Virchows Archiv A Pathol Anat (1992) 421:533–537

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Adrenocortical oncocytoma: case report with immunocytochemical and ultrastructural study

Louis R. Bégin

Department of Pathology, The Sir Mortimer B. Davis Jewish General Hospital, 3755 Chemin de la Cote Ste-Catherine, Montreal, Quebec, Canada H3T 1E2

Received May 27, 1992 / Accepted July 20, 1992

Summary. An adrenocortical oncocytic neoplasm was detected incidentally in a 58-year-old man. The tumour weighted 315 g, showing haemorrhagic areas and broad fibrous bands. It was composed exclusively of large eosinophilic cells packed with mitochondria showing flat and infrequent tubulovesicular cristae and regression of steroid-related organelles. Occasional annulate lamellae and mitochondrial osmiophilic inclusions were present. Vimentin was diffusely expressed, whereas AE1/AE3 cytokeratin was detected in half of the cells; a focal punctate pattern of staining was exclusively observed for cytokeratin peptides 8 and 18. The patient had no evidence of disease 21 months after surgery.

Key words: Adrenal – Adrenal cortex – Oncocytoma – Adenoma – Carcinoma

Introduction

Oncocytoma is a well-recognized entity in kidney, salivary tissue or endocrine glands such as thyroid, parathyroid and pituitary (Erlandson 1981; Ghadially 1985). Oncocytic neoplasms of the adrenal gland are very rare and their existence has only recently been recognized (El-Naggar et al. 1991; Erlandson and Reuter 1991; Sasano et al. 1991). A case of an adrenocortical oncocytoma with an immunocytochemical and ultrastuctural study is reported.

Materials and methods

Tissue was stained with haematoxylin and eosin for light microscopic examination. Immunohistochemical studies were done on formalin and alcohol-fixed sections. The streptavidin-biotin-peroxidase complex method was performed with antibodies against vimentin (Dakopatts, Mississauga, Ontario; dilution 1/100), AE1/AE3 cytokeratin (Boehringer Mannheim, Indianapolis, Ind., USA; dilution 1/400), cytokeratin CAM 5.2 (recognizing peptides 8 and 18) (Becton Dickinson, Mountain View, Calif., USA; dilution 1/10), and cytokeratin 8.12 (recognizing peptides 13 and 16) (ICN, Immunobiologicals, Lisle, Ill., USA; dilution 1/20). The avidin-biotin-peroxidase complex method was performed with an antibody against factor-VIII-related antigen (Dakopatts; dilution 1/250).

Ultrastructure was done on glutaraldehyde-fixed tissue obtained from different areas of the tumour. Thin sections were stained with uranyl acetate and lead citrate.

Case report

A 58-year-old white man presented with dysuria and difficulty in initiating and terminating urination. There was no history of weight loss, pain, discomfort, flushing or palpitation. Physical examination was normal except for mild prostatic enlargement on digital rectal examination. His blood pressure was 135/75 mm Hg. Cystoscopic examination was within normal limits. Am abdominal ultrasound examination revealed an incidental, right suprarenal solid tumour estimated to measure about 11×9 cm. Chest radiography was normal. Serum biochemistry values, including levels of sodium, potassium, chloride and glucose, were normal. The haemogram was within normal limits. A 24-h urine collection, repeated on 3 consecutive days, revealed the following values: 17-ketosteroids, 27–33 μmol/dl (normal: 37–70); total 17-ketogenic steroids, 23–43 μmol/dl (normal: 32–59); free cortisol, 16–177 nmol/dl (normal: up to 276); creatinine, 13.6–14.4 mmol/dl (normal: 13.3–17.7); vanillylmandelic acid, 34.3 μmol/dl (normal: 7–40); and catecholamine, 568 nmol/dl (normal: 0–768). The serum level of oestradiol was 110 pmol/l (normal: 37–220).

Laparotomy revealed a retroperitoneal, right supra-renal tumour which was circumscribed and encapsulated. It was easily mobilized and resected by blunt and sharp dissection. The adrenal vein looked normal. The patient's postoperative course was uneventful and there was no evidence of disease at 21-month follow-up.

Pathological findings

The tumour had a circumscribed and lobulated contour, weighing 315 g and measuring $13 \times 10 \times 5$ cm. Cut surface revealed soft and pale brown nodules which were confluent or separated by broad fibrous bands (Fig. 1). Large haemorrhagic areas were present whereas necrosis was absent (Fig. 1). A 3-mm-thick peripheral adrenal crescent was seen in continuity with the tumour.

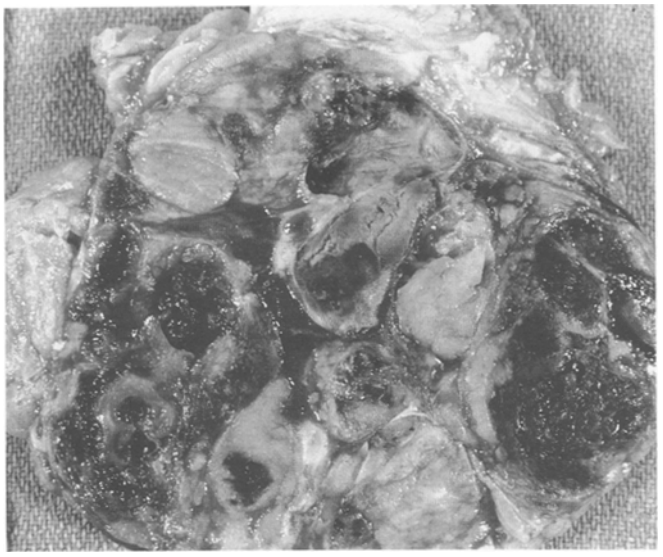

Fig. 1. Adrenocortical oncocytoma characterized by solid brown tumour nodules and large haemorrhagic areas

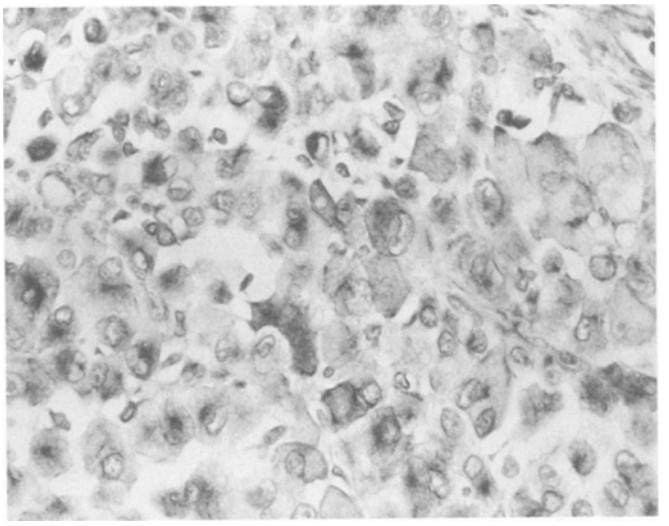

Fig. 3. Strong and diffuse cytoplasmic expression of vimentin. ×250

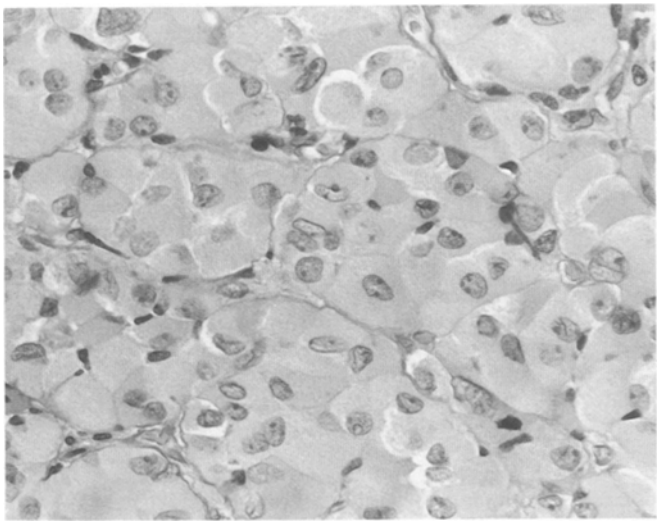

Fig. 2. Cohesive polygonal cells with abundant granular and eosinophilic cytoplasm, and frequently grooved nuclei. ×250

Histological examination revealed a dominant solid pattern of cohesive, large and polygonal cells containing abundant and granular eosinophilic cytoplasm (Fig. 2). Most cells had a round to ovoid, frequently grooved, nuclear contour and a small distinctive nucleolus (Fig. 2). Occasional nuclear pseudoinclusions were present. There were scattered and haphazardly distributed atypical cells with large or multilobulated, hyperchromatic nuclei and/or eosinophilic macronucleoli. The tumour was punctuated with areas of hyaline fibrous sclerosis entrapping groups or individual cells and with focal cellular atrophy. There were large areas of haemorrhage and/or fibrin deposition, with associated thrombosed cavernous thin-walled vessels. Minute foci of dystrophic calcification were present. Features such as mitotic activity, clear cell component, vascular invasion, necrosis or capsular invasion were absent.

Immunohistochemical characterization revealed a moderate to marked cytoplasmic expression of AE1/AE3 cytokeratin and cytokeratin CAM 5.2 of variable and regional distribution, involving about 40–50% of the cell population and often with enhancement of a thin peripheral cytoplasmic rim. In addition, a punctate (dot-like) pattern of staining was exclusively observed for cytokeratin CAM 5.2 in a small proportion of cells. Staining for cytokeratin 8.12 was negative. There was a strong and diffuse cytoplasmic expression of vimentin with peripheral enhancement (Fig. 3). A prominent, ramifying capillary network was enhanced by staining for factor-VIII-related antigen.

Ultrastructural examination revealed groups of cohesive round or polygonal tumour cells with a smooth plasmalemmal contour and united by rudimentary cell junctions (Fig. 4). There were some discrete foci of basal lamina and the presence of an intervening capillary vascular framework composed of a layer of endothelial cells and pericytes. All tumour cells had their cytoplasm packed with innumerable round mitochondria predominantly containing flat cristae (Fig. 4). Tubulovesicular cristae were seen only in some mitochondria (Fig. 5). Whereas occasional intramitochondrial round and non-membrane bound, osmiophilic dense bodies of 140–480 nm in diameter (likely representing lipidic inclusions) were present (Fig. 5), intramatrical 20–50 nm dense granules were not observed. A few cells had annulate lamellae or sparse intracytoplasmic lipid droplets (Fig. 5). Occasional strands or rare circular/parallel arrays of rough endoplasmic reticulum and a few lipofuscin bodies were present in the subplasmalemmal region. Smooth endoplasmic reticulum or intermediajte filaments were not detected. Nuclei were frequently grooved or polysegmented, depicting delicate heterochromatin and small dense nucleoli. There were occasional nuclear pseudoinclusions.

Discussion

The present tumour, being exclusively composed of large eosinophilic cells shown ultrastructurally to be oncocytes after thorough sampling, fulfils the criteria for designation as an oncocytoma (Erlandson 1981; Ghadially 1985). To our knowledge, seven cases of adrenocortical oncocytic neoplasm have been reported in the English literature, of which four were probably benign (Erlandson and Reuter 1991; Sasano et al. 1991), two had no follow up (Erlandson and Reuter 1991) and one was invasive ab initio (El-Naggar et al. 1991). Except for the case reported by El-Naggar et al. in 1991 which pre-

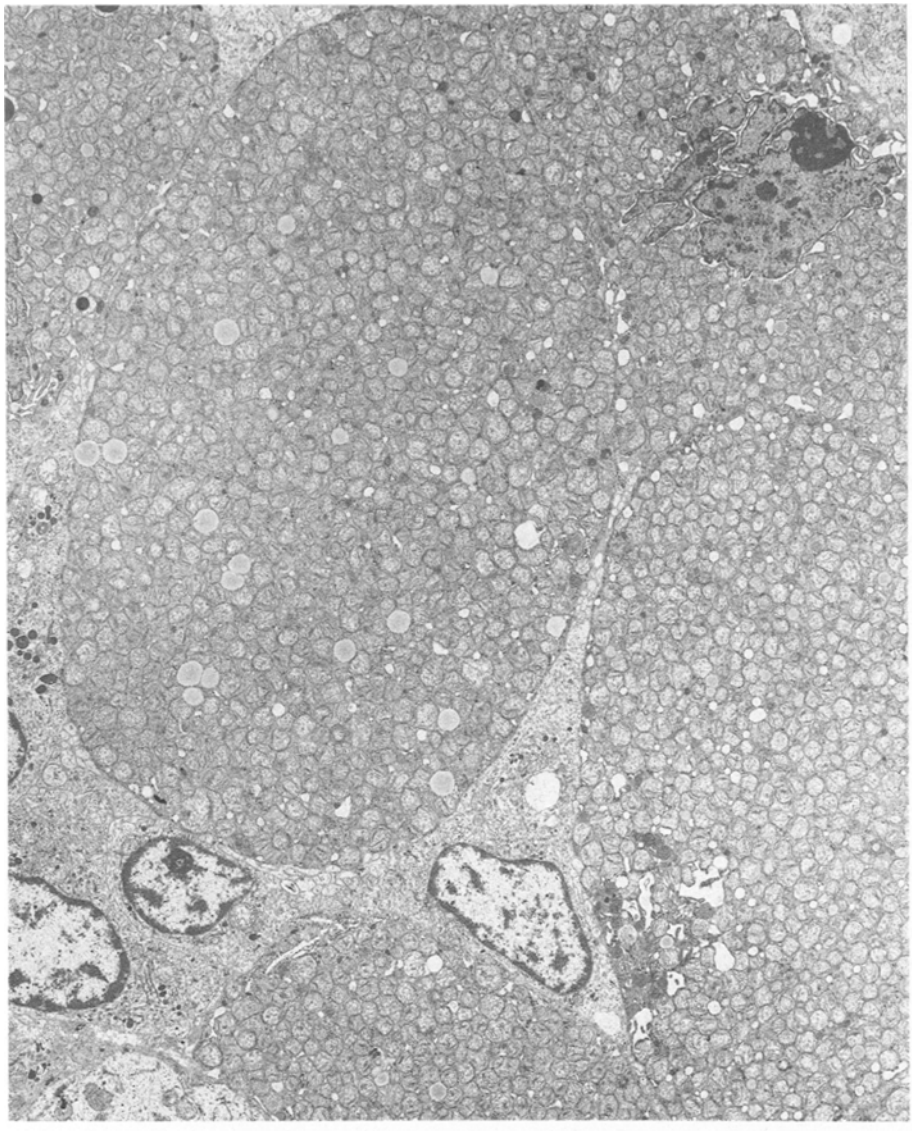

Fig. 4. Cohesive arrangement of large oncocytic cells whose cytoplasm is packed with mitochondria. ×3800

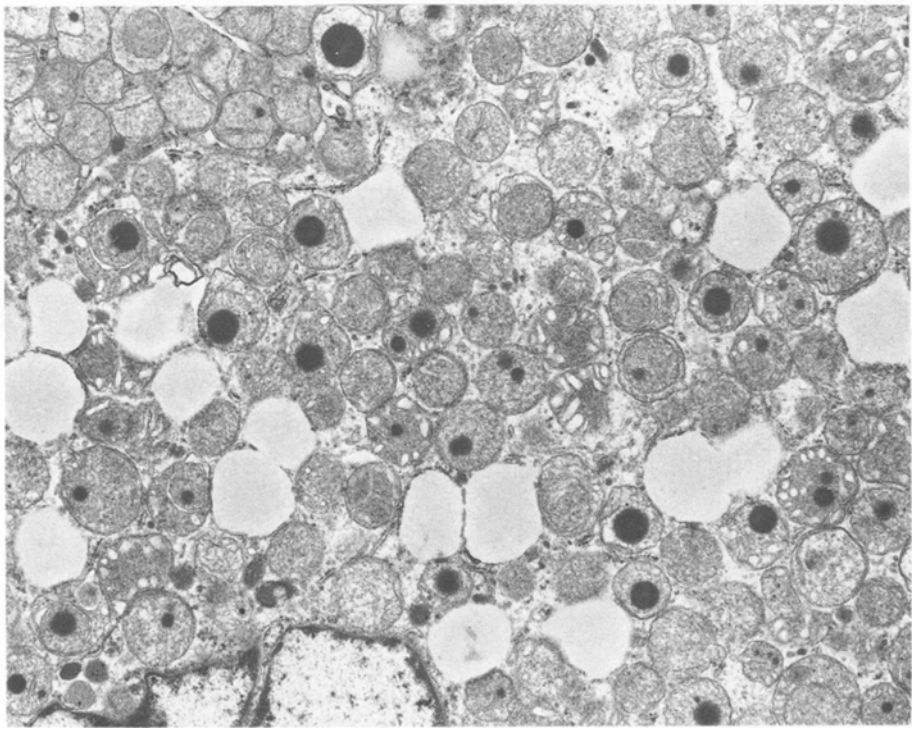

Fig. 5. Occasional oncocytes have cells with intramitochondrial osmiophilic inclusions of probably lipidic nature, mitochondrial tubulovesicular cristae, and intracytoplasmic lipid droplets. ×11 500

sented with acute abdominal pain, the other adrenocortical oncocytic neoplasms were detected incidentally by imaging studies. All cases lacked functional manifestations, although one case reported by Erlandson and Reuter in 1991 was associated with a markedly elevated urinary level of 17-ketosteroids (which returned to normal 1 week after surgery).

Of the three immunocytochemically studied cases of adrenocortical oncocytic neoplasm, the tumours expressing cytokeratin were associated with a benign outcome (Erlandson and Reuter 1991), whereas the malignant case was negative for cytokeratin (El-Naggar et al. 1991). It has been suggested that negative immunoreactivity for cytokeratin in an adrenocortical tumour at large was associated with malignant potential (Cote et al. 1990). However, Schröder et al. in 1992 detected cytokeratin in 1 adenoma and 1 carcinoma only among 72 adrenocortical tumours. The differential prognostic value of cytokeratin expression in a tumour of adrenocortical derivation is therefore doubtful. The single reported case of adrenocortical oncocytoma which was stained for vimentin was negative (Erlandson and Reuter 1991).

The absence of intramitochondrial 20–50 nm granules in our tumour corroborates the ultrastructural experience with oncocytoma at large (Erlandson 1981; Ghadially 1985). Intramitochondrial osmiophilic inclusions of varying size, as observed in our tumour have been described in occasional oncocytomas (Ghadially 1985), and resemble inclusions seen in some adrenocortical adenomas (Gorgas et al. 1976; Page et al. 1986), carcinomas (Silva et al. 1982) and the reported case of oncocytic adrenocortical carcinoma (El-Naggar et al. 1991). These inclusions have been described as of proteinaceous (Page et al. 1986), glycoproteinaceous (Gorgas et al. 1976) or probably lipidic nature (Ghadially 1985). The presence of annulate lamellae in a few cells of adrenocortical oncocytoma is of unknown significance. Most commonly seen in malignant or embryonic cells, annulate lamellae have been occasionally observed in benign endocrine tumours (Erlandson 1981; Ghadially 1985). Except for Warthin's tumour (Tandler 1966), we are unaware of their occurrence in cells of oncocytomas.

Adrenocortical oncocytoma appears to be non-functional even when of large size. Like other oncocytomas, our tumour was characterized by regression of specialized organelles. Only the presence of few mitochondria with tubulovesicular cristae and sparse lipid droplets were reminiscent of an adrenocortical derivation. However, the case reported by Erlandson and Reuter in 1991 with associated elevated urinary 17-ketosteroids was characterized by mitochondria with predominantly tubulovesicular cristae and a well-developed smooth endoplasmic reticulum. Except for scattered cells weakly immunoreactive for the enzyme P-450 scc, Sasano et al. in 1991 did not observe steroidogenic enzymatic activity in their three cases of adrenocortical oncocytoma.

Some reported cases of adrenocortical oncocytoma (Erlandson and Reuter 1991; Sasano et al. 1991), as well as the present tumour, had morphological features suggesting malignant potential. These include a weight over 100 g, haemorrhage, diffuse growth pattern, broad fibrous septa, absence of clear cell areas or marked nuclear atypia (Hough et al. 1979; Lack et al. 1990; Page et al. 1986; Weiss 1984). However, none of these cases had more than three additive criteria indicative of malignant potential in the scheme defined by Weiss in 1984. However, the case of adrenocortical oncocytic carcinoma reported by El-Naggar et al. in 1991 had more than three additive criteria in the Weiss scheme (Weiss 1984). Except for the latter case which presented with invasion of the liver and inferior vena cava (El-Naggar et al. 1991), adrenocortical oncocytic neoplasms have not been associated with malignant behaviour within a follow-up interval of 8–27 months (Erlandson and Reuter 1991; Sasano et al. 1991). Therefore it is reasonable to suggest that these tumours are benign, as adrenocortical carcinoma has been associated with metastasis at presentation in 24–52% of cases, and with local invasion in 41% of cases ab initio (Didolkar et al. 1981; King and Lack 1979).

Some benign (Fisher and Danowski 1973; Gorgas et al. 1976; Mitschke et al. 1978) or malignant (Valente et al. 1978) virilizing adrenocortical tumours were characterized ultrastructurally by a few cells packed with mitochondria and resembling oncocytes. These tumours had a significant proportion of cells without regression of specialized organelles, and which contained a prominent smooth endoplasmic reticulum, lysosomes and lipofucsin granules (resembling zona reticularis cells; Fisher and Danowski 1973; Gorgas et al. 1976; Mitschke et al. 1978; Valente et al. 1978). Some had cells with intramitochondrial 20–50 nm granules seen within oncocytic cells (Gorgas et al. 1976; Mitschke et al. 1978). It is generally recognized that cells of oncocytomas lack such mitochondrial dense granules (Erlandson 1981; Ghadially 1985). In our opinion, these changes are best viewed as focal oncocytic transformation, and such tumours do not deserve the designation of oncocytoma if stringent criteria are used. Whereas occasional cells with large numbers of mitochondria and even true oncocytes are seen in some cases of adrenocortical carcinoma (Erlandson and Reuter 1991; Valente et al. 1978), considerable quantitative and qualitative mitochondrial changes are usually seen (Silva et al. 1982).

Adrenocortical oncocytoma is a rare tumour which can be confidently diagnosed with stringent criteria, ideally including ultrastructural analysis. The pathologist should be aware of its existence, as computed tomography and magnetic resonance imaging are likely to disclose increasing numbers of non-functional adrenocortical tumours. Although the current information is limited, adrenocortical oncocytic neoplasms appear to be non-functional and probably benign.

Acknowledgements. The author thanks Mrs. L. Rhéaume for secretarial assistance and Mrs. M. Wittowa for photographic assistance.

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