Case Report-I

Status Epilepticus and Hypertension in a Child with Ganglioneuroblastoma

PRERNA BATRA, GAYATHRI SUBRAMANIUM, K.Y. VILHEKAR, PUSHPA CHATURVEDI AND ABHIJEET SAHA

ABSTRACT

Neurogenic tumours (Neuroblastoma, ganglioneuroma and ganglioneuroblastoma) are common among children. We here report a case of three year old female child with ganglioneuroblastoma who presented with status epilepticus at diagnosis. Such a presentation has been decribed rarely. Pertinent literature is being reviewed.

INTRODUCTION

Neuroblastic tumours include ganglioneuroma; ganglioneuroblastoma (GNB) and neuroblastoma (NB), and are derived from the primordial neural crest cells. They are the most common extra cranial solid tumours of childhood constituting 10% of childhood cancers.[1] Variation in tumour location and histopathological differentiation results in myriad presentations. Here we are reporting two rare presentations of GNB i.e. status epilepticus and hypertension in a patient.

CASE :

A 3-year-old female child, product of non-consanguineous marriage presented in status epilepticus. There was no history of fever, cough, rash, urinary or bowel disturbances, headache, vomiting, aura, change in personality, visual disturbance, episodic palpitations, hot flushes or family history of similar complaints.

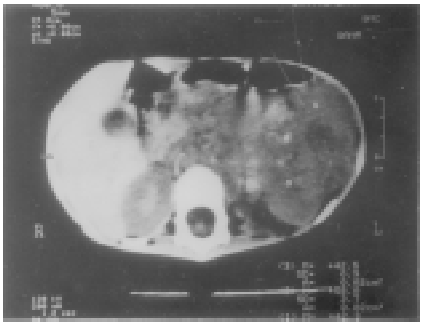
The child had tachycardia with pulse rate of 160/minute, regular, normal volume; respiratory rate of 30/min and blood pressure (B.P) of 90/60 mm Hg. She was pale and had a firm, non-tender lump with dimensions of 4×5 cms palpable in the left hypochondrium. Liver was one cm below the costal margin in the right mid-clavicular line, soft, smooth and non-tender with a span of 9.5cms. Central Nervous System (CNS) examination revealed extensor planters bilaterally with exaggerated deep tendon reflexes. Fundus was normal. Patient was managed conservatively with intravenous fluids, antibiotics and anticonvulsants.

Investigations : Hb 7.7 Gm/dl, WBC-9,900/mm^3, with 79% neutrophils and platelets count of 581,000/mm^3. Peripheral smear showed anisopoikilocytosis with predominantly microcytic hypochromic RBCs and a few target cells.

Abdominal ultrasound (USG) revealed a mass present in the para-aortic region anterior to the spine and spreading through the splenic hilum with encroachment of the vessels. Spleen was enlarged with coarse echotexture containing within it a lesion with heterogeneous echo texture (predominantly hypoechoic). Mass was 7.2×6.2×4.1 cms (including the splenic mass) with evidence of aortic and peripancreatic lymphadenopathy. Left kidney was displaced laterally. USG guided fine needle aspiration cytology of the lump done from two sites were suggestive of small round cell neoplasm of the neuroblastoma and ganglioneuroma component.

CAT scan abdomen showed a suprarenal mass with areas of necrosis (fig 1). Renal artery doppler was normal. CT scan brain showed punctate vesicular calcifications in the high parietal region suggestive of metastasis. Chest radiograph and bone marrow biopsy from bilateral iliac crests were normal. A diagnosis of ganglioneuroblastoma, stage 4 was thus made in accordance with the international criteria for neuroblastoma diagnosis and staging.[2]

Department of Paediatrics, Sewagram, MGIMS
Wardha-4420102, Maharastra
Correspondence to: **ABHIJEET SAHA**
E-mail: drabhijeetasha@yahoo.com



CT Scan abdomen showing left suprarenal mass extending in spleen with areas of necrosis.

On fifth day of admission, the patient developed hypertension, B.P. 140/100 mm Hg. Patient was put on nifedepine. Persistent tachycardia recorded during hospital stay warranted the use of propranolol. Surgical debridement along with radio and chemotherapy was planned. However, patient's parents took him away against medical advice on seventh day of admission.

DISCUSSION

Neuroblastic tumours are the most common extra cranial tumour of childhood. Despite high frequency of dissemination of this tumour to the bones and bone marrow spread to CNS is rare. A report by the Children's Cancer Group (CCG) of the metastatic sites in 567 patients with stage 4 disease between 1989-1996 revealed that only 4 patients (0.7%) at diagnosis and 13(2.2%) at recurrence presented with CNS involvement.[3] Matthay et al in a review of 434 patients with stage 4 disease reported a three year estimated risk of 8% for CNS involvement. Almost all the cases occurred at the time of recurrence rather than at diagnosis. The symptoms of the CNS lesions were usually referable to the anatomical localisation of the tumour. Headache, nausea and vomiting were more common with parenchymal lesions while pain, fever and motor signs with meningeal involvement. Seizures were recorded only in 5 / 23 patients with CNS metastasis.[4]

Tumour cells are known to infiltrate CNS by haematogenous route during a period of active disease and may remain dormant for months to years. However, they retain their proliferative potential. Cerebrospinal fluid (CSF) appears to be the major conduit of tumour spread in the neuroaxis, as is indicated by diffuse meningeal involvement, multiple subarachnoid "drop metastasis", cord encasement or free floating lumps of tumour cells in most patients[5]. CNS metastasis is associated with a poor prognosis.[4] Our patient presented with CNS metastasis and status epilepticus. Although seizures have been reported as a presenting complaint in patients with neuroblastic tumours status epilepticus has been rarely reported in GNB. In India, CNS metastasis has been encountered infrequently and incidence has been recorded as low as <5 %.[6, 7]

Except a few sporadic case reports[8,9] hypertension primarily is a rare complication in patients with NB or GNB, developing only in 10% of the patients.[11-13] In two large case series conducted in India, no patient was found to have hypertension.[6,7] Patients with NB, GNB and Pheochromocytoma have elevated levels of circulating catecholamines and their metabolites including dopa, dopamine, norepinephrine, metanephrine, normetanephrine, VMA and homovalinic acid.[14,17] Poor differentiation of the tumour is associated with higher catecholamine level.[18] However patients with Pheochromocytoma have a higher incidence of hypertension than in NB and GNB due to the presence of many storage granules to store the catecholamines in the former[8,17] The storage mechanism is inefficient in NB and GNB, thereby causing increased intracellular breakdown of catecholamines by mono-amine oxidase and catechol-o-methyl transferase and subsequent release of pharmacologically inactive compounds into circulation.[17] Only

patients having abundant storage granules seem to demonstrate blood pressure patterns like patients with pheocromocytoma.[8] Renal artery stenosis secondary to pressure exerted by the tumour mass causing elevated renin levels, increased angiotensin production, vasoconstriction, salt retention and hypertension has been reported.[19] Even in the absence of arterial constriction, renin levels can be elevated.[20] Vasopressin causing hypertension due to fluid retention has been seen in primary nasal NB.[9]

Elevated cortisol levels similar to those in Cushing's disease can also result in salt retention and hypertension. The cause of cortisol elevation is not clear although an unexplained association of Cushing's syndrome with neurogenic tumours has been noted.[10] Some reports indicate the appearance of hypertension after the initiation of therapy[21] or intra-operatively.[20] Foetal NB can give rise to raised catecholamine levels in mothers causing pre-eclampsia.[13] In our patient colour doppler of renal vessels was normal, however serum levels of catecholamine or renin could not be done due to unavailability of these tests at our centre.

Alpha-1 blockers are indicated for the management of hypertension while beta-blockers like propranolol are known to be useful in controlling the tachycardia. The final effect of the anti- hypertensives could not be assessed in our patient as she left against medical advice and was lost to follow up.

To conclude, one must rule out neuroblastic tumours in patients presenting with seizures or hypertension with a lump in abdomen, as these uncommon complications exist in such cases. Extensive investigative workup including serum catecholamines, renin, cortisol, and vasopressin levels should be done in neuroblastic tumours presenting with hypertension, to pin point the exact cause of hypertension.

REFERENCES:

1. *Welson LMK, Draper GJ. Neuroblastoma: its natural history and prognosis: A study of 487 cases BMJ 1974;3:301.*
2. *Brodeur GM, Seeger RC, Barett A, Berthold F. International criteria for diagnosis, staging and response to treatment in patients with neuroblastoma. J Cin Oncol 1998;6:1874-1881.*
3. *Dubois SG, Kalika Y, Hukens JN. Metastatic sites stage IV & IV S neuroblastomas co-relate with age, tumour biology and survival. J Pediatr Hematol Oncol. 1999;21: 181-189.*
4. *Matthay KK, Brisse H. Central Nervous System Metastasis in Neuroblastoma. Radiologic, Clinical and Biological Features in 23 patients. Cancer 2003;98:155-165.*
5. *Kellie SJ, Hayner FA, Bowman L, Kounar EH. Primary extra cranial neuroblastoama with CNS metastasis characterization by clinicopathological findings and neuro-imaging. Cancer 1991; 68: 1999-2006.*
6. *Marwaha RK, Choudhary VP. Neuroblastoma in Indian children. Indian J Pediatrics 1982;49:811-813.*
7. *Kusukumary P, Ajithkumar TV, Ratheesan K, Chellam VG, Nair MK. Pattern and outcome of neuroblastoma: A 10 year study. Indian Pediatrics. 1998;35:223-229.*
8. *Kedar A, Glassman M, Voorhess ML, et al. Severe hypertension in a child with ganglioneuroblastoma. Cancer 1981;47:2077-2080.*
9. *Singh W, Ramage C, Best P, et al. Nasal neuroblastoma secreting vasopressin. Cancer 1980;45:961-966.*
10. *Kogut MD, Donnell GN. Cushing's syndrome in association with renal gangloneuroblastoma. Pediatrics 1961;28:566-577.*
11. *Puyo A, Lewin G, Aramando I, Barontini M. Total plasma dopamine / noradrenaline ratio in catecholamine - secreting tumors. Its relation to hypertension.Hypertension 1988;11:1202-1206.*
12. *Steinmetz JC. Neonatal hypertension and cardiomegaly associated with a congenial neuroblastoma. Pediatr Pathol 1989;9:577-582.*
13. *Newton ER, Louis F, Dalton ME, Feinglold M. Fetal neuroblastoma and catecholamine induced maternal hypertension. Obstet Gynecol 1985;65:49S-52S.*
14. *Alvarado CS, Faraj BA, Kim TH, Camp VM, Bam RP, Ragab AH. Plasma dopa and catecholamine in the diagnosis and follow-up of children with neuroblastoma. Am J Hematol Oncol 1985;7:221-227.*
15. *Voorhess ML. Neuroblastoma – Pheochromocytoma: Products and pathogenesis. Ann NY Acad Sci 1974;230:187-194.*
16. *Von Studnitz W, Kaser H, Sjoerdama A. Spectrum of catecholamine biochemistry in patients with neuroblastoma. N Engl J Med 1963;269:232-235.*
17. *Kaser H, Turler K, Wanger HP. Catecholamine metabolism in sympathetic tumor cells. Lancet 1970;2:469-470.*
18. *Abramowsky CR, Taylor SR, Anton AH, Berk AL, Roederer M, Murphy RF. Flow cytometry DNA ploidy analysis and catecholamine secretion profiles in neuroblastoma. Cancer 1989;63:1752-1756.*
19. *Londe S.Causes of hypertension in the young. Pediatr Clin North Am 1978;25:55-65.*
20. *Weinblatt ME, Heisel MA, Siegel SE. Hypertension in Children with Neurogenic Tumors. Pediatrics. 1983;71(6):947-951.*
21. *Wolf JEA, Bauch HJ, Roessner A. Development of hypertension in neuroblastoma during therapy: A case report. Medical and Pediatric Oncology 1993;21:460-464.*