Androgen Producing Adrenocortical Carcinoma
A Histological and Ultrastructural Study of Two Cases

Marialuisa Valente, Natale Pennelli, Patricia Segato, Luciano Bevilacqua, and Gaetano Thiene
Institute of Pathological Anatomy, University of Padova, Medical School, Padova, Italy

Summary. Two cases of androgen secreting adrenocortical carcinoma have been described by light and electron microscopy. The histological and ultrastructural features of the tumour cells were similar to those of compact cells of zona reticularis and to those described in virilizing adenomas. They possess numerous mitochondria with lamellar and tubular cristae, abundant smooth endoplasmic reticulum, lipofuscin bodies and scanty lipid. Irregularly shaped, crenated mitochondria, with outpouchings of the outer limiting membrane have also been observed. The clusters of neoplastic cells were surrounded by basement membrane which demonstrated a focal discontinuity, probably reflecting malignancy of the tumours. Hyperplasia of smooth endoplasmic reticulum and the presence of outpouchings of the mitochondrial outer limiting membrane might be the morphological manifestation of endocrine activity of the tumours.

Key words: Adrenal cortex hormones — Endocrinology — Microscopy, Electron — Neoplasms — Virilism.

Introduction

Adrenocortical carcinomas are relatively rare neoplasms (Hutter and Kayhoe, 1966) which are of particular interest. Although malignant, they may exhibit endocrine activity, thus producing specific clinical features. Huvos et al. (1970) reported 34 cases of adrenocortical carcinoma, among which 18 were endocrinologically active. A similar incidence was observed by Hajaar et al. (1975) who, in a study based on 32 malignant cases, described Cushing's syndrome in 7 patients, Cushing's syndrome and virilization in 4, and virilization alone in other 4.

Although the ultrastructural features of carcinomas producing Cushing's syndrome have been described (Mitschke et al., 1973; Tannenbaum, 1973; Thiele, 1974), no ultramicroscopic investigation of androgen secreting malignant tumours has been published. However the ultrastructure of two cases of andro-
gen secreting adenoma has been reported (Fisher and Danowski, 1973; Akhtar et al., 1974).

We report here clinical, histological and ultrastructural data from two patients with adrenocortical carcinomata causing virilization.

Case Reports

Case 1

A 2.5 year old boy was admitted to the University Hospital with the somatic picture of the adrenogenital syndrome. The testes were normal but the penis was precociously developed and pubic hair was present. Muscular hypertrophy was also observed, and the voice was deep and coarse. Routine laboratory studies gave normal results, but urinary 17-Ketosteroid values were 15 mg per day (normal values up to 2 mg); 17-OH corticosteroid values were normal; dexamethasone administration did not produce any change. A retroperitoneal pneumogram showed an enlarged right adrenal gland covering the renal shadow in part. The diagnosis of adrenocortical tumour with androgen secretion was made. The child underwent surgical exploration and right adrenalectomy was performed. The post-operative course was uneventful and 17-Ketosteroids fell to normal values. Five months after the operation the patient was readmitted to the hospital because of progressive liver enlargement. Surgical exploration disclosed multiple hepatic metastases and a biopsy was taken. The patient died one month later; autopsy could not be carried out.

Case 2

A 13 year old prepubertal girl was admitted to the University Hospital with signs of virilization. She had facial acne and growth of facial, axillary and pubic hair with a male distribution. The voice was deep. The breasts were not developed and the external genitalia were hypoplastic. Routine laboratory findings were in the normal range. X rays of the hands showed ossification of the epiphyseal plates. The 17-Ketosteroid value was 24.8 mg per day (normal values up to 12 mg) and there was no change after dexamethasone administration; 17-OHcorticosteroid values were normal. Gas chromatography revealed a pronounced increase in dehydroxyepiandrosterone. A retroperitoneal pneumogram revealed a large mass above the right kidney shadow. The diagnosis of androgen secreting adrenocortical tumour was made and the girl underwent surgery. Right adrenalectomy was performed. The patient had a normal post-operative course and was discharged with normal 17-Ketosteroid values. Unfortunately we were not able to follow up this case.

Material and Methods

Portions of surgically removed adrenal tumours of both patients and a biopsy of a hepatic metastasis in Case I, were fixed in formalin and embedded in paraffin. 5–7 micron thick sections were stained with hematoxylin and eosin and PAS for histological examination.

For the ultrastructural study, fragments of both tumours were immediately fixed in 4% phosphate-buffered glutaraldehyde (pH 7.2), post-fixed in osmium tetroxide and embedded in Epon. Semithin sections (0.5–1 micron) were stained with toluidine blue and observed at the light microscopy. Ultrathin sections (600–700 Å) of selected areas were stained with uranyl acetate and lead citrate for electron microscopic observation.

Results

Gross Findings

The two adrenal neoplasms had similar macroscopic features, appearing as brownish encapsulated irregular masses, about 4–5 cm in diameter. Small yellow