Case Report

Peripheral neuroblastoma in an adult: Rare disease at a rare site

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ABSTRACT

Adult peripheral neuroblastoma represents less than 1% of all malignant primary tumors of peripheral nerves. We report a young adult who presented with swelling over the left wrist with left epitrochlear and axillary lymph nodes. Incision biopsy of the swelling was suggestive of malignant small round cell tumor. On immunohistochemistry, cells were positive for synaptophysin, chromogranin and nonspecific enolase and negative for leucocyte common antigen, cytokeratin, CD99 and myogenin. Urinary vanillyl mandelic acid and homovanillic acid levels were elevated. The patient received 8 cycles of chemotherapy (OJEC). Reassessment positron emission tomography-computed tomography scan showed a complete metabolic response at the primary site and partial response at left axillary lymph nodes. The patient underwent axillary lymph node clearance followed by radiotherapy to the tumor bed and lymph node regions. The patient could not afford autologous haematopoetic stem cell transplant and was started on isotretinoin maintenance. He is on follow-up for 12 months and disease free.

Key words: Isotretinoin, peripheral neuroblastoma, positron emission tomography computed tomography scan

INTRODUCTION

Neuroblastoma is the most common extracranial solid tumor in children.[1] It is an embryonal cancer of autonomic nervous system, and the cell of origin is the developing and incompletely committed precursor cell derived from neural crest tissues. The tumors arise in tissues of the sympathetic nervous system, typically in the adrenal medulla or paraspinal ganglia, presenting as mass lesions in the neck, thorax, abdomen, or pelvis.[2] Neuroblastoma in adults is a rarity.[3,4] Moreover neuroblastoma arising from sympathetic nerves of the forearm has not been described in the literature. We describe a patient who presented with a swelling over the wrist which on evaluation was found to be a peripheral neuroblastoma.

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CASE REPORT

We describe a 22-year-old man who presented with a swelling over the left wrist noticed after an injury. Swelling progressively increased over 2 months and was associated with dull aching pain. He also had significant weight loss. There was no history of fever or night sweats. His performance score (ECOG) was 1. He had a fusiform swelling above the left wrist, firm in consistency and nontender. His left epitrochlear and axillary lymph nodes were palpable. Systemic examination was unremarkable. His complete blood count was normal, LDH, renal function, and liver function test were within normal limits. MRI of left forearm showed a loculated soft tissue mass surrounding the distal radius with the permeative destruction of the cortex and marrow infiltration. Fluorodeoxyglucose-positron emission tomography (FDG-PET) computed tomography (CT) showed a heterogeneously enhancing mass lesion in the left distal forearm and wrist involving the muscles of flexor

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and extensor compartment (size 8.5 cm × 6.3 cm × 8.1 cm, maximum standardized uptake value [SUVmax] 6.8) [Figures 1 and 2]. FDG uptake was also seen in left axillary and left epitrochlear lymph nodes. Incision biopsy of the forearm swelling was suggestive of malignant small round cell tumor. On immunohistochemistry, malignant cells were positive for synaptophysin, chromogranin, and nonspecific enolase and negative for leucocyte common antigen, cytokeratin, CD99 and myogenin [Figure 3]. Conventional cytogenetics was unsatisfactory. The patient did not have N-MYC amplification. Urinary vanilly mandelic acid and homovanillic acid levels were greater than twice the upper limit of normal. Bone marrow aspiration and biopsy did not reveal any abnormal tumor cells. Multiple-gated acquisition scan showed left ventricular ejection fraction of 68%. A diagnosis of peripheral neuroblastoma was considered. Patient received 4 cycles of chemotherapy with OJEC (vincristine 1.4 mg/m^2, carboplatin 240 mg/m^2, etoposide 200 mg/m^2, and cyclophosphamide 600 mg/m^2 in a 21 days cycle). Reassessment PET-CT scan showed interval resolution of left forearm mass (complete metabolic response) and interval decrease in the size of left epitrochlear and axillary lymph nodes (partial response). The patient received 4 more cycles of chemotherapy OJEC. Reassessment PET-CT scan showed no focal enhancing lesion at the distal end of the forearm, and interval decrease in the size of FDG nonavid left axillary lymph nodes (partial response) [Figure 4]. The patient underwent left axillary lymph node clearance, and 18 lymph nodes were removed. The largest lymph node showed residual viable tumor cells (25%) and large areas of necrosis (75%). The patient received intensity-modulated radiotherapy 50 Gy in 25 fractions to the tumor bed, left epitrochlear and left axillary regions. The patient could not undergo myeloablative chemotherapy followed by autologous stem cell transplant due to financial constraints. Patient was started on isotretinoin. He is on follow-up for 12 months and is disease free.

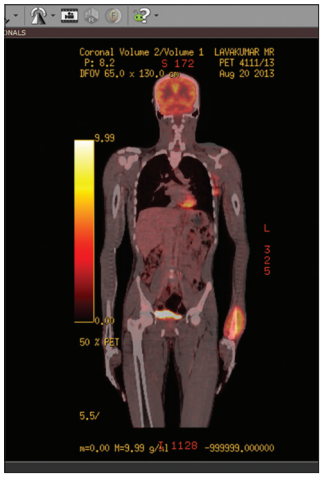

Figure 1: Positron emission tomography computed tomography (prior to chemotherapy) showing a mass lesion in the left distal forearm and wrist

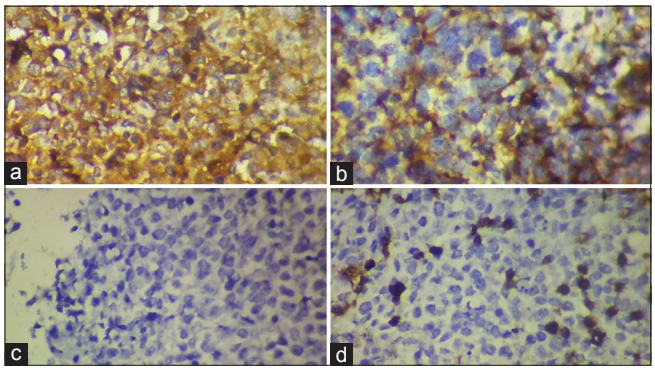

Figure 3: Immunohistochemistry - (a) Nonspecific enolase positive, (b) synaptophysin positive, (c) cytokeratin negative, (d) leucocyte common antigen negative

DISCUSSION

Neuroblastoma is rarely reported in adults, with <10% of the cases diagnosed after 10 years of age.[3] Incidence rate

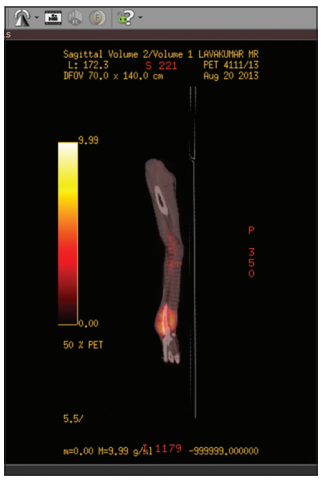

Figure 2: Positron emission tomography-computed tomography (prior to chemotherapy) showing a mass lesion in the left distal forearm and wrist (magnified image)

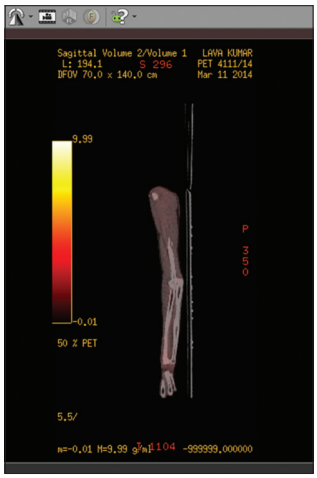

Figure 4: Positron emission tomography-computed tomography scan (after 8 cycles of chemotherapy) showed no focal enhancing lesion at distal end of forearm

for patients aged 30–39 years is about 0.2 cases/million years.[4] In many ways, neuroblastoma in adults is different from that in children [Table 1]. Most data suggest that adult neuroblastoma presents with advanced stage and has a poorer prognosis.[5] This may be due to tumor biology with the more aggressive clinical course, or possibly due to the fact that adults are less sensitive or have poor tolerance to pediatric chemotherapy regimens. Adult peripheral neuroblastoma represents <1% of all malignant primary tumors of peripheral nerves.[6,7] Immunohistochemistry, electron microscopy and cytogenetics have permitted a more accurate diagnosis of adult neuroblastomas differentiating it from the small round cell tumors, which include lymphomas, primitive neuroectodermal tumor, undifferentiated small cell carcinoma, Ewing's sarcoma and embryonal rhabdomyosarcoma. The most common site of involvement of neuroblastoma in adults is the abdomen. Neuroblastoma arising from sympathetic nerves of the forearm has not been described in the literature. In the index case, elevated urinary catecholamine level, and immunohistochemistry supported the diagnosis of neuroblastoma.

123I-metaiodobenzylguanidine scintigraphy is the nuclear imaging modality of choice for neuroblastoma, being valuable for diagnosis, staging, and response assessment. 18F-FDG PET/CT has significant prognostic implications in high-risk neuroblastoma patients. Tumoral metabolic activity (SUVmax) and extent of 18F-FDG–avid bone and bone marrow disease (18F-FDG skeletal scores) were identified as poor prognostic factors associated with decreased survival in some studies.[8] Our patient had a complete metabolic response at the primary site after chemotherapy and absence of N-MYC amplification which might have been responsible for a good prognosis.

Treatment of neuroblastoma in adults is extrapolated from pediatric studies. Our patient was considered high risk because of age >18 months. Current treatment for high-risk neuroblastoma can be divided into three distinct phases: Induction of remission, consolidation and finally a maintenance phase focused on the eradication of the minimal residual disease. Our patient was treated with chemotherapy followed by lymphadenectomy which showed viable tumor cells. After radiotherapy patient should have undergone myeloablative chemotherapy followed by autologous stem cell transplant. However, because of financial constraints he received isotretinoin instead. Isotretinoin acting to cause terminal differentiation of immature progenitor cells prevents relapse[9] and is now part of standard therapy during the first remission in patients with high-risk neuroblastoma.[10] The index patient had a good response to multimodality treatment and were on follow-up for 12 months.

Table 1: Difference between neuroblastoma in pediatric and adult patients

Characteristics	Pediatric neuroblastoma	Adult neuroblastoma (age >20 years)
Incidence	The most common extracranial solid tumor	Rare
Shimada histology	Favourable	Unfavourable is more common
Growth rate	High	Slow
N-MYC amplification (%)	20	Rare
Catecholamine secretion (%)	95	40-57
Metastatic disease (%)	50	Higher
Outcome		
3 years overall survival (%)	86	45
5 years overall survival (%)	85	36

CONCLUSION

Peripheral neuroblastoma is rare in adults. It should be considered in the differential diagnosis of neurogenic tumors with small round cell histology. With multimodality treatment (surgery, chemotherapy, and radiotherapy) disease control is possible. FDG-PET CT can be used to monitor response to therapy and also for prognostication.

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Conflicts of interest
There are no conflicts of interest.

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