Cushing's Syndrome due to Adrenocortical Carcinoma
Report of a Case*

Burhan Say, M.D.**

Cushing's syndrome in childhood associated with adrenocortical carcinoma is a rare condition. Guin and Gilbert [1] collected 29 cases from the world literature in 1956 and stressed that Cushing's syndrome in childhood is almost always due to adrenocortical carcinoma. Occasionally it may be caused by a benign adrenal adenoma or by simple adrenal hyperplasia. One case has been described which was associated with a neuroblastoma of the adrenal gland. Williams [2] stresses that in most cases of adrenal hyperplasia there is evidence of Cushing's syndrome at or very soon after birth whereas cases developing symptoms of Cushing's syndrome in later years are due to an adrenal adenoma or carcinoma.

In cases of Cushing's syndrome which are caused by an adrenal tumor there will be an increased production of androgens and glucocorticoids as well as oestrogens. As a result of this the signs and symptoms will depend on the relative proportions of the hormones produced by the tumor. In most cases the hormone which is most excessively produced is glucocorticosteroid but recently a case of Cushing's syndrome in a 2 1/2 year old child with an adrenocortical carcinoma was reported in which there was an excessive production of aldosterone with symptoms related to it. [3]

In a typical case the somatic alterations involve buffalo type obesity, plethora, moon-face, hirsutism and hypertension, cessation of growth, and atrophy of skin, muscles and bone. Osteoporosis may be present in the vertebrae, ribs, pelvis and less frequently in other bones. Gynecomastia is rarely present. Although the fasting blood sugar is usually within normal limits many patients show a diabetic type of glucose tolerance curve. If diabetes is present, it is usually insulin-resistant. The red cell and hemoglobin values may be elevated but the total eosinophile count will be well below normal.

Particularly useful investigations in these cases include:

1 — Estimation of plasma and urinary 17 - hydroxycorticosteroids, which are always raised.

2 — Urinary 17 - ketosteroids, which are usually raised.

3 — ACTH stimulation, which does not produce a rise of the above mentioned steroids in cases of adrenocortical carcinoma.

---

* From the Reaserch Institute of Child Health. Hacettepe, Ankara.

** Associate in Pediatrics.

4 — Excretion urography, which may show depression of the kidney on the side of the tumor.

5 — Perirenal or presacral insufflation of air, which may outline the tumor.

We feel that all cases of Cushing's syndrome in children should be regarded as cases of adrenocortical carcinoma until proved otherwise by full investigation and even exploration of the adrenal glands.

The treatment of choice is adrenalectomy as soon as the patient is fully prepared. Post-operative radiotherapy is advisable as the tumor is often adherent to surrounding structures. As the contralateral adrenal gland in these cases is almost always hypoplastic it is essential to administer cortisone before, during and after the operation and to stimulate growth and function of the remaining adrenal gland by the administration of ACTH postoperatively. This subject is fully discussed by Williams [4]. An immediate postoperative fall of blood pressure commonly occurs and this must be treated with noradrenaline.

Three approaches to an adrenal tumor are available :

a) Posterior, through the bed of the 11th or 12th rib: This gives a very direct approach but has the disadvantages that the liver and peritoneal cavities cannot be explored for metastases and that the tumor must be fully mobilised before its blood supply can be ligated.

b) Anterior or transperitoneal: The vessels to the adrenal gland can be ligated early on in the operation so as to avoid malignant emboli during the manipulation of the tumor and the peritoneal cavity can be explored, but on the other hand the exposure is a poor one as the tumor is so far from the anterior abdominal wall.

c) Thoraco-abdominal approach: This is the method of choice with modern anesthesia as it combines the advantages of the two above mentioned approaches and has none of their disadvantages,

The prognosis following surgical extirpation must be guarded as the tumor tends to metastasize early but a sustained fall of the ketosteroids to normal levels is in favor of a good prognosis as the metastases are usually hormone-excreting.

Case Report

An 8 year old boy was admitted with the complaint of excessive appetite and lassitude for the past 30 days. He had also gained considerable weight during this time and the parents had noticed changes in his physical appearance. The past history and family history were negative except that the mother was being treated for tuberculosis.

On examination the boy had a plethoric face, most marked on the cheeks, and obesity of the trunk but not of the extremities. There was very marked gynecomastia, the external genitalia were enlarged and there was some pubic hair. The blood pressure was 170/120.

Investigations : Hemoglobin 14.9 gms%; RBC 4.3 million. No eosinophiles seen on smear. Plasma proteins: 7.7. gms %; (alb. 5.1, globulin 2.6.).

Carbon dioxide 24 mEq/L.

Urinary 17-ketosteroids 18 mgm/24 hours.

Urinalysis : no abnormality.

X-ray of the bones showed no abnormality and a chest radio gram was normal.

Excretion urography was normal but presacral air insufflation showed a large tumor above the left kidney.

In view of the physical findings and the results of the investigations a carcinoma of the left suprarenal gland was diagnosed.

Details of the pre-and post-operative steroid therapy are given below:

1 day pre-operative:	2 × 25 mgm cortisone,	
Day of operation :	4 × 25 mgm cortisone,	2 × 25 mgm ACTH
1st postoperative day	7 × 25 mgm cortisone,	4 × 25 mgm ACTH
2nd ,, ,, ,,	7 × 25 mgm cortisone,	2 × 25 mgm ACTH
3rd ,, ,, ,,	2 × 5 mgm Deltacortil,	2 × 25 mgm ACTH
4th ,, ,, ,,	2 × 5 mgm Deltacortil,	2 × 25 mgm ACTH
5th ,, ,, ,,	2 × 5 mgm Deltacortil,	2 × 10 mgm ACTH
6th ,, ,, ,,	2 × 5 mgm Deltacortil,	2 × 10 mgm ACTH
7th ,, ,, ,,	1 × 5 mgm Deltacortil,	2 × 10 mgm ACTH
8th ,, ,, ,,	1 × 5 mgm Deltacortil,	2 × 10 mgm ACTH
9th ,, ,, ,,		1 × 10 mgm ACTH

Operation

Dr. Herbert Eckstein, (Dr. Emel Berker, anaesthetist).

The abdomen was opened through a transverse left supra-umbilical incision and the tumor palpated and its operability assessed. The liver was normal and no metastases were felt. The incision was then extended through the costal margin and the 9th intercostal space opened and the diaphragm split. The posterior peritoneum was divided and the adrenal vessels were doubly ligated and divided. The tumor was mobilised and removed without undue difficulty; it was about the size of an orange. The wound was enclosed in layers and the tumor-bed was drained through a stab-hole. A total of 800 cc of blood

was given during and after the operation. The blood-pressure rose to 200 mm Hg during the procedure but at the end of the operation the patient collapsed and the blood pressure fell to 70/40. He responded to intravenous cortisone and to nor-adrenalin and was in fact maintained on nor-adrenalin for the next 12 hours. Antibiotics and intravenous fluid threrapy were given post-operatively.

His convalescence was uneventful except that a slough developed in the calf as a result of the intravenous nor-adrenalin infusion but this was later skin-grafted successfully. A course of deep x-ray therapy was given to the tumor-bed.

Urinary 17-ketosteroids fell to normal values post-operatively (once steroid therapy had been stopped) and repeated estimations have given values ranging from 2. 2 to 6.8 mgm/24 hours. The blood pressure a week after the operation was 120/60 and has remain so since.

Pathology Report

Macroscopic : A tumor as big as an orange with an irregular surface, lobulated. The mass has a thin very vascular capsule.

Microscopic : Slides prepared by the routine methods and also those stained with potassium bichromate revealed a neoplastic tissue with typical polygonal cells showing columnar as well as alveolar appearances. Areas of necrosis, haemorrhage and calcification were seen. In many areas cells with large nuclei and excessive chromatin were found. In some slides marked differentation was seen and there were rows of cells resembling the fasciculate layer of the adrenal cortex. As only few chromaffin cells were seen this tumor is regarded as arising from the cortex of the gland. Conclusion : Adrenocortical carcinoma.

Summary

A case Cushing's syndrome with adrenocortical carcinoma is presented and the diagnosis and treatment are discussed.

The author wishes to acknowledge the kind assistance of Dr. Herbert Eckstein, F.R.C.S., in the preparation of this paper.

REFERENCES

1. Guin, G. H., Gilbert, E. F.: Cushing's Syndrome Due to Adreno-cortical Carcinoma. A. M. A. J. Dis. Child., 92: 297, 1956.
2. Williams, D. I.: Urology of Childhood, 1. 1931, London, 1958.
3. Jackson, W. P. U. et. al.: Cushing's Syndrome in Childhood. Brit. Med. J., 2: 130, 1958.
4. Williams, R. H.: Textbook of Endocrinology, 284. W. B. Saunders Co. Philaladelphia, 1955.