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Case report

Ectopic thyroid follicles in the submucosa of the duodenum

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Summary. Ectopic microscopic thyroid follicles were encountered fortuitously in the submucosa of the duodenum in a 63-year-old man undergoing pancreaticoduodenectomy for pancreatic carcinoma. The follicles, filled with a colloid-like substance, were intermingled with Brunner's glands of the duodenum. There were no signs or symptoms of a thyroid tumour. The epithelial cells and colloid-like substance were both immunoreactive for thyroglobulin but no cells stained for calcitonin. The possibility of a metastatic origin for the follicles from an occult thyroid carcinoma was excluded by the clinical and histopathological findings. These ectopic thyroid follicles cannot be explained by developmental inclusions or metastasis and may be metaplastic in nature.

Key words: Choristoma – Thyroid – Thyroglobulin – Duodenum

Introduction

Ectopic thyroid tissue usually occurs between the base of the tongue and the mediastinum. We have observed ectopic thyroid follicles in the submucosa of the duodenum in a patient with pancreatic carcinoma. The occurrence of ectopic thyroid follicles with typical histological and immunocytochemical appearances is difficult to explain by developmental inclusion or metastasis. The primordium of the thyroid is too distinct and the mature thyroid gland is too distant from the duodenum for developmental inclusions and the duodenum is an unlikely site for metastasis.

Clinical summary

A 63-year-old Japanese man with a brief history of diabetes was admitted to Hokkaido University Hospital because of a tumour in the head of the pancreas. His past history included tuberculosis of the lung, but there was no history of thyroid disease. No tumour was evident in the neck region and clinical examinations, including palpation and hormonal function tests, revealed a normal thyroid. Thyroid echography and scintigraphy were not performed. A pancreaticoduodenectomy was performed, the post-operative recovery was uneventful and he was discharged from hospital. Two years later, the patient was re-admitted with cachexia. He died of a recurrent pancreatic cancer. Permission for autopsy was refused.

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Pathological findings

On gross examination of the resected pancreas and duodenum, a tumour was present in the pancreas but there were no evident abnormalities in the duodenum. The tumour was a moderately differentiated tubular adenocarcinoma of pancreatic duct origin. There was lymphatic invasion by the adenocarcinoma cells surrounding the pancreas. There was no evidence of invasion of the duodenal parenchyma or lymphatics by the adenocarcinoma cells.

Ectopic follicles were seen in the second portion of the duodenum. Round or oval follicles were present among or adjacent to the duodenal glands of Brunner in the submucosa of the duodenum and were filled with a colloid-like substance (Fig. 1a). The colloid-like substance was intensely stained by periodic acid-Schiff (PAS) stain. Psammoma bodies or papillary proliferation of the follicular epithelium was absent. The follicles were composed of a monolayer of cuboidal epithelial cells. Nuclear atypia or hyperchromatism was absent (Fig. 1b) and there were no mitotic figures. The arrangement of the follicles resembled the lobular structure of the thyroid gland (Fig. 1a). The follicles were intermingled with the Brunner's glands in some areas (Fig. 1c). There were no follicular structures in the lymphatic vessels and no fibrotic or inflammatory reaction was seen in the connective tissue surrounding the follicular structures. Similar tissues were not seen in any other tissue, including peripancreatic lymph nodes.

In 34 other cases of resected duodenum of patients with pancratic carcinoma, and in 60 other cases of duodenal endoscopic biopsies, thyroid follicles were not detected.

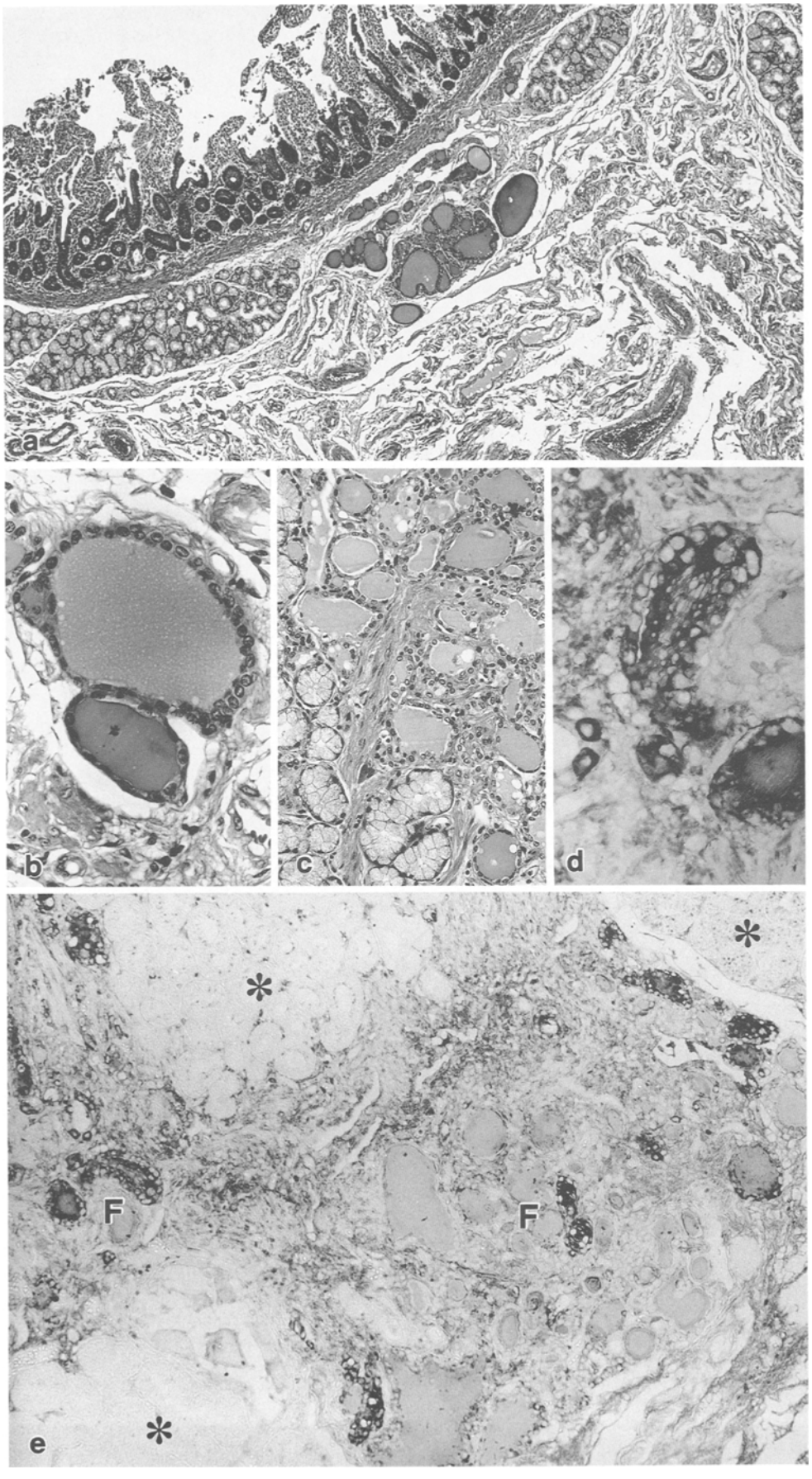

Fig. 1a. Ectopic thyroid follicles in the submucosa of the duodenum. H&E, ×40. **b** Egg-shaped and distorted follicles are filled with a colloid-like substance and are lined with a monolayer of epithelial cells. Note the absence of papillary growth and desmoplastic reaction by the stroma. H&E, ×400. **c** Follicles are intermingled with Brunner's gland in a portion different from that shown in **a.** H&E, ×200. **d** Immunohistochemical staining by the peroxidase-antiperoxidase method. The cytoplasm of follicular epithelial cells and colloid-like substance is positive for thyroglobulin. Peroxidase- antiperoxidase method, ×400. **e** Ectopic thyroid follicles (*F*), which were variously stained for thyroglobulin, are distributed among thyroglobulin-negative Brunner gland (*). Peroxidase-antiperoxidase method, ×100

Immunohistochemical staining by the peroxidase-antiperoxidase (PAP) method was performed on formalin-fixed, paraffin-embedded sections using rabbit antiserum against human thyroglobulin and calcitonin, goat anti-rabbit immunoglobulin, and rabbit PAP complex (Dako, USA). The epithelial cells and colloid-like substance in the follicles were positive for thyroglobulin (Fig. 1d, e), but negative for calcitonin. The follicular epithelial cells stained positively for thyroglobulin consisted of 35% of all thyroid-like cells (955 positive cells out of 2725), and colloid-like substance positively stained for thyroglobulin was seen in 44 (strongly positive) and 130 (weakly positive) out of a total of 180 follicular structures.

Non-immune rabbit serum yielded no reactivity in the follicles in the present case, or in a control adenoma. Cells immunoreactive for thyroglobulin or calcitonin were not seen in 60 cases of fibercoptic duodenal biopsies used as controls. Renal tubular epithelial cells in eighteen autopsied patients showing so-called "thyroidization" of the kidney also proved negative for both thyroglobulin and calcitonin.

Discussion

Ectoptic thyroid tissue has been detected in various organs, including the base of the tongue, sublingual, perihyoid, subhyoid, intratracheal, and heart regions (Kantelip et al. 1986; Okstad et al. 1986; Walling 1987; Hashimoto et al. 1988; Rosai 1989). From an embryological point of view, ectopic thyroid tissue can be found anywhere along the thyroglossal duct (Okamoto 1983; Sadler 1984), the most frequent location being the base of the tongue (Rosai 1989). In rare instances, ectopic thyroid has been reported to occur in the diaphragm (Okstad et al. 1986), but ectopic thyroid below the diaphragm, even as a microscopic deposit, has apparently never been documented with the exception of struma ovarii. The microscopic appearance of struma ovarii is usually that of normal thyroid tissue (Novak and Woodruff 1979; Rosai 1981).

The close, morphological resemblance of the follicular structures in the present case to normal thyroid follicules, as well as the specific staining for thyroglobulin in the colloid-like substance and follicle-lining cells, confirm that the follicles are thyroid. The intense staining by PAS of the colloid-like substance demonstrated that the content was a glycoprotein; also consistent with the notion that the substance was thyroglobulin.

Eleven cancers metastatic from the thyroid to the duodenum were detected in 672 patients with thyroid carcinomas, as reported in the Pathological Autopsies in Japan (The Japanese Society of Pathology 1987, 1988). The possibility that the thyroid follicles in this case are metastatic from an occult thyroid cancer must be considered. Indeed, extensive metastases from occult carcinomas of the thyroid have often been reported (Sampson et al. 1969; Strate et al. 1984; Yamashita et al. 1986; Hoie et al. 1988; Allo et al. 1988). Most of these were limited to lymph nodes in close proximity to the primary tumours. However, several distant metastases were also noted (Strate et al. 1984; Allo et al. 1988). Strate et al. (1984) described two cases of occult thyroid papillary carcinoma, the first was a 2.4 mm carcinoma with a solitary pulmonary metastasis, and the second was a lethal tumour with extensive metastases to hilar and mediastinal lymph nodes, lung, pericardium, epicardium, pleura, left kidney, liver, adrenals, prostate, and vertebral column. There were some histological features in common in these metastatic occult carcinomas; they were generally a papillary lesion, the border between the metastases and normal tissue was clearly demarcated and not intermingled with normal tissues (Strate et al. 1984). To distinguish non-neoplastic thyroid tissue from metastatic thyroid carcinoma cells, Meyer and Steinberg (1969) proposed the following criteria; microscopic size, follicles round or oval, non-papillary, uncrowded, nuclei uncrowded, not enlarged, no stromal proliferation, and no psammoma bodies.

Thus the possibility that thyroid follicles of microscopic size in the duodenum represent a metastasis from an occult thyroid carcinoma is unlikely, because neither cellular atypia nor papillary proliferation was observed in the cells forming round to oval thyroid follicles, there was no evidence that the thyroid follicles involved lymphatic vessels of the duodenum or peripancreatic lymph nodes, and there was no destructive invasion by the follicle cells or desmoplastic reaction by the surrounding connective tissue.

Nicastri et al. (1965) suggested that the thyroid inclusions might derive from transport of thyroid tissue through the lymphatics. In the present case, the location of the ectopic thyroid was so distant from the thyroid gland that it is unlikely to have occurred through developmental inclusion or metastasis. The possibility that the thyroid follicles in the duodenum were derived from metaplasia of the Brunner's glands must be considered as they are intermingled with the Brunner's glands in some areas. Chronic stimulation such as inflammation, which is usually associated with metaplastic transformation, was not present in this case.

Sauk (1970) reported microscopic detection of ectopic lingual thyroid tissues in 10% of the cadavers examined. The incidence of microscopic thyroid ectopias in the other locations may also be higher than recognized heretofore.

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