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Case Report

Polypoid Nonchromaffin Paraganglioma of the Duodenum

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Summary. A polypoid tumor was surgically removed from the second part of the duodenum of a 56-year-old male. The main body consisted of large epithelioid cells arranged in an adenoma like pattern of strands and nests. These cells were argyrophil and had marked nonspecific esterase activity. Unmyelinated nerves with proliferated Schwann cells accompanied these epithelioid cells together with scattered gangliocyte like elements. Ultramicroscopically, the epithelioid cells were seen to contain round electron dense granules, 150 nm in diameter on average. The tumor is considered to be a nonchromaffin paraganglioma, as it probably developed from paraganglion cells associated with small arteries or branches of the vagus nerve, or from the undifferentiated pluripotent APUD cells of the duodenum.

Key words: Nonchromaffin paraganglioma – Duodenal polyp – APUD cell tumor.

Introduction

Dahl et al. (1957) were the first to describe a duodenal ganglioneuroma, drawing attention to strange adenomatous structures at the periphery of the tumor. Among 167 duodenal tumors, Taylor and Helwig (1962) found 9 polyp like structures which they classified as nonchromaffin paragangliomas. Lukash et al. (1966), Weitzner (1970), Kepes and Zacharias (1971), Lauzon and Cadotte (1972), Qizilbash (1973) and Friesen et al. (1974) all reported on similar cases.

The histogenesis of these rare duodenal growths, their relationship to local tissue and their functional effects are as yet undefined, which justifies a report on one single case.

Clinical History

The 56-year-old patient was admitted to the Städt. Krankenhaus München-Schwabing[1] because of severe gastrointestinal bleeding following treatment with angicoagulants. He had suffered, for many years, from hypertension and arteriosclerosis.

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Endoscopically, a polypoid tumor was found, situated in the pars descendens duodeni. At surgery the polyp was seen to have a long wide stalk which was firmly embedded in the duodenal wall above the papilla of Vater. Six month later, the duodenum was found to be free of tumor.

Materials and Methods

The tumor was fixed in 4% formalin, was examined by light- and electronmicroscopes and was investigated histochemically. Frozen and paraffin sections were treated with the following stains: haemalum-eosin, haematoxylin-van Gieson elastica, Goldner's trichrome, azan, periodic acid Schiff, Best's carmine, mucicarmine, Maldonado's phloxine-B in Loeweneck et al.'s modification, Solcia and Capella's lead haematoxylin, Nissl's cresylviolet, Sudan III and Sudan black. The silver impregnations used were those of Gomori, Bielschowsky-Gros, Bodian and Masson-Hamperl. The tissue was also tested for chromaffinity; nonspecific esterase activity was measured by the α-naphtyl acetate method with fast-blue.

Formol-fixed tissue pieces, refixed in osmium tetroxide solution and embedded in Epon 812 were employed for electronmicroscopy (Zeiss EM 10).[2]

Results

Macroscopically, the 3.1:2.6:1.5 cm sized, formalin-fixed tumor is egg-shaped, and is covered by an intact mucous membrane. It is greyish-white on section and slightly lobular.

Microscopically, the tumor tissue spreads mainly in the submucosa, splitting up the neighbouring layers of the muscularis. It is also seen in the lamina propria of the mucosa (Fig. 1 b), and in part in the connective tissue of the villi. It consists of different-sized cell masses, separated by delicate vessel-containing connective tissue septa. There is no connective tissue capsule. The main body of the tumor is made up of large cytoplasm-enriched epithelioid cells, arranged in adenoma like formations, in cell balls and strands (Fig. 1 a and b). In the loose connective tissue of the lamina propria, where the growth exists in small masses, it is composed of nests with scanty, mainly polygonal cells which are seen to be surrounded by argyrophil fibres in Gomori's silver impregnation. However, in the submucosa, where the tissue forms large dense roughly spherical areas, the strand structure predominates with bands of cylindrical, prismatic to spindle-sphaped cells, lying close together, separated by thin connective tissue septa (Fig. 1 a). The cytoplasm is palely eosinophilic, slightly granular, a pale greenish-grey in Goldner's trichrome stain; the phloxin-B stain shows up areas of lighter and darker cells. The nuclei are mainly oval and uniform in size, having a medium chromatin density, well defined nucleoli, mitotic figures are not seen. The cell units often cling, sometimes closely, to sinuous dilated capillaries. Individual groups of degenerate, calcified cells are to be found in clusters, sometimes with single cells containing calcium granules in their cytoplasm, in their vicinity. The cytoplasm is PAS negative, does not stain with mucicarmine, Best's carmine, Sudan III or Sudan black. The cells

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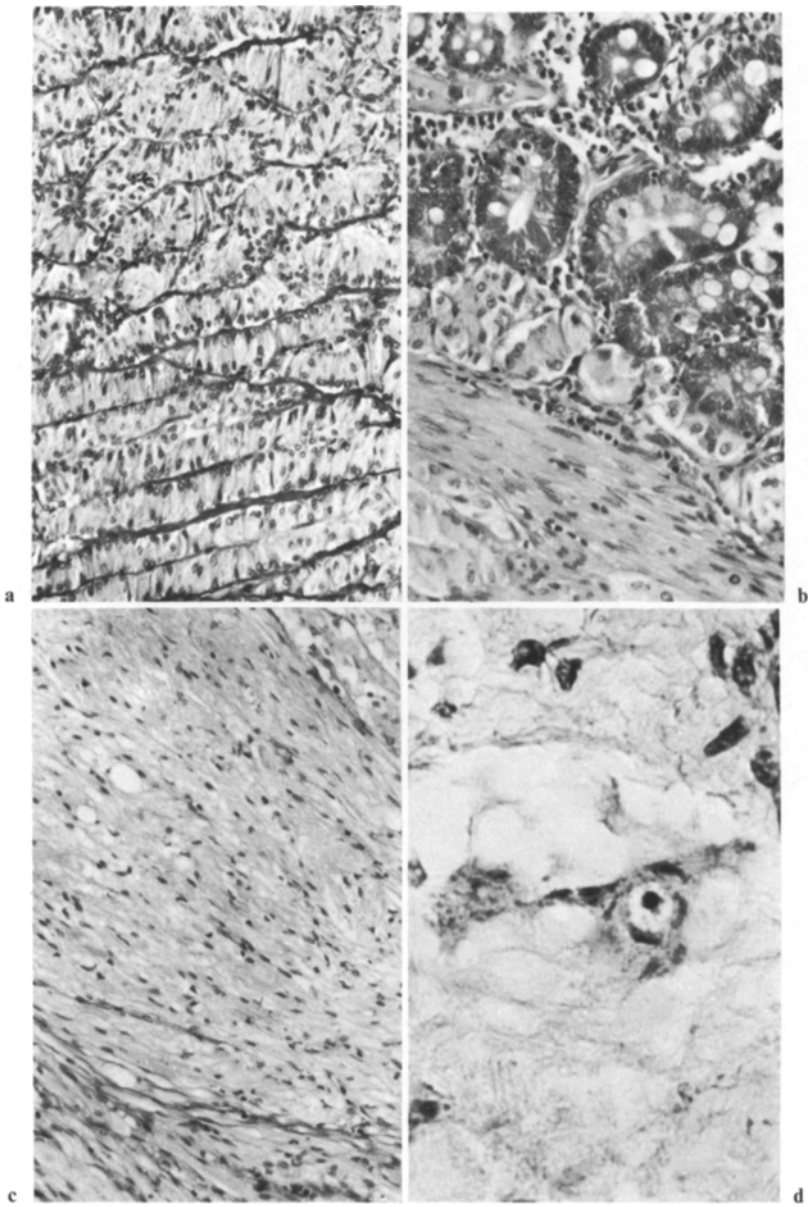

Fig. 1a–d. The various tissue components in the tumor: epithelial like, arranged in cords (**a**), small epithelioid tumor cell clusters in the L. propria of the T. mucosa (**b**), spindle-shaped cells (**c**), and gangliocyte like cell with Nissl granules (**d**). El. v. Gieson. ×120 (**a**), HE. ×150 (**b**), El. v. Gieson. ×120 (**c**), Nissl's stain. ×700 (**d**)

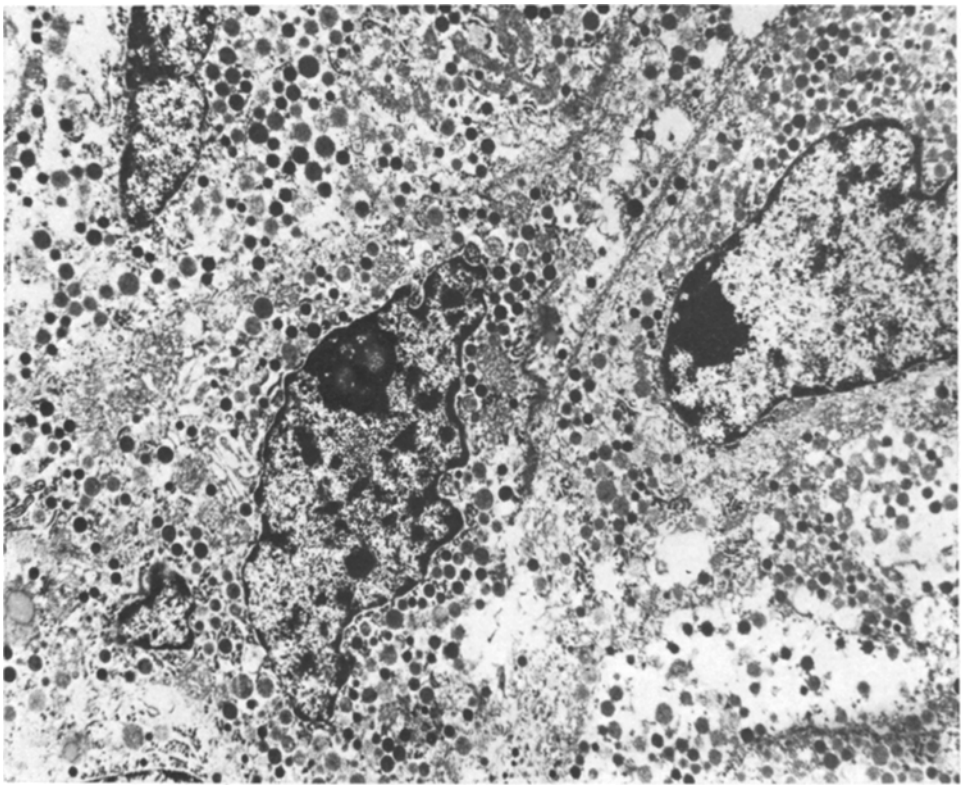

Fig. 2. Typical submicroscopical dense-cored granules in the cytoplasm of tumor cells. ×12,100

are neither chromaffin nor argentaffin, but are argyrophil. One cell pole is often drawn out, with a vague, delicate silverblackened projection. There is distinct histochemical activity by nonspecific esterase in the tumor cells, in fine granular form. Long spindle cells in slightly wavey arrangements, with intermediate delicate collagen fibres are found in other parts of the tumor. These few in number, and presumably represent Schwann cells and unmyelinated nerves (Fig. 1c). There are smooth transitions into epithelial areas, when both components combine closely. The spindle-shaped cell complexes are mainly at the tumor periphery.

In addition, the tumor tissue contains formations of gangliocyte type cells, which occur sometimes singly, sometimes in groups, and are situated mainly within the spindle cell component. These cells are rich in cytoplasm, spherical in form, and have large, clearly-outlined vesicular nuclei (Fig. 1d). They also have a definite nuclear membrane and unusually large nucleoli. Their cytoplasm contains single nissl-type granules, and often two or more nuclei, as demonstrated by Nissl's cresylviolet stain. Histochemically, these cells have a high activity of nonspecific esterase, with almost complete blackening of their cytoplasm.

Ultramicroscopically, the tumor cells adhere closely to the capillaries. They contain electron dense granules in their cytoplasm, which are bound by a single membrane, and vary between 100 and 300 nm in size (Fig. 2). The cytoplasm also contains a Golgi apparatus, cristatype mitochondria, granular endoplasmatic reticulum, and free ribosomes. However, they have no microtubuli or plasma filaments.

Discussion

The tissue structure, staining reactions and histochemical behaviour of the epithelial-like main component of this tumor resemble the nonchromaffin paragangliomas. However, the tumor tissue differs in that it is combined with unmyelinated nerves and gangliocyte like elements. Thus the tumor is a variation on nonchromaffin paraganglioma, like those described by Taylor and Helwig (1962). The structure of epithelioid and spindle shaped cells with gangliocytes is obviously typical for nonchromaffin paragangliomas of the duodenum, and for this reason they were called "gangliocytic paragangliomas" by Kepes and Zacharias (1971). In mixed-cell paragangliomas, the amounts of the different cell types can vary enormously, so that transitions from almost purely epithelial to ganglioneuroma forms occur. The intense vascularity of the tumor tissue, the argyrophilia of its cells and the lack of argenta- and chromaffinity, are also typical for these tumors. The argyrophilia, demonstrated by Feyrter (1951) and Hamperl (1952) in the cells of paraganglia and paragangliomas, also suggests that the tumor belongs to the nonchromaffin paragangliomas. Nonspecific esterase activity in duodenal paragangliomas has not as yet been described, but this is a further characteristic of this type of tumor, for Glenner and Grimley (1974) have reported typically high activity of this enzyme in paragangliomas of the carotid bodies. According to Carvalheira et al. (1969) the enzyme is also a regular constituent of all argyrophilic cells in the APUD cell system.

The hyperplastic unmyelinated nerves, with proliferation of Schwann cells and gangliocyte like formations are atypical for nonchromaffin paragangliomas. Ábrahám (1969) and Pryse-Davies et al. (1964) found nerve fibres in normal carotid bodies and in their tumors, these were also accompanied by gangliocytes. Most of the gangliocytic elements in our case cannot be definitely identified as true neurones, only a few cells seem to possess axons. The compressed spindle-shaped epithelioid cells in the band like areas often have small argyrophil tail-like elongations, which Kepes and Zacharias (1971) have also observed in two paragangliomas. The electron dense secretory granules seen here are identical with those presented by Kepes and Zacharias (1971).

Nonchromaffin paragangliomas of the digestive tract have been found in the duodenum and in the stomach, at the latter site by Pack (1964) and Delamarre et al. (1975). The majoritiy occurs in the second part of the duodenum; Lukash et al. (1966) and Lauzon and Cadotte (1971) found cases in the fourth part. Paraganglia, or cells of paraganglion type have not been found in the stomach or duodenal wall as normal structures. It might be assumed that cells of the widespread paraganglia found in fetal life build the matrix of upper

gastrointestinal tumors of this type, since according to Elliott (1965), "glomus like bodies" occur distal to the root of the superior mesenteric and coeliac arteries, and Goormaghtigh (1936) in mice, and Chen and Yates (1970) in syrian hamsters have found knotshaped collections of paraganglion cells in the perineurium of small abdominal branches of the vagus nerve.

The *main cell* component of the paraganglia belong to the APUD series of Pearse et al. (1973). Their tumors are thus APUD cell adenomas or -carcinomas, emphasising their similarity to other argyrophil-cell growths of the duodenum, such as those described by Weichert et al. (1971a and 1971b) as "carcinoid-islet cell tumors". If one assumes, like Weichert (1970), that the APUD cells of the foregut are hardly differentiated, and have a large potential for growth and developement then these cells acquire great significance in the histogenesis of duodenal paraganglioma. Multipotent neuroectodermal cells differentiate diversly and demonstrate all possible functions of APUD cells in their tumors, the component cells of which may evolve from them into typical paraganglion or gangliocyte like cells. In this way it is possible to explain the strange tissue structure of the duodenal paraganglioma as a "hybrid" between the typical paragangliomas and ganglioneuromas.

References

Ábrahám, A.: Elektronenmikroskopische Untersuchungen an menschlichen Karotiskörpern. Z. mikro-anat. Forsch. **81**, 413–453 (1969)

Carvalheira, A.F., Welsch, U., Pearse, A.G.E.: Cytochemical and ultrastructural observations on the argentaffin and argyrophil cells of the gastro-intestinal tract in mammals, and their place in the APUD series of polypeptid-secreting cells. Histochemie **14**, 33–46 (1968)

Chen, J., Yates, R.D.: Ultrastructural studies of vagal paraganglia in Syrian hamsters. Z. Zellforsch. **108**, 309–323 (1970)

Dahl, E.V., Waugh, J.M., Dahling, D.C.: Gastrointestinal ganglioneuromas. Brief review with report of a duodenal ganglioneuroma. Amer. J. Path. **33**, 953–965 (1957)

Delamarre, J., Poket, F., Capron, J.-P., Hoang Ngoo Minh, Lorriaux, A.: Chémodectome gastrique. Etude d'un cas et revue de la littérature. Arch. Fr. Mal. App. Dig. **64**, 339–346 (1975)

Elliott, G.B.: Glomus-like bodies on the superior mesenteric artery. Canad. Med. Ass. J. **19**, 1303–1305 (1965)

Feyrter, F.: Zur Normung der Silberimprägnation neuraler und nicht neuraler Gewebe. Virchows Arch. **320**, 551–563 (1951)

Friesen, S.R., Hermreck, A.S., Mantz, F.A.: Glucagon, gastrin and carcinoid tumors of the duodenum, pancreas and stomach: polypeptide "apudomas" of the foregut. Amer. J. Surg. **127**, 90–101 (1974)

Glenner, G.G., Grimley, P.M.: Tumors of the extra-adrenal paraganglion system. Published by Armed Forces Instituts of Pathology, Washington (1974)

Goormaghtigh, N.: On the existence of abdominal vagal paraganglia in the adult mouse. J. Anat. **71**, 77–90 (1936)

Hamperl, H.: Über argyrophile Zellen. Virchows Arch. **321**, 482–507 (1952)

Kepes, J.J., Zacharias, D.L.: Gangliocytic paragangliomas of the duodenum. A report of two cases with light and electron microscopic examination. Cancer **27**, 61–70 (1971)

Lauzon, A., Cadotte, M.: Paragangliome gangliocytaire du duodenum. Union Med. Can. **101**, 1584–1586 (1972)

Loeweneck, H., Brückner, W.L., Maass, U., Appel, G., Schmidt, G.P.: Die Funktion des Pankreas nach trunkulärer Vagotomie. Eine tierexperimentelle Studie am Schwein und an der Ratte. Z. Gastroenterol. **13**, 457–463 (1975)

Lukash, W.M., Hyams, V.J., Nielson, O.F.: Neurogenic neoplasmas of the small bowel: benign nonchromaffin paraganglioma of the duodenum. Amer. J. dig. dis. **11**, 575–579 (1966)
Pack, G.T.: Unusual tumors of the stomach. Ann. N.Y. Acad. Sci. **114**, 985–1011 (1964)
Pearse, A.G.E., Polak, J.M., Rost, F.W.D., Fontaine, J., Le Lièvre, C., Le Donarin, N.: Demonstration of the neural crest origin of Type I (APUD) cells in the avian carotid body, using a cytochemical marker system. Histochemie **34**, 191–203 (1973)
Pryse-Davies, J., Dawson, I.M.P., Westbury, G.: Some morphologic, histochemical, and chemical observations on chemodectomas and the normal carotid body, including a study of the chromaffin reaction and possible ganglion cell elements. Cancer **17**, 185–202 (1964)
Qizilbash, A.H.: Benign paraganglioma of the duodenum. Case report with light and electron microscopic examination and brief review of literature. Arch. Path. **96**, 276–280 (1973)
Solcia, E., Capella, C., Vassallo, G.: Lead-haematoxylin as a stain for endocrine cells. Significance of staining and comparison with other selective methods. Histochemie **20**, 116–126 (1969)
Taylor, H.B., Helwig, E.B.: Benign nonchromaffin paragangliomas of the duodenum. Virchows Arch. **335**, 356–366 (1962)
Weichert, R.F.: The neural ectodermal origin of the peptide-secreting endocrinic glands. Amer. J. Med. **49**, 232–241 (1970)
Weichert, R.F., Roth, L.M., Harkin, J.C.: Carcinoid-islet cell tumor of the duodenum and associated multiple carcinoid tumors of the ileum. Cancer **27**, 910–918 (1971)
Weitzner, S.: Benign nonchromaffin paraganglioma of the duodenum, report of a case and review of the literature. Amer. J. Gastroenterol. **53**, 365–369 (1970)

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