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Nonchromaffin Paraganglioma of the Duodenum

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Summary. A benign nonchromaffin paraganglioma of the duodenum is described and compared with other reported cases. Duodenal location is extremely rare but the morphology, based on the optical microscopic pattern (Zellballen) and the ultrastructural appearance is, comparable with paragangliomas of other sites. The lack of nerve fibres and ganglion cells in this tumour, together with the absence of a positive chromaffin reaction permits us to classify it as a pure nonchromaffin paraganglioma. This finding constitutes indirect evidence of the probable existence of a paraganglion in the duodenal wall, a structure not yet demonstrated in the adult.

Key words: Pure duodenal nonchromaffin paraganglioma – Benign nonchromaffin paraganglioma – Gangliocytic paraganglioma – Duodenal ganglioneuroma – Duodenal wall neoplasms.

Introduction

The extra-adrenal nonchromaffin paragangliomas originate, in more than 98% of cases, in a number of structures with a chemoreceptive function ("chemodectomas") (Helpap, 1978) and very rarely develop in other sites (Dahl, Waugh and Dahlin, 1957). Nonchromaffin paragangliomas can arise along the vagus nerve but occur most frequently in its cervical portion (Fernandez, Hernandez and Staley, 1975; Moncure and Goodman, 1975; Someren and Karcioglu, 1977). Taylor and Helwig (1962) described a group of rare polypoid tumours in the duodenum as "benign nonchromaffin paragangliomas", for which, when they include ganglion cells, the terms "duodenal ganglioneuroma" (Dahl, Waugh and Dahlin, 1957; Gemer and Feuchtwanger, 1966; Goldman, 1968) or "gangliocytic paraganglioma" (Kepes and Zacharias, 1971; Lauzon and Cadotte, 1972; Reed and Daroca, Daroca, Jr. and Harkin, 1977) have been used.

A total of 23 cases of these duodenal tumours have been reported (Table 1) of which eleven were considered to be paragangliomas and twelve to be ganglio-

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Table 1. Paragangliomas of the duodenum

	Author	Nr. Cases	Age, Sex	Terminology	Ganglion-like cells and nerve fibrils	Argyrophil granules	E.M.	Follow-up
1	Dahl et al.	1	49, F	Duodenal ganglioneuroma	Present	–	No	Four months
2	Taylor and Helwig	9	32–72, 7M, 2F	Benign nonchromaffin paragangliomas of the duodenum	Present	Positive	No	Three years
3	Gemer and Feuchtwanger	1	64, F	Ganglioneuroma of the duodenum	Present	Negative	No	–
4	Lukash et al.	1	46, M	Benign nonchromaffin paraganglioma of the duodenum	Present	Negative	No	–
5	Goldman	1	51, M	Ganglioneuroma of the duodenum	Present	Negative	No	–
6	Kepes and Zacharias	2	68, M 61, M	Gangliocytic paraganglioma of the duodenum	Present	Not mentioned[a]	Yes	Three and two years
7	Lauzon and Cadotte	1	49, F	Paragangliome gangliocytaire du duodenum	Present	Negative	No	–
8	Qizilbash	1	39, M	Benign paraganglioma of the duodenum	Present	Negative	Yes	–
9	Reed et al.	6	26–61, 4M, 2F	Gangliocytic paraganglioma	Present	Positive	Yes	Three and half years (except for the 2nd and 5th cases)
10	Present case	1	56, M	Nonchromaffin paraganglioma of the duodenum	Absent	Positive	Yes	Two years

[a] Dense-core granules in the ultrastructural study

cytic paraganglioma. In all instances ganglion-like cells were present. This report presents an ultrastructural study of a pure non gangliocytic nonchromaffin paraganglioma of the duodenum.

Case Report

A 56-year old man, with a previous history of gastric ulcer, underwent a subtotal gastrectomy 15 years ago. In 1978 he was admitted with symptoms of polyarthritis which was treated with gold salts and phenylbutazone. This was presumed to be the cause of a mild nephrotic syndrome which was treated with corticosteroids and remitted after two months. Gastric discomfort was more marked after steroid treatment.

Radiologic examination of the upper gastrointestinal tract revealed an oval filling defect in the first part of duodenum. Endoscopically, a sessile polypoid mass of approximately 5 mm in diametre was discovered, with intact mucosa overlying the tumour. The mass was removed endoscopically.

Serial histologic sections revealed that the tumour was originated in the submucosa and did not involve other layers. The nests of epithelioid cells (Zellballen) (Fig. 1), were separated by slender richly vascularized connective tissue tract (Fig. 2); a reticulin impregnation demonstrated different shapes and sizes of cellular nests (Fig. 3). The proliferating cells were usually polygonal, with ill defined outlines and slightly granular cytoplasm and oval or spindle-shaped hyperchromatic

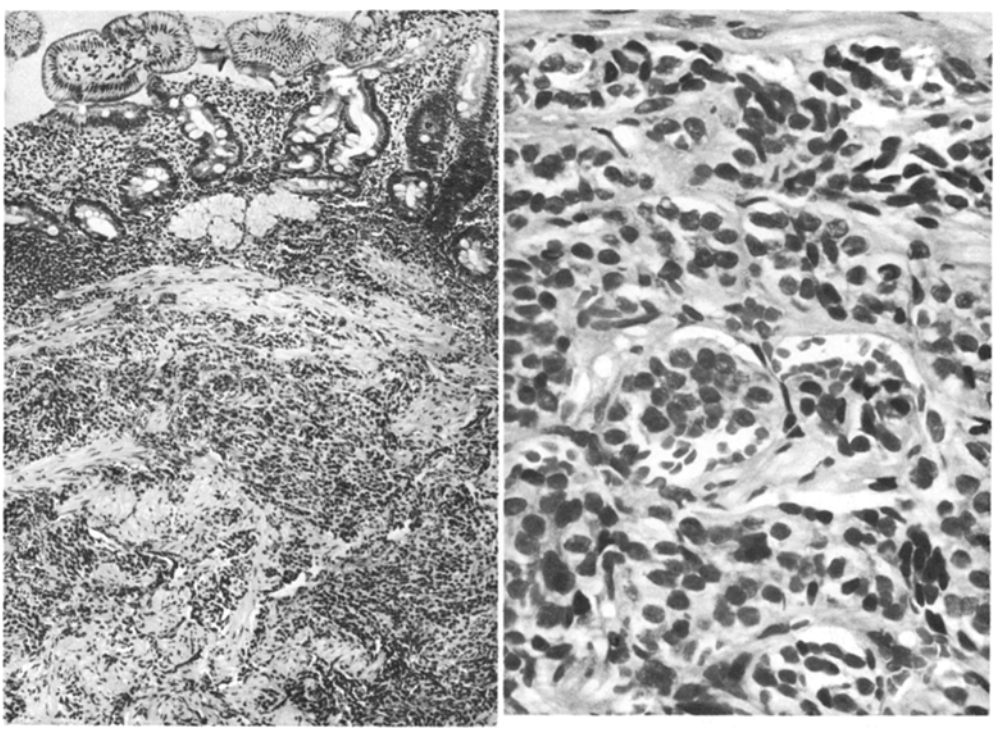
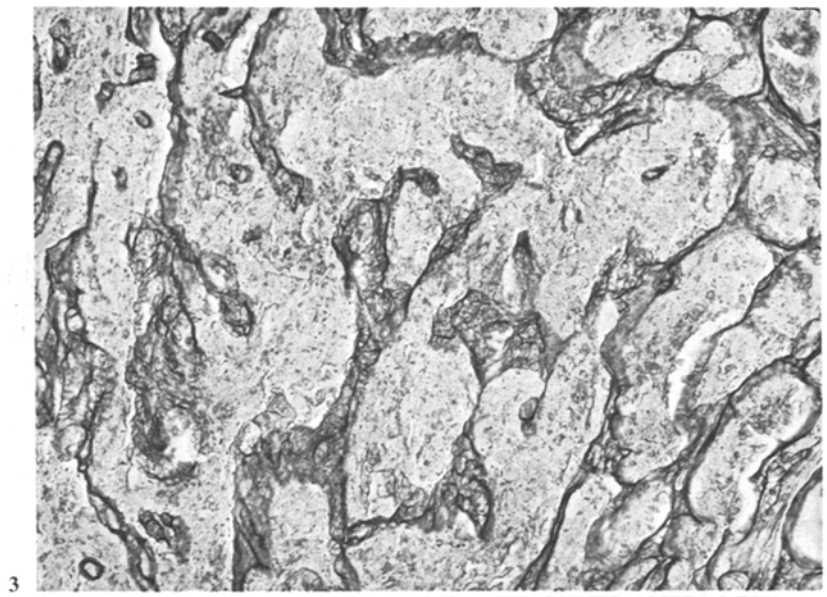


Fig. 1. Panoramic view, showing the submucosal location (× 125)

Fig. 2. Nests of polygonal cells surrounded by a slender richly vascularized stroma (× 500)



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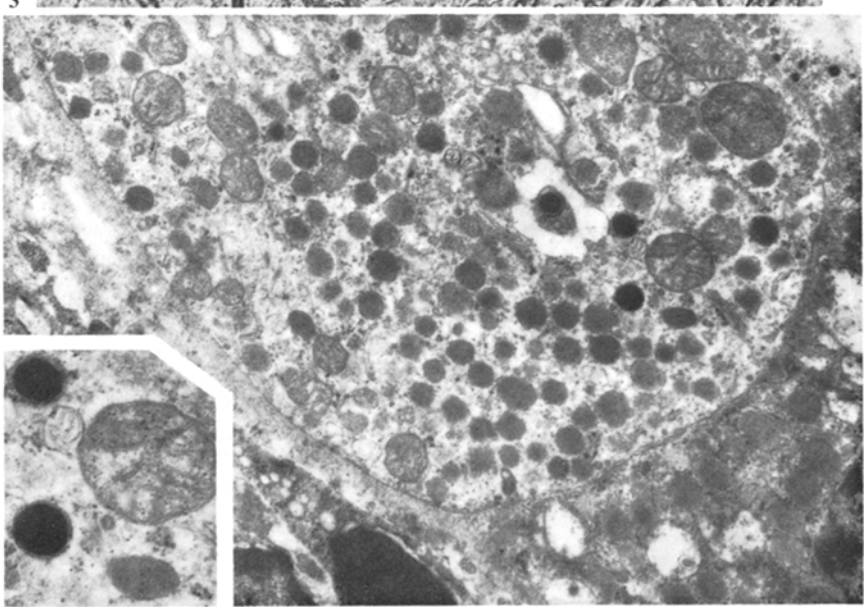

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Fig. 3. Wilder reticulin impregnation demonstrate the alveolar pattern of the stroma and Zellballen arrangement of the tumour cells ($\times 250$)

Fig. 4. This electron micrograph shows numerous dense-cored granules in the cytoplasms of chief cells ($\times 25{,}000$, inset $\times 30{,}000$)

nuclei. The cells exhibited a moderate number of argyrophil granules with the Grimelius's stain; chromaffin reaction was negative with the Masson-Fontana method, post formalin fixation. No mitotic activity nor ganglion-like cells were evident.

A fragment of the formalin-fixed tumour was processed for electron microscopy and showed relatively good preservation. In the ultrastructural study two types of cells were seen, which were either dark or light depending on the amount of hyaloplasm and cytoplasmic organelles; in both types secretory granules with an electron-dense core and membranous envelope were present (Fig. 4). The granules in the "light" cells were scanty, round, 160 nm in diameter; those in the "dark" cells were more numerous and irregularly shaped, the largest – with a lysosomal appearance – reaching a diameter of up to 600 nm. Few mitochondrion and endoplasmic reticulum profiles were seen, and were more evident in the "light" cells. Lipofuscin aggregates were sometimes observed; no microfibrils were present. The cells showed cytoplasmic processes and were attached be well developed junctional complexes. Neither specialized synaptic contacts (chemoreceptor units) nor micropinocytotic vesicles were present. Some cells, probably satellite or sustentacular, contained very few membrane-bound granules and an angular nucleus with stippled chromatin; they provided an obvious contrast to the appearance of those we have considered to be chief cells. The cellular clusters sometimes were surrounded by an irregular basement membrane, in the extracellular space collagen fibrils and a large number of capillaries with endothelial fenestrations were found. No neurite endings or unmyelinated nerve fibres were evident. These findings correlated with the negative Bodian's impregnation of fibres in optical microscopy.

Discussion

In the fetus and newborn there is a more extensive distribution of paraganglion cells than in the adult and the cells are prominent (Coupland, 1965). This observation probably explains the occurrence of well differentiated paragangliomas in sites where, in the adult, the existence of paraganglia has not been demonstrated. It is assumed that there may be cellular nests present during fetal development which remain in adult life (Glenner and Grimley, 1974). Alternatively there exists the possibility that visceral-autonomic paraganglia could be related to vagal paraganglia, perhaps on the terminal branches of the vagus nerve (Goormaghtigh, 1936). It is interesting to note that both, benign (Fernandez, Hernandez and Staley, 1975) and malignant (Moncure and Goodman, 1975; Someren and Karcioglu, 1977) intravagal paragangliomas have been described. Recently, an extensive review of the extra-adrenal nonchromaffin paraganglia and its tumours has been carried out by Helpap (1978).

The lack of evidence for the existence of paraganglia in the duodenum of the adult explains the controversy which has arise concerning the terminology and classification of these tumours in the duodenal wall. The neoplasms described as "ganglioneuromas" and gangliocytic paragangliomas contain mature ganglion-like cells and stroma similar to that of neurofibromata and could presumably be derived from an abdominal sympathetic ganglion. We consider the term ganglioneuroma to be inappropriate, as it is usually applied to tumours representing the full maturation of neuroblastoma. Furthermore, no case of primary neuroblastoma has ever been reported in this location. However, ganglion-like cells are present within the normal paraganglia (Costero and Barroso-Moguel, 1961). Nevertheless, as both sympathetic ganglia and paraganglia seem to be closely related (Taylor and Helwig, 1962), it is not surprising that pure ("nonchromaffin paraganglioma") or mixed paragangliomas ("gangliocytic

paraganglioma") are found, without the latter necessarily representing an intermediate histologic form.

Review of the literature on this subject shows that some cases, previously referred to as nonchromaffin paragangliomas (Lukash, Hyams and Nielsen, 1966; Qizilbash, 1973; Taylor and Helwig, 1962) really correspond to mixed forms (which included ganglion cells) and should therefore be called gangliocytic paraganglioma.

The present case is the first recorded pure duodenal nonchromaffin paraganglioma, since neither ganglion cells nor nerve fibres were present and both its optical ("Zellballen" patterns) and electron-microscopical characteristics (dense-core storage granules, sometimes of catecholaminic type) correspond to nonchromaffin paragangliomata in other locations (Fernandez, Hernandez and Staley, 1975).

The three previous electron microscopic studies of mixed forms (Kepes and Zacharias, 1971; Qizilbash, 1973; Reed, Daroca, Jr. and Harkin, 1977) showed similar finding to those of the present study, although amyloid fibrils were found in one instance (Reed, Daroca, Jr. and Harkin, 1977).

This group of tumours often form a polypoid mass in the duodenum and can either be an incidental radiological finding or may present with haemorrhage. Most of the patients were middle aged; there were 17 males and seven females. The behaviour of the tumour reported here has been benign (after two years of follow-up) which is customary for this type of duodenal tumour. In our case, as in those previously reported, no functional activity due to the release of catecholamines and/or their metabolites was found. The differential diagnosis should include intestinal endocrine tumours and haemangiopericytoma; however, this tumour was limited to the submucosa and did not extend into the muscle coats, moreover, the findings from optical and electron microscopy provide sufficient evidence for confident differential diagnosis.

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