

Adrenal crisis in metastatic adrenal cortical carcinoma in an infant with neurofibromatosis type 1

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Introduction

Neurofibromatosis type 1 (NF-1) is associated with a high risk of benign and malignant neoplasms, especially related to the nervous system and endocrine organs, although there is no definite association with adrenal cortical carcinoma (ACC)¹. Similarly, ACCs are very rare malignancies which may occur at any age but are commoner among children less than 5 years old and adults over 40 years of age and two thirds of them are capable of secreting an excess of corticosteroid hormones^{1,2,3}.

Case report

A five month old baby boy was born to non-consanguineous healthy parents as the fourth child. He had numerous café au lait patches, which were noted from birth and multiple neurofibromas that were of recent onset. Hence a diagnosis of NF-1

was made. An ultrasound scan of the abdomen at 3 months of age did not show any intra-abdominal or retroperitoneal masses. He was admitted to the Lady Ridgeway Hospital for Children, Colombo, at 5 months of age for fibro-optic laryngoscopy for further evaluation of congenital stridor. During this admission, he underwent general anaesthesia (GA) during which he had a cardiorespiratory arrest which was resuscitated successfully, and he was transferred to the intensive care unit (ICU). The investigations done during the resuscitation revealed severe hyperkalaemia, hyponatraemia and hypoglycaemia. During the ICU stay he had repeated episodes of cardiorespiratory depressions and arrests, which were always associated with hyperkalaemia, hyponatraemia and hypoglycaemia. His venous blood gas, capillary blood sugar and serum electrolyte reports are shown in Table 1.

Table 1: Venous blood gas capillary blood sugar and serum electrolyte reports of the 5 month old baby

Investigation	22/12/2016 9.00am	22/12/2016 2.00pm	23/12/2016 1.13pm	23/12/2016 3.40pm
pH	7.103	7.08	7.58	7.40
pCO ₂ (mm Hg)	85.4	71.0	15.4	33.8
pO ₂ (mm Hg)	20.2	23.3	120.2	91.3
Bicarbonate (mmol/L)	27.0	21.0	14.4	21.2
Base excess	-2.8	-3.7	-7.8	-3.8
Capillary blood sugar (mg/dl)	42	41	37	63
Sodium (mmol/L)	121.8	129.4	122.4	132.0
Potassium (mmol/L)	19.74	12.15	9.13	3.99

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Despite treatment with hydrocortisone and fludrocortisone, his condition deteriorated and he needed inotropic support. In spite of repeated fluid boluses and regular doses of glucocorticoids and mineralocorticoid, baby progressed to circulatory failure and succumbed within two days of the initial cardiorespiratory arrest.

The computed tomography (CT) scan of abdomen revealed a poorly enhancing hypodense mass, measuring 3.1 cm (antero-posterior), 4.3 cm (cephalo-caudal) and 3.4 cm (transverse) in size, in the region of left adrenal gland, with no separately identifiable left adrenal gland. There were numerous focal lesions involving all segments of the liver, suggestive of liver metastases (Figure 1).



Figure 1: Computed tomography scan of abdomen with adrenal carcinoma and liver metastasis

← Liver metastasis ← Adrenal carcinoma

Discussion

NF-1 is an autosomal dominant disease, inherited due to loss of function mutation in NF-1 gene, in chromosome 17q11.2, with the prevalence of 1: 3000 live births⁴. Clinical diagnosis of NF-1 was considered with the presence of multiple neurofibromas and more than six café au lait patches more than 5mm in size. NF-1 is associated with high risk of benign and malignant neoplasms, especially in nervous system, skin, gastrointestinal system stroma cells, lungs, muscles and pheochromocytoma^{1,4,5,7}. On the other hand, thyroid nodules, parathyroid adenomas, carcinoid tumors are also reported⁷. There are cases of ACCs reported in patients with NF-1 in the medical literature. Child with ACC and systemic metastasis has been described⁶. Definite association between these two conditions is still not established²⁻⁵.

ACCs are very rare malignant tumours which may occur at any age. They are commoner among children less than 5 years old and adults over 40 years of age^{1,3}. Ten to fifteen percent of ACCs are inherited with a mutated gene, such as Li Fraumeni syndrome, Lynch syndrome and multiple endocrine neoplasia type 1 (MEN1) but there is no evidence to suggest an association between NF-1 and ACCs^{2,3,5}. Two thirds of ACCs are capable of secreting excess hormones which can result in malignant hypertension, Cushing disease and virilization¹.

This patient presented with adrenal crisis but did not reveal clinical features of long standing corticosteroid excess. In addition, ultrasound scan

of abdomen was done at 3 months of age which did not reveal any intra-abdominal or retroperitoneal masses. ACCs are generally fast growing malignancies, detected at late stages⁹. Treatment depends on the tumour spread, general wellbeing and fitness of the patients for combined surgery, chemotherapy and radiotherapy⁹.

Hypersecretion of adrenal cortisol, which is called 'adrenal hypercortisolism', can have wide variability in the degree of hyper secretion as well as in the degree of clinical manifestations^{9,10}. The presentation can vary from sub-clinical hypercortisolism to full blown Cushing syndrome^{7,10}. Patients who had undergone unilateral adrenalectomy for subclinical hypercortisolism had progressed to adrenal insufficiency after surgery^{9,10}. This can be explained theoretically, as hypercortisolism of the diseased adrenal gland has suppressed the normally functioning contra-lateral adrenal gland and child later presented with adrenal crisis when the diseased gland and the hypercortisolism were absent after surgical removal⁷⁻¹⁰. The patient had adrenal crisis due to the same reason where the contralateral adrenal gland had been suppressed due to tumour in the left adrenal gland. When the gland had bleeding and necrosis, the contralateral suppressed adrenal gland was not able to produce stress hormones resulting in adrenal crisis. There is no biochemical evidence for cortisol excess, as this infant did not survive through the disease process and was not stable enough for the investigations during the presentation.

ACC is a rare association in NF-1 and unilateral ACC can present with adrenal crisis, due to suppression of contralateral non affected adrenal gland with sub-clinical hypercortisolism of the affected gland.

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