

Case Report (V)

Adrenal Cortex Tumour in a Six Year Girl – A Case Report & Review of Literature.

K S BUDHWANI, RAJENDRA K GHRITLAHAREY, MANASH K DEBBARMA

ABSTRACT

A 6-year-old girl was admitted with complains of acne over face, hair over pubic area & deepening of voice for 4 months. She was investigated for virilizing adrenal tumour. Her hormonal assay confirmed functioning adrenal tumour. Exploration & excision of right adrenal tumour was done. Postoperative period was uneventful & she was discharged on 13th postoperative day. Histopathological report was adrenocortical carcinoma. Two months later she was admitted in shock & could not be revived. Pertinent literature is reviewed.

INTRODUCTION

Adrenal cortical tumours (ACTs) constitute less than 0.2% of all pediatric neoplasms & account for 6% of all adrenal tumours in children with an estimated incidence of 0.3 per million population.¹ There is bimodal occurrence by age, with a peak incidence at less than 5 years & a second peak in the 4th & 5th decades. Because of the relative rarity of these tumours, little is known about their causation & the influence of genetic factors.⁴ Virilization is most common presenting features followed by Cushing's syndrome or a combination of the two. Some tumours may present without features of hyper function of adrenal cortex.⁵ Diagnostic work up consist of clinical examination, biochemical, hormonal, & radiological investigations, all are needed to document size of tumour, invasion, hyper function, distant metastases, & to rule out benign adrenal adenoma from adrenocortical carcinoma.^{6,7} Complete surgical excision remains the only effective treatment. Adjuvant

radiotherapy or chemotherapy has been advocated for incompletely excised tumour or patients with metastases.^{9,10,14} A number of criteria have been identified in adults. Adrenocortical tumour allow some prognostication & these include; cellular & nuclear pleomorphism, high mitotic activity with atypical mitosis, vascular & capsular invasion, weight greater than 250 gms, size more than 10 cms, sheets of necrosis, etc. Such criteria have not been identified in pediatric adrenocortical tumours.

Case:

Six years old girl was admitted on July 31, 2002 with complaints of acne over face, pubic hairs & deepening of voice for 4 months. There was no history of drug intake, headache, weakness, bladder or bowel changes, etc. There was no history of chronic illness or diseases in past. There was history of death of a brother due to brain tumour.

General examination revealed; her pulse rate was 130/minutes & blood pressure 140/90 mmHg. Respiratory System, CVS, & CNS are normal. There were no lump palpable or organomegaly or ascitis detected on abdominal examination. Local examination revealed acne over face, pubic hairs, and clitoromegaly. Her weight was 26kgs.

Hormonal assay revealed Serum cortisol (AM) 22.7ug/dl, (PM) 7.20ug/dl, LH < 00.10mu/ml, FSH < 01.00mu.ml, Testosterone 06.60 ng/ml (increased), DHEA -SO₄ above 800.00ug/dl (increased).

Ultrasonography of abdomen showed a heterogeneous lesion with cystic area seen in upper pole of right kidney. It measures 5x5cms.

A soft tissue density area, partially occluding inferior vena cava was also seen. Her uterus & ovaries were normal. Minimal ascitis also detected. CT scan of abdomen with oral & I/V contrast revealed a large hypodense smooth walled area, seen in right suprarenal location of 57x45mm. Aorta & inferior vena cava were normal. No retroperitoneal lymphadenopathy detected.

Exploratory laparotomy through right supra umbilical transverse incision was done. There was a right adrenal tumour of 5x5cms. Tumour was excised with its capsule intact. Tumour was not adherent to inferior vena cava, diaphragm, and liver. No lymphadenopathy was detected. Her postoperative period was uneventful. She was given hydrocortisone in perioperative periods & maintained in postoperative periods also. Her blood pressure returned to normal limits after a week & She was discharged on 13th postoperative day.

Gross weight of excised specimen was 40 Gms, it was grayish - white to yellow measuring 5.5x5x4.5cms. Its cut surface was grayish yellow. Microscopic examination revealed round & oval shaped neoplastic cells with abundant acidophilic cytoplasm & bizarre hyperchromatic nuclei. Although mitotic activity was less, the large size of tumour, & other features favoured the diagnosis of carcinoma of adrenal cortex.

She was admitted 2 months later with complaint of not feeling well for one day. She was in shock, & could not be revived. Relatives were reluctant to elaborate any details of past illness or improper / inadequate medication or stressful events, so the exact cause of death could not be made out. We presumed death is not directly related to the malignancy itself but may be due to some stressful condition or inadequate hormonal replacement etc, leading to adrenal insufficiency, shock & death.

DISCUSSION

Little is known about the etiopathogenesis, clinical characteristics, & management of

pediatric adrenocortical tumours because of the limited number of case reports in the literature & many large series consist mostly of adult & few pediatric cases collected from the literature or gathered from several centres & very few of these consist of both adenomas & carcinomas.¹

Adrenocortical tumours (ACTs) may be associated with various congenital conditions suggesting a possible genetic predisposition. Most commonly seen in children with adrenal hyperplasia usually of 21-hydroxylase deficiencies. These may be associated with MEN I, Beckwith - Wiedemann syndrome, hemihypertrophy, astrocytoma etc. Rarely adrenocortical carcinoma may occur among siblings & there may be a family history of cancer.^{2,3}

Children may present with mixed clinical findings but the most common is virilization followed by Cushing's syndrome. More than 50% of patients with adrenocortical carcinoma present with virilization symptoms. Boys present with precocious puberty as increase in size of penis, scrotum, increased pubic, axillary & facial hair, acne & deepening of voice. Girl's exhibits with increased clitoral size, enlargement of labia majora, acne, increased pubic & axillary hair, deepening of voice, lack of appropriate breast development & lack of menarche.^{2,4}

Cushing's syndrome is due to excess of adrenocortical hormones & is seen in about one third of patient with adrenocortical tumours. There is progressive generalized obesity, Moon face, buffalo hump, failure of growth velocity & hypertension. Rarely feminization may occur & Boys presented with gynecomastia & hypertension while girls presented with precocious sexual development & hypertension.⁴

Approximately 30 -40% of adrenocortical carcinoma may present without any findings of over production of hormones. In sixty percent of patients functional & palpable adrenal mass is carcinoma rather than adenoma. Physical examination findings almost always include a palpable mass in the abdomen that usually

involves the center of the abdomen rather than flanks. The mass is hard & non-mobile.⁴ Metastatic spread of adrenocortical tumour is to local lymph nodes, lungs, liver, bones, kidneys, brain, and thigh. The differential diagnosis of adrenal mass in children must include adenoma, carcinoma, neuroblastoma, Wilms' tumour, lymphoma, etc.⁴ The median interval between onset of symptoms & diagnosis is 18 months range 2 to 60 months.⁵

A critical diagnostic factor is a biochemical demonstration of adrenal hyperfunction. Lab studies of adrenocortical carcinoma include serum glucose, serum cortisol, androgen, and adrenal hormones, urinary vanillylmandelic acid (VMA) & homovanillic acid (HVA). Urinary steroids typically show a markedly elevated 17-ketosteroid level. This investigation helps in differentiating between functioning & non-functioning adrenal neoplasm, also helps to differentiate between adrenal cortex neoplasms from neuroblastoma.^{4,5}

Radiological investigations include Ultrasonography, CT scan, and MRI etc. CT scan is more sensitive than ultrasonography in identifying tumour mass & CT scan seems to be the best for localization of adrenal tumours. Iodocholesterol scans or more invasive procedures such as arteriography, venography are only used in cases where CT scan is not helpful. CT scan of chest & bone scintigraphy should be performed to detect metastases.^{5,6}

The size of tumour, if larger than 5cm in diameter, there is more likelihood of carcinoma. Fine needle aspiration for cytology of an adrenal mass has limited ability to differentiate benign from malignant primary adrenal lesions & for the same it is not recommended as a routine. Fine needle aspiration may be catastrophic in a patient with an unsuspected pheochromocytoma & for the same reason urinary catecholamines are indicated to exclude a pheochromocytoma before needle biopsy.⁷ CT guided fine needle aspiration biopsy may be helpful in

differentiating whether hepatic mass is metastatic or otherwise.⁸

Surgery is the mainstay & most effective treatment for adrenal carcinoma & currently appears to be the only hope of cure. Every reasonable attempt should be made to render the patient disease free at the primary site, at the site of local invasion & at the site of metastatic disease. Adrenocortical carcinomas are usually well encapsulated & differentiation between adenoma & carcinoma may be difficult.^{2,4, 9 10} Preoperative Corticosteroids replacement is essential in the surgical management of cases of adrenocortical carcinoma, since the contralateral adrenal gland is often suppressed. Patients with symptomatic, biochemical evidence of over production of hormones should be suppressed in the postoperative period & maintained & tapered accordingly. Percutaneous ethanol injection therapy (PEIT) is an established treatment for hepatocellular carcinoma in adults & is performed under ultrasound guidance under local anesthesia. PEIT has been successfully used to treat liver metastasis of adrenocortical carcinoma in a two years old girl.¹¹

Tobias-Machado et al in 2002, performed first case of retroperitoneoscopic adrenalectomy in a one & half year's child. The child presented with clinical features of virilization. Ultrasonography confirms 5 cms of adrenal tumour on right side. Pathological report was as adrenal cortical carcinoma with capsular invasion. The authors believe that laparoscopic surgery is a promising option in selected cases, for the treatment of children with localized adrenal tumours that do not show invasion of neighboring structures.¹²

Miller et al in 2002 reported their experiences with seventeen cases of lateral tranperitoneal laparoscopic adrenalectomies in children. Laparoscopic adrenalectomy can be performed safely & effectively with a short hospital stay, minimal blood loss, & excellent functional outcome in pediatric patients.

Authors believe laparoscopic adrenalectomy is an excellent approach for the management of benign pediatric adrenal pathology.¹³

Although radiotherapy has been used to treat adrenocortical carcinoma, there is little convincing evidence of much effect. Radiation therapy may be helpful in palliation of unresectable disease that is unresponsive to medical therapy. The role of chemotherapy other than for metastatic disease is still controversial. Chemotherapy has been used in the patients with adrenocortical carcinoma when tumour could not be completely excised or there is evidence of metastases. Mitotane (o, p'-DDD) has been the most successful agent in the treatment of adrenocortical carcinoma in adults & in children. The mode of action is selective necrosis of the adrenal gland. Mitotane can be used alone or as a combination with cisplatin & etoposide.¹⁴

Prognosis of adrenocortical carcinoma is always guarded. Cure has been reported in patients who underwent complete removal of a small (<9 cm), encapsulated tumour. Reported long-term survival of children with adrenocortical carcinoma is between 10 to 46%. Prognosis is poor in patients in whom surgery could not be performed or in whom metastases is detected. Patients with regional & metastatic disease had a very poor prognosis & in spite of aggressive surgical therapy, the 5 years survival rate is less than 30%. Survival after partial resection is unusual, even when adjuvant chemotherapy or radiotherapy was used.

The prognostic significance of tumour size, weight, & histological grade are still very much unclear. None of the clinical, laboratory, or pathological features are reliable predictors for recurrence & discrimination of malignancy in adrenocortical tumours. Early diagnosis & total excision is the best for adrenocortical carcinoma.^{1, 4, 5, 9, 11, 15}

Conclusion:

Adrenocortical carcinoma in children is a well known to occur albeit with relative rarity. Virilization is most common presenting feature followed by Cushing's syndrome, or a combination of the two. Diagnostic work up consists of clinical examination, hormonal assay & radiological investigations. Larger weight, bigger size of tumour, lobulated appearance, presence of necrotic area, calcifications & hemorrhage, vascular & capsular invasions, frequent mitoses, nuclear atypia & hyperchromasia, all are the common features suggestive of malignancy of adrenal cortex. The most important aspect of therapy for adrenocortical carcinoma is early diagnosis & total excision. Surgery is the main stay in the treatment & currently appears to be the only hope of cure. Newer modality, like laparoscopic adrenalectomy is also a promising option in selected patients. Partial excision & advanced stage disease are the major determinants of poor outcome.

REFERENCES:

1. Ciftci AO, Senocak ME, Tanyel FC, et al. Adrenocortical tumours in children. *J Pediatr Surg* 2001;36:549-54.
2. Howard McC, Snyder III. *Genitourinary Tumours. Clinical Pediatric Urology by Kelalis PP, King LR, Belman AB. 1992, III Ed: 1400-03.*
3. Hertel NT, Carlsen N, Kerndrup G, et al. Late relapse of adrenocortical carcinoma in Beckwith-Wiedemann Syndrome. *Clinical, endocrinological & genetic aspects. Acta Paediatr* 2003;92:439-43.
4. Lawrence C Wolfe. *Adrenal Carcinoma. eMedicine Journal* 2003;4:(3).
5. Mayer SK, Oigny LL, Deal C, et al. Childhood Adrenocortical Tumours: Case Series & Reevaluation of Prognosis - A 24-Year Experience. *J Pediatr Surg* 1997;32:911-15.
6. Ribeiro J, Ribeiro RC, Fletcher BD. Imaging findings in Pediatric adrenocortical Carcinoma. *Pediatr Radiol* 2000;30:45-51.
7. Jeffrey A Norton, Hop N LE. *Adrenal Tumours. Cancer: Principles & Practice of Oncology by Vincent T. DeVita Jr, Samuel Hellman, Steven A Rosenberg. 2001; Ed 6th: 1770-80.*

8. *Serrano R, Rodriguez-Peralto JL, Santos-Briz A, et al. Fine needle aspiration cytology of metastatic hepatic adrenocortical carcinoma mimicking hepatocellular carcinoma: a case report. Acta Cytol 2001;45:768-70.*
9. *Mishra A, Agarwal G, Misra AK, et al. Functioning adrenal tumours in children & Adolescents: An institutional experience. Australian & New Zealand Journal of Surgery 2001,71:103-7.*
10. *Narasimhan KL, Samujh R, Bhansali A, et al. Adrenocortical tumours in childhood. Pediatr Surg Int 2003;19:432-5.*
11. *Fujio H, Teruaki K, Hirokazu T, et al. A child with adrenocortical carcinoma who underwent percutaneous ethanol injection therapy for liver metastasis. J Pediatr Surg 2003;38:1237-40.*
12. *Tobias-Machado M, Cartum J, Santos-Machado TM, et al. Retroperitoneoscopic adrenalectomy in an infant with adrenocortical virilizing tumour. Sao Paulo Med J 2002;120:87-9.*
13. *Miller KA, Albanese C, Harrison M, et al. Experience with laparoscopic adrenalectomy in pediatric patients. J Pediatr Surg 2002;37:979-82.*
14. *Hovi L, Wikstrom S, Vettenranta K, et al. Adrenocortical carcinoma in children: A role for etoposide & cisplatin adjuvant therapy? Preliminary report. Med Pediatr Oncol 2003;40:324-6.*
15. *Upadhye PS, Desai MP, Colaco MP, et al. A Clinicopathologic Profile of adrenocortical tumours. Indian Pediatr 1997;34:481-90.*



**XIII BIENNIAL CONFERENCE OF
THE INDIAN SOCIETY OF MEDICAL & PAEDIATRIC ONCOLOGY
&
XI CONFERENCE OF
INDIAN SOCIETY OF ONCOLOGY**

8-10th Oct. 2004

Will be held at Convention Centre NIMHANS, Bangalore

Please Contact/Write to

Dr. PP Bapsy

Organising Secretary

Professor & Head

Department of Medical Oncology

Kidwai Memorial Institute of Oncology

Hosur Road, Bangalore-560029

E-mail : ppbapsy@yahoo.com