. They arise from the neuroectodermal elements, which probably develop from migrating embryonic cells of the neural crest.^[6] These tumors have similar characteristic translocation t(11, 22) and express CD99 cell surface antigen on immunohistochemistry.^[7] Most common extraosseous sites include lower extremities, head and neck, pelvis, and prevertebral spaces.^[8] It most commonly affects children and young adults between the ages of 10 to 20 years.^[9] The positive expression of CD99 cell surface adhesive glycoprotein plays an essential role in diagnosing

ES/PNET. But other tumors also express CD99. Thus, the differential diagnosis includes other members of ESFTs along with neuroendocrine carcinoma, lymphoma, metaplastic carcinoma of the breast, and rhabdomyosarcoma.^[10] It is a highly aggressive tumor with a high incidence of local recurrence and distant metastases. According to the National Comprehensive Cancer Network (NCCN) guideline, the treatment plan for all members of ESFT is the same. It includes a multimodality approach consisting of local treatment (surgery and radiation therapy) and chemotherapy.^[11] As these tumors have a high tendency for distant metastasis, they should be treated with multiagent systemic chemotherapy to control the micrometastases and improve overall survival. The most commonly used multiagent chemotherapy combines Vincristine, Adriamycin, Actinomycin D, Cyclophosphamide, Ifosfamide, and Etoposide chemotherapeutic agents. For patients with metastatic disease, a combination of Vincristine, Adriamycin, and Cyclophosphamide (VAC regimen) is preferred. ES/PNETs are responsive to chemotherapy initially, but later on, they become resistant to chemotherapy, which results in disease progression. The role of radiation therapy in managing ES/PNETs is unclear. Whole lung radiation is used in patients with lung metastasis, and the combination of local radiation therapy after surgery is used to control disease after they become resistant to further treatment with chemotherapeutic agents. The good prognosis of ES/PNETs depends on their early diagnosis, with the prognosis of metastatic disease being dismal.

4. Conclusion

Primitive neuroectodermal tumors (PNETs) are rare tumors constituting only 1% of all sarcomas, with PNETs of the axilla in an adult 71-year-old male patient being extremely rare. Thorough physical examination, HPE, and IHC analysis are required for accurate diagnosis, with IHC playing a significant role in differentiating PNETs from other tumors. Our patient was diagnosed with a PNET of the right axilla based on HPE and IHC and was treated with surgery, multiagent systemic chemotherapy, and local radiation therapy.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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How to Cite this Article: Mahawar R, Swer D, Singh LJ. Primitive Neuroectodermal Tumor of Axilla: A Case Report. *International Journal of Scientific Research in Dental and Medical Sciences*. 2023;5(3):171-173. <https://doi.org/10.30485/IJSRDMS.2023.414119.1528>.