

# Left inguinal lymphadenopathy as the solitary metastatic presentation of primitive neuroectodermal tumor of unknown origin

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## ABSTRACT

Primitive neuroectodermal tumor (PNET)/ewing's sarcoma is a rare neural crest tumor of central nervous system, thoracopulmonary regions, pelvis, and lower extremities. Visceral involvement by PNET is a rare phenomenon, with kidney being the most commonly involved organ. We report a 35-year-old Asian female presenting with left inguinal swelling, with computed tomography scan evidence of conglomerate lymph nodal mass in the left external iliac and inguinal region. A clinico-radiological diagnosis of lymphoproliferative disorder was made. She subsequently underwent excision biopsy. Histopathology of the biopsy specimen revealed completely effaced lymph nodal architecture, which was replaced by a tumor composed of nests of small, round, blue cells. On immunohistochemistry, the tumor cells were positive for CD99 and negative for CD3, CD20, leucocyte common antigen, epithelial membrane antigen, cytokeratin, desmin, vimentin, synaptophysin, and chromogranin A. Extensive search regarding any possible different site of involvement by the tumor was negative. The clinical presentation and histological, cytological, and immunohistochemical pattern, lead to the diagnosis of metastatic PNET of the left external iliac and inguinal lymph node with unknown primary origin. To the best of our knowledge, it is the first ever reported case of inguinal lymphadenopathy as the solitary metastatic presentation of PNET of unknown origin.

**Key words:** Ewing's sarcoma, inguinal lymphadenopathy, primitive neuroectodermal tumor

## INTRODUCTION

Primitive neuroectodermal tumor (PNET) is a rare aggressive neural crest tumor of adolescents and young adults aged 10-20 years, with a slight male preponderance.<sup>[1]</sup> It mainly occurs in the central nervous system, thoraco-pulmonary regions, and pelvis and lower extremities. It has a high incidence of local recurrence and distant metastasis.<sup>[1-3]</sup> PNET presenting as inguinal lymphadenopathy is extremely rare. This case report describes a rare case of metastatic PNET observed in a 35-year-old Asian woman, who presented with a painless left inguinal lymphadenopathy as the solitary metastatic site of PNET with unknown primary origin.

## CASE REPORT

A 35-year-old Asian lady presented with gradually progressive painless swelling in her left inguinal region for the last 3 months. She had no other complaints and her past history was unremarkable. On clinical examination, no abnormality was found except a 3 × 3 cm, firm, non-tender, mobile palpable lump in the left inguinal region. All routine hematological and biochemical parameters were within normal limits. Computed tomography (CT) scan of the abdomen and pelvis revealed multiple enlarged necrotic conglomerate lymph nodes in the left external iliac and inguinal region with no other abnormality in the abdomen or pelvis [Figure 1]. A clinico-radiological diagnosis of lymphoproliferative disorder was made. The patient subsequently underwent excision biopsy of the left inguinal mass. Histopathology of the biopsy specimen revealed completely effaced lymph nodal architecture, which was replaced by a tumor composed of nests of medium-sized round or oval tumor cells with high nucleo-cytoplasmic ratio, enlarged round or oval nuclei with few mitotic figures, and scant cytoplasm [Figure 2].

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The Ki-67 index was 10-15%. On immunohistochemistry, the tumor cells were immunoreactive for CD99 [Figure 3] and negative for CD3, CD20, leucocyte common antigen (LCA), epithelial membrane antigen (EMA), cytokeratin, desmin, vimentin, synaptophysin, and chromogranin A. A search for any other site of involvement by the tumor using bone marrow biopsy, bone scan, whole-body CT scan, and MRI of brain yielded negative results. The clinical presentation and histological, cytological, and immunohistochemical characteristics of the tumor lead to the diagnosis metastatic PNET of the left external iliac and inguinal lymph node with unknown primary origin. The patient received combination chemotherapy with vincristine, adriamycin, and cyclophosphamide alternating with ifosfamide and etoposide (VACA/IE regimen) for 3-48 weeks and 55.8 Gray/31 fractions involved field radiation to the left external iliac and inguinal region with 6 MV photons. A positron emission tomography scan, done after 3 months of treatment completion, showed complete radiological response. She has been doing well after 1 year of treatment and is currently on regular follow-up in our department.

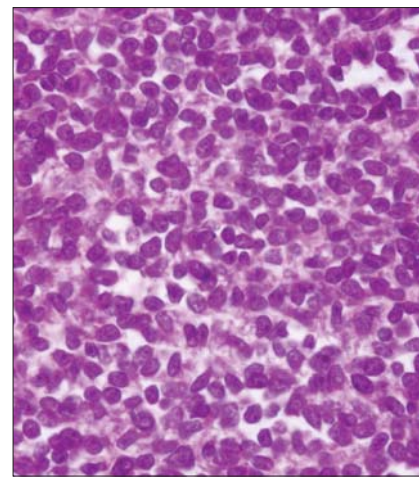
## DISCUSSION

PNET is classified on the basis of the site of origin into CNS PNET and peripheral PNET. The peripheral PNET, first recognized by Arthur Purdy Stout in 1918, is a member of the family of "small, round, blue cell tumors." Peripheral PNET occurs outside the CNS and has considerable overlap with Ewing's Sarcoma (ES), both sharing a common and unique translocation [t(11;22)(q24;q12): Fusion gene designated EWS/FLI-1]. PNET constitutes 1% of all sarcomas.<sup>[3]</sup> PNET outside the CNS is mostly found within the deep soft tissue of the extremities and the paravertebral areas. Although PNETs can occur in numerous solid organs such as the kidney, ovary, vagina, testis, uterus, cervix uteri, urinary bladder, breast, parotid gland, heart, lung, liver, rectum, pancreas, and gall bladder, it is an extremely rare tumor entity.<sup>[3-5]</sup> The kidney is the most common visceral organ involved by PNET.<sup>[6,12]</sup>

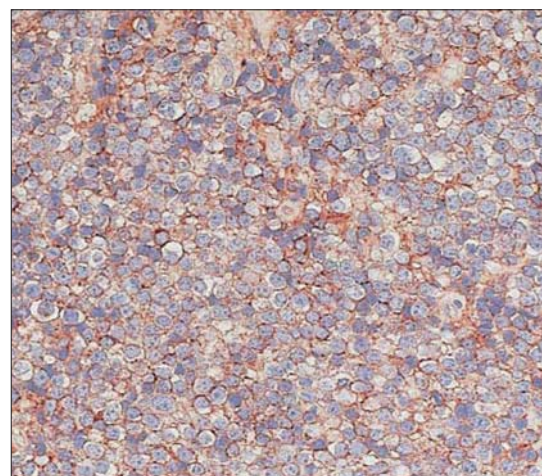
The diagnosis of PNET/ES requires panels of immunohistochemical study. The positive expression of CD99 (MIC2), a cell-surface glycoprotein involved in cell adhesion, plays a crucial role in the diagnosis of PNET/ES.<sup>[4]</sup> However, CD99 may also be expressed in other tumors, including metaplastic carcinoma of the breast, neuroendocrine carcinoma, lymphoblastic lymphoma, mesenchymal chondrosarcoma, synovial sarcoma, and alveolar rhabdomyosarcoma.<sup>[7]</sup> In our patient, small cell carcinoma, neuroendocrine carcinoma, and lymphoblastic lymphoma were excluded by negative staining for cytokeratins, chromogranin A, synaptophysin, and LCA.



**Figure 1:** CT scan of the abdomen and pelvis showing multiple enlarged necrotic conglomerate lymph nodes in the left external iliac and inguinal region



**Figure 2:** Photomicrograph of the histopathology of the inguinal lymph node biopsy, showing small, round, blue tumor cells with hyperchromatic and rounded nuclei and scanty cytoplasm (H and E,  $\times 400$ )



**Figure 3:** Photomicrograph showing immunoreactivity for CD99 on cell membranes of tumor cells (H and E,  $\times 200$ )

A combination of multiple modalities, including surgery, chemotherapy, and radiation therapy, is the most appropriate treatment of PNET.<sup>[1]</sup> It has a high propensity for

metastatic spread. Consistent use of systemic chemotherapy to treat localized PNET effectively improved the 5-year survival rate from 5 to 10% up to 65%, which is primarily due to the elimination of micrometastases.<sup>[8-10]</sup> 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.<sup>[8]</sup> In patients with unresectable or metastatic disease, palliative chemotherapy may be useful. The role of radiation therapy in the treatment of PNET/ES is unclear. However, the use of radiation therapy combined with surgery, in order to control local disease, is proving to be helpful.<sup>[11]</sup>

Survival in PNET depends on multiple factors, one of the important being the degree of dissemination of disease, and various studies have shown a 5-year survival of 58-61% with a median survival of 120 months.<sup>[11]</sup> Our patient in this report responded well to multimodality treatment and is asymptomatic and doing well even after 1 year of treatment completion.

## CONCLUSION

In conclusion, we have reported a rare case of metastatic PNET presenting as left external iliac and inguinal lymphadenopathy without any other site of involvement. Clinical presentation mimicked lymphoproliferative disorder. The tumor responded well to multimodality treatment, and there was no evidence of disease 1 year after treatment completion.

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