Virchows Arch. A Path. Anal. and Histol. 377, 91–96 (1977)

Virchows Archiv A

Case Report

Carcinoid Tumour of the Thymus

A Case Report Including Discussion of the Morphological Diagnosis and the Cell of Origin

Sandra Chalk[1] and Kenneth J. Donald[2]

[1] Department of Pathology, The Prince Charles Hospital, Chermside, Queensland 4032, Australia
[2] Department of Pathology, University of Queensland Medical School, Herston, Queensland 4006, Australia

Summary. This report concerns a 49 year old asymptomatic male who had a mediastinal mass demonstrated on routine radiography. A large encapsulated tumour composed of small regular cells arranged in clumps and acini with fine vascular stroma was removed. The differential diagnosis on routine H&E section included parathyroid tumor, medullary carcinoma arising in ectopic thyroid tissue, epithelial thymoma or carcinoid tumor of the thymus. The presence of compressed thymic tissue around the tumor, and of argentaffin granules together with the electron microscopic appearance characteristic of the "enterochromaffin" or "APUD" group of cells allowed the diagnosis of carcinoid tumor of the thymus to be made. Electron microscopy showed that the cell cytoplasm contained electron dense membrane bound granules, together with bundles of microfilaments. Vesicles of smooth surfaced reticulum were present but rough surfaced reticulum was inconspicuous. No desmosomes were demonstrated. Special stains for amyloid and glycogen were negative.

Key words: Carcinoid thymus.

Introduction

Primary carcinoid tumor of the thymus is rare and the present case is the eighteenth reported. Rosai and Higa (1972) illustrated eight cases at the light microscope level and reviewed eight others from the literature. Hughes et al. (1975) described a further case at light microscopic level. Because of the rarity of the tumor it is not usually considered in the pre-operative diagnosis and can provide difficulties on frozen section when one considers the histologically

For offprints contact: Dr. S.M. Chalk, Department of Pathology, The Prince Charles Hospital, Rode Road, Brisbane 4032, Australia

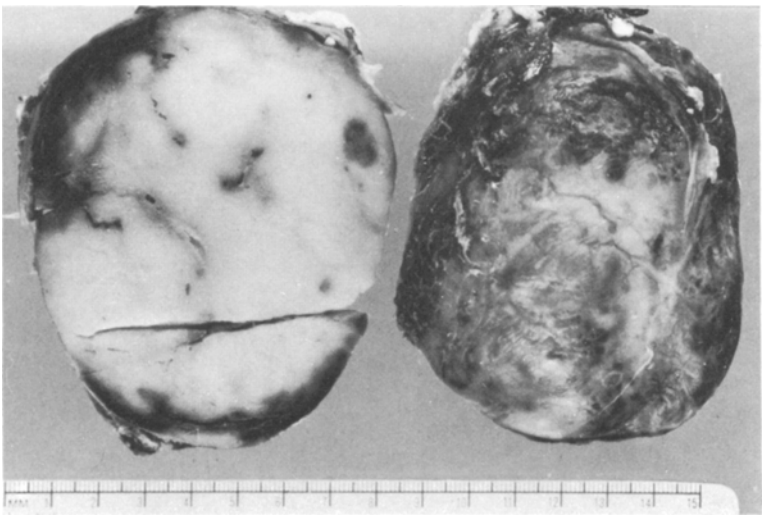

Fig. 1. Macroscopic appearance of tumour

similar tumors which may occur in this area. Both situations arose in our case. A detailed ultrastructural study is lacking in the literature although Rosai and Higa briefly mentioned ultrastructure without illustrations.

Clinical Detail

The patient was a forty-nine year old asymptomatic male with a large anterior mediastinal mass which was detected on mass radiography. He had been treated for two years for hypertension, and chest X-ray taken two years previously had been normal. Blood urea and serum creatinine were at the upper limits of normal. There was no evidence of carcinoid syndrome.

A left thoracotomy was performed and an encapsulated tumor was found in the anterior and middle mediastinum infero-lateral to the aortic arch. The vascular pedicle appeared to be coming from the neck. The tumor was removed in toto along with two mediastinal lymph nodes. Eighteen months after surgery he was well and asymptomatic. He was still under treatment for hypertension.

Pathology

Macroscopic examination showed a smooth surfaced encapsulated tumor $12 \times 10 \times 7$ cm with a fleshy texture, creamy-white in colour with areas of recent and old haemorrhage (Fig. 1).

On light microscopy (Fig. 2), the tumor was composed of small regular cells with poorly defined borders. The cytoplasm was lightly eosinophilic to clear, with a few cells showing either granularity or vacuolation. Most of the nuclei were round to oval, vesicular and contained a single small nucleolus. Other nuclei were round and densely chromatic. A few mitotic figures were present. Delicate vascular branching connective tissue septa divided the tumor into small pseudolobules. Within the lobules the cells had a predominantly

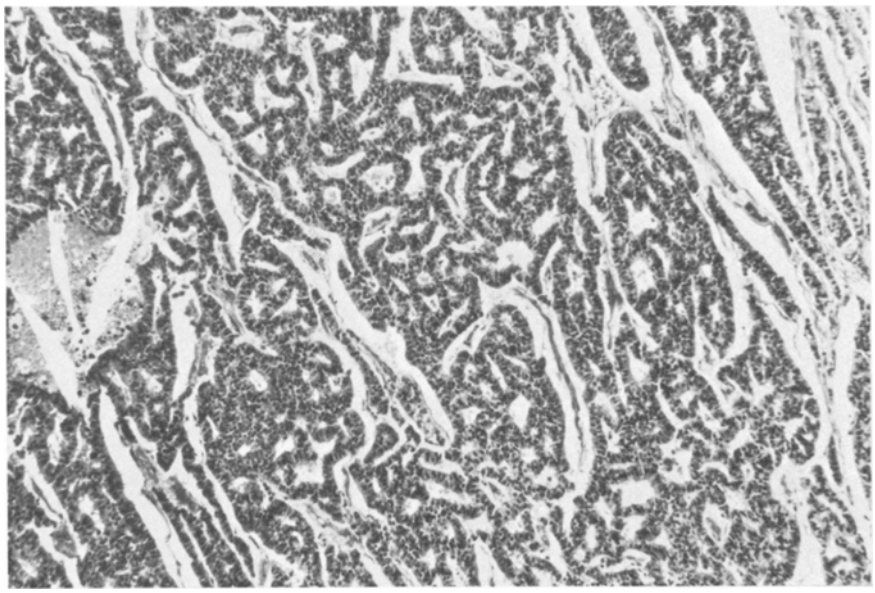

Fig. 2. Histological appearance of the tumour demonstrating uniformity of the cells and their arrangement in tubules, festoons and acini with minimal intervening stroma. (H&E × 90)

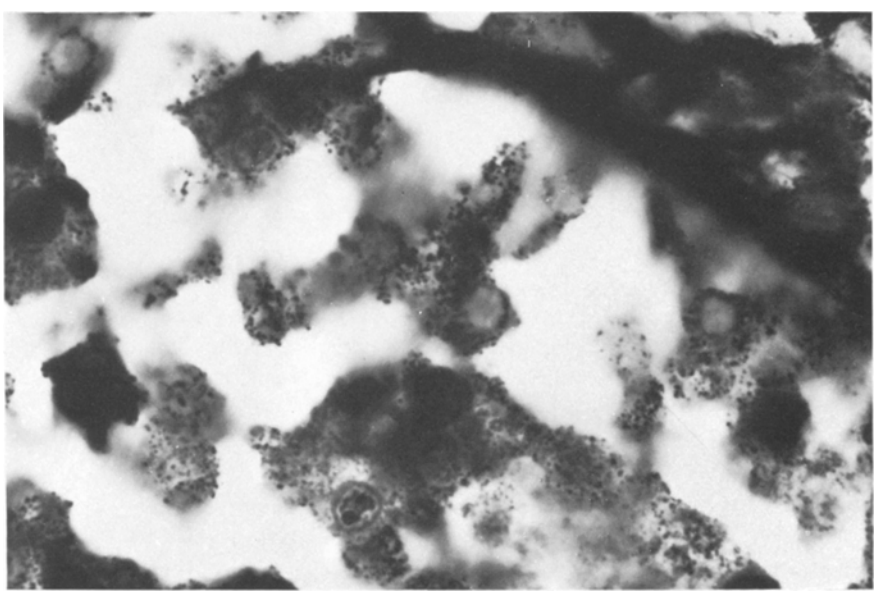

Fig. 3. Silver staining to demonstrate the presence of argentaffin granules. (Sevier-Munger × 1500)

acinar arrangement. Tubular and festooned patterns and solid clumps were also present. Small areas of necrosis with calcification were present within some solid areas. Some acini contained eosinophilic granular material, others appeared empty.

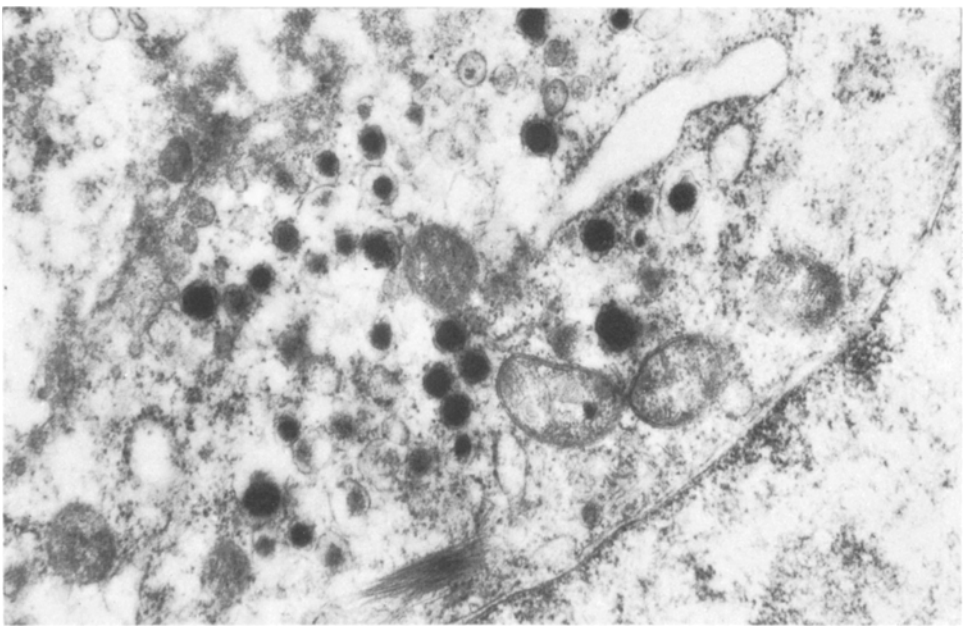

Fig. 4. Ultrastructural appearance showing membrane bound electron-dense granules together with bundles of microfilaments. Abundant free ribosomes are also evident. (×29, 700). Stained with Uranyl Acetate and Lead Citrate

Thymic tissue was present within the capsule and vascular and capsular invasion were noted. Most of the cells showed argyrophilic granules when stained by the Sevier-Munger and Grocott techniques. Some of the cells were also argentaffin positive when stained by the Masson-Fontana and Gomeri-Burtner methods (Fig. 3). Stains for amyloid and glycogen were negative.

At the ultrastructural level (Fig. 4), the cytoplasm contained numerous randomly distributed spherical electron dense granules. These were bound by a single layered membrane and showed some variation in both size and density. They had an average diameter of 180 nm. Smooth surfaced endoplasmic reticulum was present. Rough surfaced reticulum was rare although free intracytoplasmic ribosomes were plentiful. Bundles of microfilaments coursed through the cytoplasm. No desmosomes or other junctional modifications were noted.

Discussion

On haemotoxylin and eosin sections the differential diagnosis included parathyroid tumor, medullary carcinoma of the thyroid, thymoma and carcinoid tumor.

Parathyroid tumor was considered unlikely because no surrounding parathyroid tissue could be found and the cells gave a negative reaction for glycogen (Black, 1969). The serum calcium was normal in the immediate post-operative period. No pre-operative calcium studies had been performed. At the ultrastruc-

tural level the lack of prominence of rough surfaced endoplasmic reticulum, the absence of desmosomes and annulate lamellae and the presence of bundles of microfilaments was against a parathyroid origin. Parathyroid adenomas do contain neuro-secretory granules similar to carcinoids and other APUDomas (Elliott and Arhelger, 1966).

Medullary carcinoma of the thyroid was eliminated because of the lack of relationship of the tumor to any thyroid tissue, the absence of amyloid from the stroma and the presence of intracytoplasmic microfilaments at the ultrastructural level (5). It should be noted that Horvath et al. (1972) reported a tumor arising in the thyroid which did have bundles of microfilaments of the type seen in the present tumor and they diagnosed a medullary carcinoma, although no amyloid was present in the stroma. In a report by Meyer (1968) on two amyloid producing medullary carcinomas of the thyroid no such microfilaments were described.

Because of the obvious origin of the tumor within the thymus gland, thymoma had to be given serious consideration. While at the light microscope level the present tumor resembled an epithelial thymoma, the presence of neurosecretory granules and the absence of desmosomes at the ultrastructural level made this an unlikely diagnosis (Levine and Bensch, 1972; Kameya and Watanabe, 1965).

A final diagnosis of carcinoid tumor was made. By light microscopy the tumor resembled a carcinoid in its architectural pattern, cellular morphology and granule staining. Ultrastructurally the cells had the appearance characteristic of carcinoids and APUDomas in general with neurosecretory granules, prominent vesicular smooth surfaced endoplasmic reticulum, inconspicuous rough surfaced reticulum and high content of free ribosomes (Pearse, 1974).

Forssmann et al. (1969) described various types of "enterochromaffin" or "argentaffin" cells occurring throughout the gastro-intestinal tract of rats. These cells all had the same basic ultrastructural features described for the cells of the APUD system. They varied from one another only in the size and shape of the neurosecretory granules and their content of microfilaments. The cells were divided into five groups on the basis of these differences and it was found that at any particular level of the gastro-intestinal tract the cells of one or other group were the predominant "enterochromaffin" component. Black (1968) published an ultrastructural study in which the appearances of the enterochromaffin cells at various levels of the gastro-intestinal tract were compared with the appearances of the cells of carcinoid tumors arising in these locations. He concluded that "the typical carcinoid found in a given tissue reflects the structure and histochemical features of the enterochromaffin cells commonly resident in that tissue".

Rosai and Higa (1972) studied thymus glands from both chickens and human subjects at the light microscope level. Argentaffin positive cells were plentiful in the chicken thymuses but no argentaffin positive cells were found in the twenty human thymuses studied. However, in four of the normal human thymuses argyrophilic cells were demonstrated. This is consistent with the finding that the enterochromaffin cells of other foregut derivatives namely stomach and bronchus contain granules which are argentaffin negative but argyrophil

positive (Black, 1968). A occasional carcinoid from the bronchus is argentaffin positive (Bensch et al., 1965).

Bensch et al., writing on bronchial carcinoid, describe small round neurosecretory granules similar to those in the present thymic carcinoid. Similar granules are also seen in gastric carcinoids (Black, 1968).

References

Bensch, K.G., Gordon, G.B., Miller, L.R.: Electron microscopic and biochemical studies on the bronchial carcinoid tumor. Cancer **18**, 592 (1965)

Black III, W.C.: Enterochromaffin cell types and corresponding carcinoid tumors. Laboratory Investigation **19**(5), 473–486 (1968)

Black III, W.C.: Correlative light and electron microscopy in primary hyperparathyroidism. Arch. Path. **88**, 225–241 (1969)

Elliott, R.L., Arhelger, R.B.: Fine structure of parathyroid adenomas with special reference to annulate lamellae and septate desmosomes. Arch. Path. **81**, 200–212 (1966)

Forssmann, W.G., Orci, L., Pictet, R., Renold, A.G., Rouiller, C.: The endocrine cells in the epithelium of the gastrointestinal mucosa of the rat. An electron microscope study. J. Cell Biol., **40**, 692–712 (1969)

Horvath, E., Kovacs, K., Ross, R.C.: Medullary cancer of the thyroid gland and its possible relations to carcinoids. An ultrastructural study. Virchows Arch. Abt. A. Path. Anat. **356**, 281–292 (1972)

Hughes, J.P., Ancalmo, N., Leonard, G.L., Ochsner, J.L.: Carcinoid tumor of the thymus glands: report of a case. Thorax **30**, 470–475 (1975)

Kameya, T., Watanabe, Y.: Electron microscopic observations on human thymus and thymoma. Acta Path. Jap. **15**(2), 223–246 (1965)

Levine, G.D., Bensch, K.G.: Epithelial nature of spindle cell thymoma. An ultrastructural study. Cancer **30**, 500–511 (1972)

Meyer, J.S.: Fine structure of two anyloid-forming medullary carcinomas of thyroid. Cancer **21**, 406–425 (1968)

Pathology Annual (1974): Review of medullary carcinomas of thyroid.

Pearse, A.G.E.: The APUD cell concept and its implications in pathology. Pathology Annual. p. 27. New York: Appleton-Century-Crofts, Division of Prentice-Hall Inc. 1974

Rosai, J., Higa, E.: Mediastinal endocrine neoplasm, of probable thymic origin, related to carcinoid tumor. Clinicopathological study of 8 cases. Cancer **29**, 1061–1073 (1972)

Received September 3, 1977