

Case Report

Bilateral Metastatic Orbital Neuroblastoma in an Adult

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Abstract: Neuroblastoma is the most common extra cranial solid malignancy in children but it is rare in adults. We report a 35 year old woman who presented with bilateral proptosis with visual loss, fever, and bone pain and weight loss. Computed tomography showed orbital adrenal mass with bony lesions of orbit and calvarium. CT abdomen revealed a pelvic mass which was suspected to be the primary. There were metastatic deposits at distant sites suggesting a diffuse infiltrative malignancy. Urine catecholamines were normal. MIBG scan was negative. Histopathology showed “small dark round cell tumor” and immuno histo chemistry confirmed the diagnosis of neuroblastoma. The patient was subjected to chemotherapy based on paediatric protocols for neuroblastoma and she is clinically stable till date. Neuroblastoma should be considered in the differential diagnosis of bilateral orbital tumor in an adult. Urine catecholamine levels may be normal in adult neuroblastoma.

Keywords: Neuroblastoma, adult neuroblastoma, “small dark round cell tumor”, urine catecholamines.

INTRODUCTION

Neuroblastoma is a malignancy of neural crest cells which is of rare occurrence in adulthood. Only 10% patients are older than 10 years of age [1]. The common sites of primary in adults are abdomen, retro peritoneum, pelvis, mediastinum, head and neck [2]. Frequent sites of metastases are bone marrow, bone, lymph node, orbit, liver, lung, brain, skin and testis. Ocular manifestations are proptosis, periorbital ecchymosis, motility restriction, subconjunctival hemorrhage, opsoclonus, Horner’s syndrome, anisocoria, strabismus, ptosis and blindness [1, 3]. The importance of considering this tumor amongst “small dark round cell tumors” in adult patients cannot be over-emphasized [4]. Urine metanephrine levels are not commonly elevated in adults [2]. In adults; neuroblastoma has distinct biological and clinical features in contrast with pediatric tumors, which explain the clinical course and poor treatment response [5, 7]. The most important prognostic factors are age at diagnosis and stage of the tumor [6]. No standard treatment guidelines currently exist for adult neuroblastoma. The survival rates in adults are poor despite treatment with pediatric regimens [5,6]. Adults are known to have multiple recurrences and are refractory to treatment [5]. The diagnosis of neuroblastoma in an adult rests on awareness of this rare tumor. This report highlights the importance of considering neuroblastoma in the differential diagnosis of an adult with bilateral proptosis even though the tumor is extremely rare in this age group.

CASE REPORT

35 year old female presented with bilateral proptosis with visual loss for 6 months. She had history of bone pain for 2 years and intermittent fever with weight loss for 6 months.



Fig 1: Proptosis

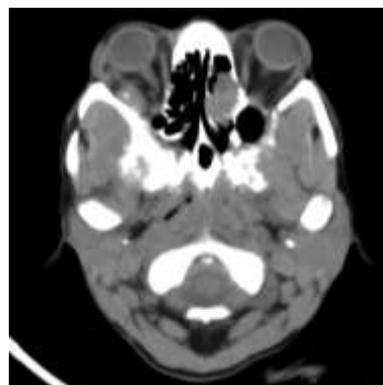


Fig 2: CT showing orbital mass

Best corrected visual acuity was 6/24 in both eyes. Exophthalmometry was 26mm and 25mm at 103mm for the right eye and left eye respectively (by Hertel's). There was no periorbital ecchymosis or lid retraction. There was no congestion of conjunctiva.

There was no palpable mass. The extra ocular movements were full range. Pupillary reactions were sluggish. Fundus examination revealed bilateral disc edema with marked pallor suggestive of secondary optic atrophy.

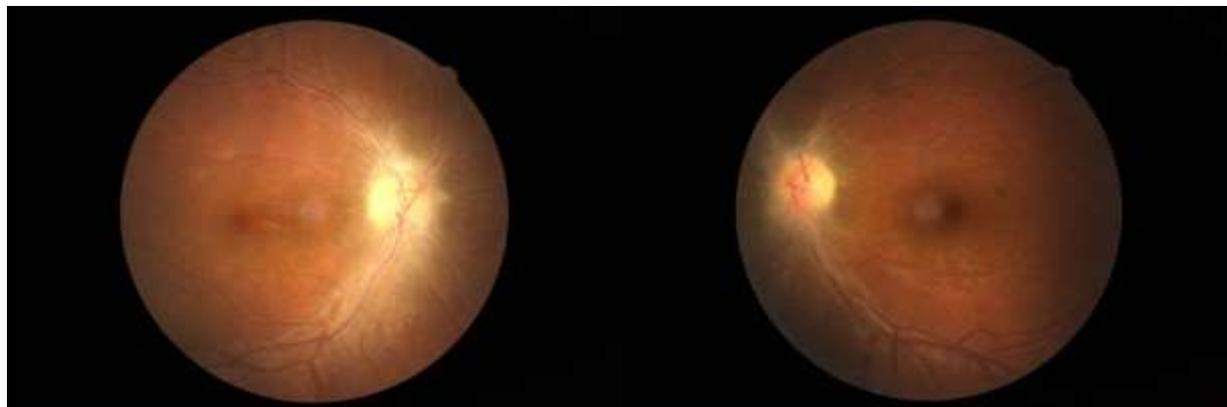


Fig-3: Fundus picture showing secondary optic atrophy

On systemic examination, she had pallor and hepato splenomegaly. There was no thyromegaly and no lymphadenopathy. Nasopharyngeal mass lesion was excluded by endoscopic examination. Breast examination and gynaecological examination were within normal limits. The Eastern Cooperative Oncology Group (ECOG) performance status was 4.

Haemogram revealed severe anaemia and thrombocytopenia (Hb- 3.9g% TLC 7600 and platelets 80,000/mm³). Thyroid function tests were normal. CECT Orbit revealed diffuse permeative bony destruction with dense sunray periosteal reaction, projecting into the orbital cavities. There was narrowing

of optic canals and orbital apex. There were calvarial and dural deposits and diffuse soft tissue thickening of para nasal sinuses. CECT of abdomen and pelvis showed a mass lesion involving left suprarenal gland and another lesion arising from left ileum with soft tissue component, speculated calcifications and periosteal reaction suggesting metastasis from the adrenal malignancy. There were liver secondaries and diffuse sclerotic-lytic lesions suggestive of bone secondaries. Urine VMA levels were normal. Iodine-131 MIBG whole body scan revealed no MIBG avid lesion. Bone marrow biopsy showed sheets of small round cells were seen with rosette and central neuropil.

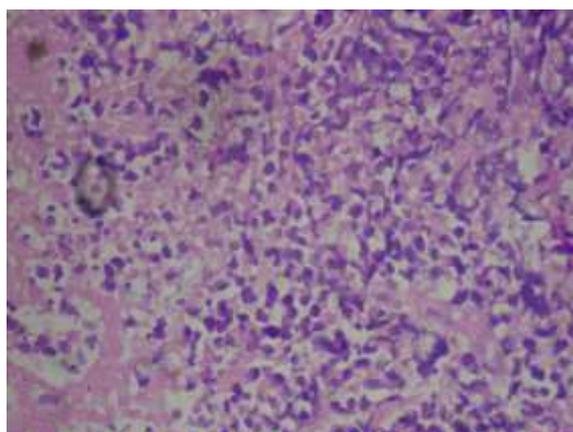


Fig 4: Histopathology showing small round cells

Immuno histo chemistry revealed cells positive for synaptophysin and negative for PAS, Chromogranin and LCA. CD99 was inconclusive. Diagnosis of neuroblastoma was made and patient was started on chemotherapy with doxorubicin, Cyclophosphamide, etoposide and vincristine. The patient has been followed

up and is stable with good tolerance to the regimen for the last 8 weeks.

DISCUSSION

Neuroblastoma originates from adrenal medulla or from sympathetic ganglia from paraspinal sites [6]. Neuroblastoma is predominantly a tumor of childhood

and there are few isolated reports of its occurrence in adults. 10-20% of patients have orbital metastasis [3].

There is little known about clinico pathologic features of adult neuroblastoma because of its rarity. The symptoms are usually due to mass effect of the tumor or bone pain from metastasis [3]. Retro bulbar metastases are the cause for proptosis, motility restriction and periorbital ecchymosis (raccoon eyes) [1, 3].

Elevated catecholamine metabolites like homo vanillic acid and vanillyl mandelic acid in urine have been reported in 90-95 % of neuroblastoma [1]. It is to be noted that urine metanephrine levels are not commonly elevated in adults and hypertension may not be observed in adults [2]. When elevated however, it provides a useful guide to the diagnosis, tumor response and relapse [4, 8].

Light microscopy reveals “small dark round cell tumors” which in adults can be confused with lymphoma, rhabdomyosarcoma, ewings sarcoma and undifferentiated small cell carcinomas. Immuno histo chemistry plays a substantial role in differentiating them [4]. The presence of dendritic processes, desmosomes, dense core granules on electron microscopy help to distinguish neuroblastoma [4].

Ocular manifestations by definition are stage 4 according to international neuroblastoma staging system [3]. Therefore aggressive chemotherapy is employed followed by resection of primary tumor if possible. Myeloablative chemotherapy and radiotherapy to the primary site may be considered later [3]. The most active chemotherapeutic agents are Cyclophosphamide, ifosfamide, cisplatin, carboplatin and doxorubicin [2].

The reasons for significantly worse outcome in adults may be tumor biology, more virulent clinical course, advanced disease at diagnosis and a poor response to pediatric chemotherapy protocols [5, 7].

CONCLUSION

The diagnosis of neuroblastoma in an adult can elude the unwary unless a high index of suspicion is entertained. The diagnosis should be considered in an

adult presenting with bilateral proptosis with unexplained fever, bone pain and weight loss. Catecholamine metabolites may be normal in 10-15% of patients. Treatment may be initiated based on pediatric guidelines. However, adults on chemotherapy require regular follow up due to high risk of recurrence. An innovative therapeutic approach is needed in adults and hence, future research is required to target tumor biology. Newer treatment regimens of this rare malignancy in adults may help in improving final outcome.

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