Virchows Archiv (1994) 425:331–334

CASE REPORT

José Cameselle-Teijeiro · Juan Varela-Durán

Intrathyroid salivary gland-type tissue in multinodular goiter

Received: 8 April 1994 / Accepted: 6 June 1994

Abstract We report a case of intrathyroid salivary gland tissue in a 66-year-old Caucasian female with multinodular goiter. Lobules of well differentiated seromucinous salivary glands were found in close relationship with cartilage and fat, and intimately associated with normal thyroid follicles and solid cell nests (SCN) of the thyroid gland. This is the first report of non-neoplastic intrathyroid salivary gland tissue. We conclude that this heterotopic tissue probably arises from the SCN as ultimobranchial vestigial structures.

Key words Salivary gland · Intrathyroid inclusions
Solid cell nests · Histogenesis

Introduction

The existence of heterotopic tissue in the thyroid gland is well-documented [2, 8]. Intrathyroidal inclusions of thymus, parathyroid gland tissue, fat, striated muscle, respiratory-type ciliated epithelium and cartilage have all been reported [2, 4, 9]. However, none of these studies has included the finding of non-neoplastic salivary gland tissue in the thyroid parenchyma.

Extensive reports of salivary gland heterotopia have described salivary gland tissue in intracranial locations, middle ear, gingiva, mandible, and in the region of the lower neck but unrelated to the thyroid [3]. This is the first report of non-neoplastic intrathyroid salivary gland tissue although a salivary gland-type pleomorphic adenoma has been described [6]. The morphological features of this unique finding and the possible histogenesis of this heterotopic tissue from the so-called solid cell nests (SCN) of the thyroid are discussed.

J. Cameselle-Teijeiro (✉) · J. Varela-Durán
Department of Pathology,
University of Santiago Medical School and Hospital,
E-15705 Santiago, Spain,
and Department of Pathology, Hospital Fundacion Verin,
Verin, Spain

Case report

A 66-year-old Caucasian female consulted for a lower neck mass that she had noted for several months. There were no symptoms of neck pain or pressure, dysphagia, or hoarseness. She had no previous history of radiation or X-ray exposure to her neck, face or thorax. Physical examination revealed multinodular enlargement of the thyroid gland. Thyroid function tests were within normal limits. The thyroid scan with 99Tc pertechnectate showed several, irregular sized, cold nodules in both lobules. At surgery, a subtotal thyroidectomy was performed. The postoperative course was uneventful, and the patient is in good health 3 1/2 years after surgery.

Material and methods

For light microscopy, sections of formalin fixed, paraffin embedded tissue were stained, with Harris haematoxilin and eosin, periodic acid-Schiff (PAS), Alcian blue (pH 2,5), PAS-Alcian blue (pH 2.5) and Mayer's mucicarmine. For immunohistochemistry, conventional 4 µm histological sections from the paraffin blocks were air dried at room temperature for 12 h, and then stained using the avidin-biotin-peroxidase technique [5] employing commercially available antibodies to the following antigens:thyroglobulin (Dakoppats, 1:300), calcitonin (Dakoppats, 1:600) and calcitonin gene-related peptide (CGRP; Amersham, 1:400). Primary antibodies were eliminated from duplicate slides as negative controls, and appropiate positive controls known to contain the antigen were processed simultaneously in every case.

Pathologic findings

On gross examination the resected thyroid gland was enlarged and distorted, measuring 10×9×7 cm in maximum diameter, with a preserved fibrous capsule. On cross section, multiple irregular-sized nodules were seen, in some areas separated by fibrous strands. Focal areas of haemorrhage, calcification and cystic change were observed.

Microscopically, the findings were those of a typical multinodular goiter, with multiple nodular structures composed of proliferating follicles of different sizes and shape. Areas of dense fibrosis with occasional calcification, haemorrhage and cholesterol clefts were found in all sections.

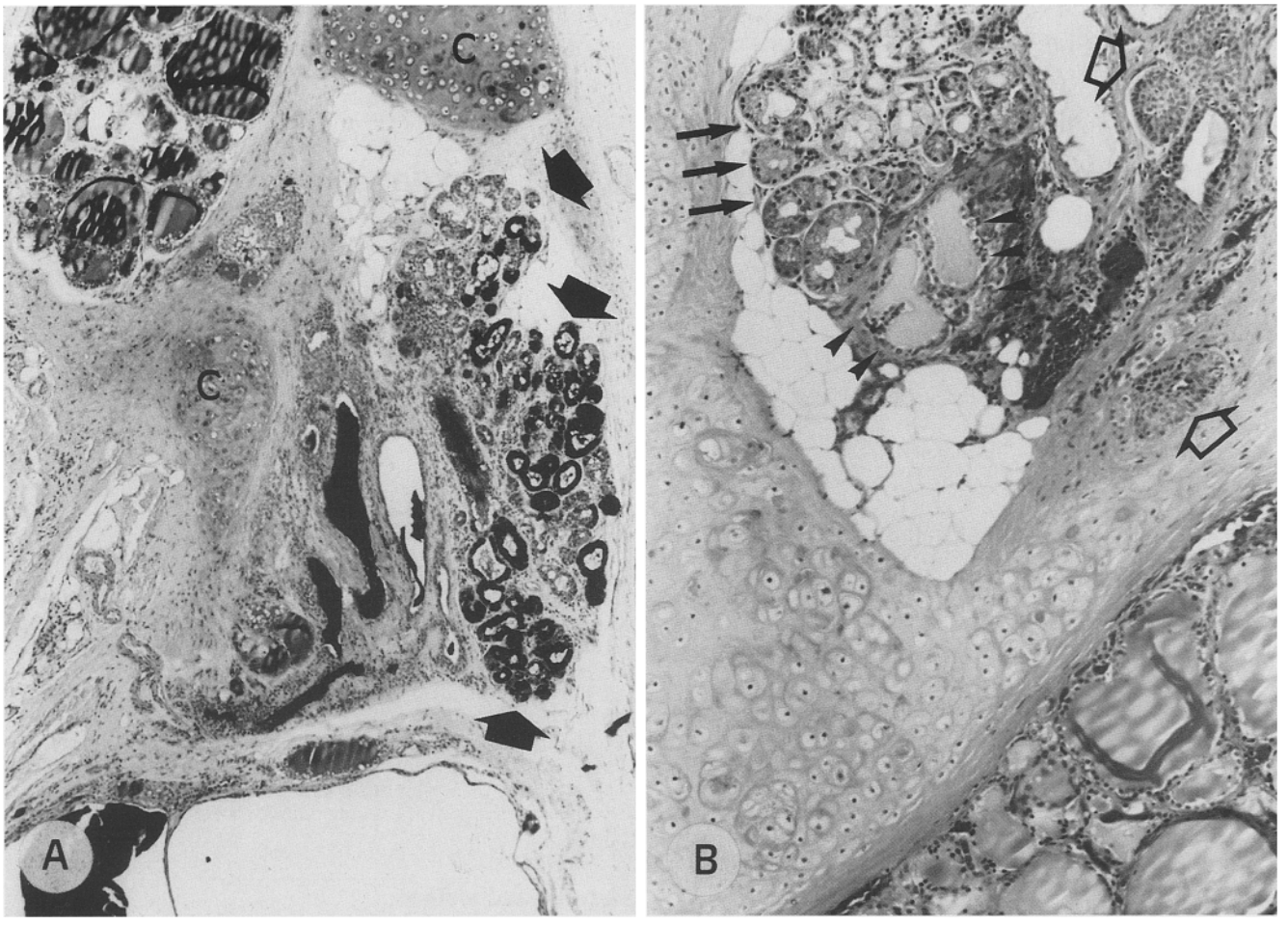

Fig. 1 **A** Lobules of mature salivary glands *(arrows)* intermingled with fat, cartilage (*C*) and thyroid parenchyma as well as with cystic spaces containing mucinous material; (PAS) periodic acid-schiff-Alcian blue, × 80. **B** The salivary gland tissue *(arrows)* is intimately associated with solid cell nests *(empty arrows)* and thyroid follicles *(arrow heads)*; haematoxylin, and eosin (H&E) ×220

Islands of mature cartilage, fat and several lobules of seromucinous salivary gland tissue were identified in only one of the sections, and were intermingled with fibrous and thyroid tissue (Fig. 1A, B).

In the same section, solid nests of polygonal or elongated cells, with abundant eosinophilic cytoplasm were found (Fig. 2A). Most of the cells forming these nests showed an epidermoid-like appearance, with nuclei displaying an oval profile and having occasional nuclear grooves (Fig. 2B). Intermingled with these cells were smaller cells with clear cytoplasm and a small compact nucleus. These structures clearly represented the SCN of the thyroid gland. Some of these nests showed cystic cavities containing PAS, Alcian blue and Mayer's mucicarmine positive material (Figs. 1A, 2A). There were also some mixed follicles composed of a solid cell proliferation in intimate connection with follicular-like lumen formation (Fig. 2B). Solid cell nests were not identified in any of the other multiple sections studied and were therefore not found bilaterally.

Immunoperoxidase studies demonstrated strong thyroglobulin immunoreactivity in the thyroid follicles as well as in the mixed follicles associated with SCN. The main cells of the SCN were negative for both thyroglobulin and calcitonin. In these cell nests there was also positive staining for calcitonin and calcitonin gene-related peptide in the smaller C cells. Both markers were negative in the salivary gland tissue.

Discussion

The major and minor glands arise as invaginations of the primitive oral epithelium. Only the parotid and submaxillary glands migrate and it is apparent that in normal development the migration of the parotid and submaxillary glands is limited to the region of the mandible. This process could not account for the existence of salivary tissue in intracranial locations or in the region of the thyroid gland [3].

However, the presence of heterotopic salivary gland tissue has been well documented in various intracranial locations including the pituitary gland, cerebellopontine angle and middle ear, as well as in lymph nodes, and in the region of the lower neck [3] where not only mature salivary gland tissue but also neoplasms originating in heterotopic salivary tissue have been described [7]. In

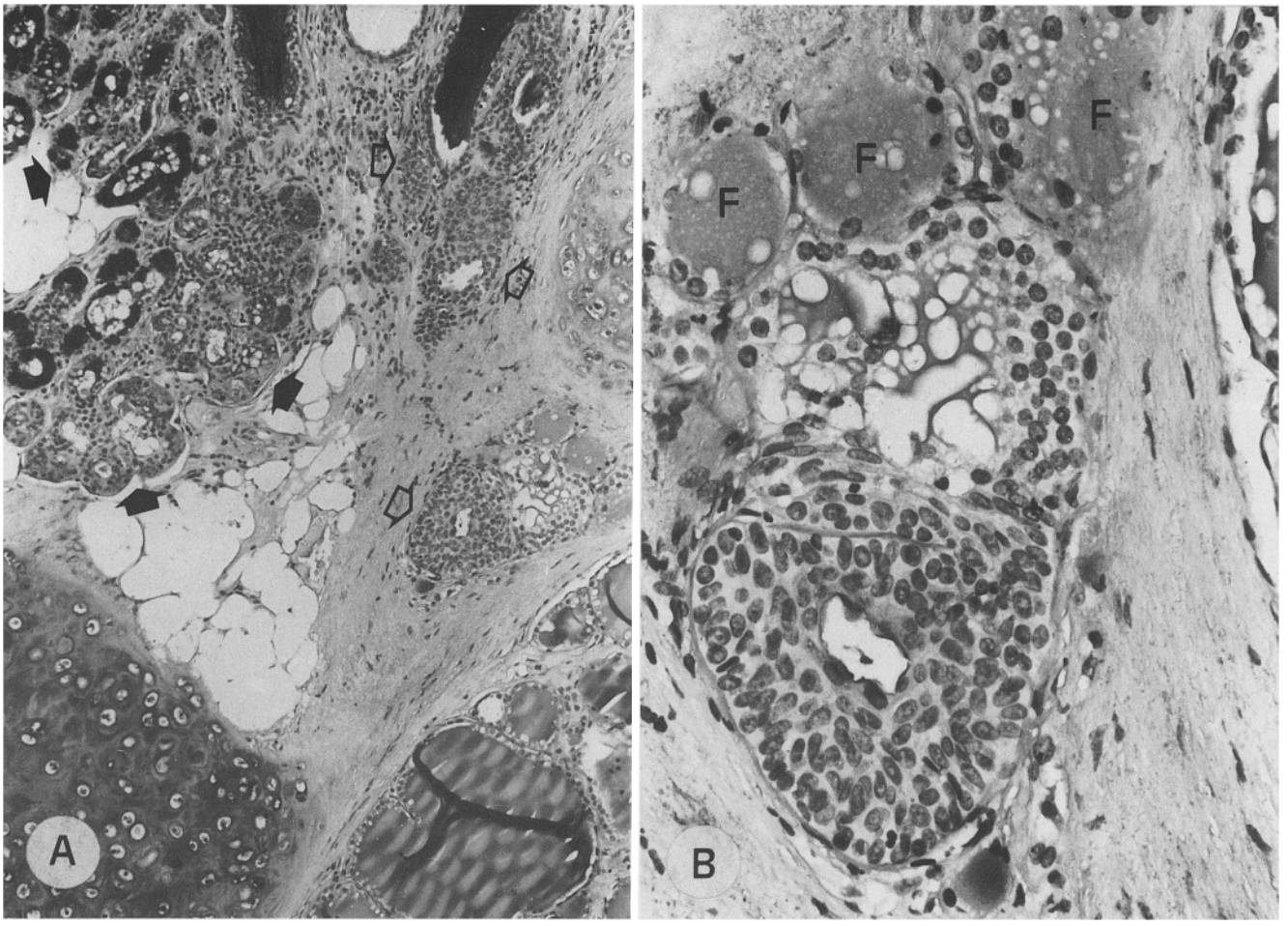

Fig. 2 **A** Salivary gland tissue *(arrows)* next to solid cell nests *(empty arrows)* and other heterotopic tissues including cartilage and fat. Thyroid follicles in the lower right corner; PAS, × 80. **B** High power view of solid cell nest in **A** connected to thyroid follicles (*F*) H&E, ×340

this latter location Youngs and Scofield [10] reported 11 patients with salivary gland heterotopia of which 10 cases were located along the medial border of the sternocleidomastoid muscle or near the sterno-clavicular joint; only one case was in the parathyroid next to the upper third of the right lobe. They also refer to another two cases in which salivary gland tissue was found in the capsules of parathyroid glands. In our extensive review of the literature, however, we have not been able to find any report of heterotopic salivary gland tissue located in the thyroid.

Inclusions of non-thyroid tissue within the thyroid capsule have been extensively illustrated, including the finding of thymus, striated muscle, adipose tissue, ciliated epithelium, parathyroid tissue and cartilage [2, 8]. None of these studies described the finding of salivary gland tissue as a sole or partial component of these inclusions. In their review of 350 thyroid glands from autopsy protocols, Carpenter and Emery [2] found different morphological types of intrathyroid heterotopic tissue among which salivary gland was not included.

In our case the lobules of well differentiated salivary gland tissue were associated with SCN of the thyroid and in very close relationship with islands of mature cartilage. This heterotopic tissue was histologically indistinguishable from the oral salivary glands and resembled submaxillary glands as in other reports of salivary gland heterotopia [10].

The location of heterotopic salivary gland tissue in the neck has been explained on the basis of the relationship between this tissue and the branchial apparatus, particularly the precervical sinus of His, in view of the association of this heterotopic salivary gland tissue with branchial cysts and sinuses [10]. In our case, however, the intimate association of intrathyroidal salivary gland tissue with SCN of the thyroid suggests a possible histogenesis of this salivary heterotopia in these vestigial structures.

SCN of the thyroid were originally described as solid cell proliferations, displaying two distinct cell types, that may be found in normal or neoplastic thyroid glands [1]. The association of SCN with remnants of thymic tissue and cartilage has been well documented and favours, together with the secretion of mucinous material by the SCN and its immunohistochemical profile, an ultimobranchial body origin for the SCN. Since the ultimobranchial body is of endodermal origin, as salivary glands are, the occurrence of this heterotopic salivary gland tissue associated with SCN in the thyroid paren-

chyma can be justified. Degenerative or metaplastic changes could be considered as possible mechanisms leading to this unusual finding, as it has been the case in other reports of intrathyroidal cartilage and fat tissue [1, 4]. However, we favour the existence of a disembryologic process on the basis of which the SCN – as remnants of the ultimobranchial body – differentiate into mature salivary gland tissue thus justifying the occurrence of salivary gland-type neoplasms in the thyroid. One such a case concerning a salivary gland-type pleomorphic adenoma was described by Lange [6] whose article contained a thorough discussion on the various histogenetic possibilities that include sequestration of salivary gland tissue and a branchial origin.

Acknowledgements The authors are grateful to Mrs. María Valeiras-Puga for her technical assistance. This project has been partially supported by grant BAE 89/0995 from the Fondo de Investigación Sanitaria (FIS), Spain, and grant COGENOR S.L., La Coruna, Spain.

References

1. Cameselle-Teijeiro J, Varela-Durán J, Sambade C, Villanueva JP, Varela-Núñez R, Sobrinho-Simoes M (1994) Solid cell nests of the thyroid: light microscopy and immunohistochemical profile. Hum Pathol 25:684–693
2. Carpenter GR, Emery JL (1976) Inclusions in the human thyroid. J Anat 122:77–89
3. Ellis GL, Auclair PL, Gnepp DR (1991) Surgical pathology of the salivary glands. WB Saunders, Philadelphia
4. Finkle HI, Goldman RL (1973) Heterotopic cartilage in the thyroid. Arch Pathol 95:48–49
5. Hsu SM, Raine L, Fanger H (1981) The use of avidin-biotin-peroxidase complex (ABC) in immunoperoxidase techniques. A comparison between ABC and unlabeled antibody (PAP) procedures. J Histochem Cytochem 29:577–580
6. Lange MJ (1974) Pleomorphic adenoma of the thyroid containing salivary gland cells with pseudocartilage and myoepithelial cells. Int Surg 59:178–179
7. Pesavento C, Perlito A (1976) Benign mixed tumor of heterotopic salivary gland in the upper neck : report of a case with review of the literature on heterotopic salivary gland tissue. J Laryngol Otol Clin Rec 10:577–584
8. Rosai J, Carcangiu ML, DeLellis RA (1992) Tumors of the thyroid gland. In: Atlas of tumor pathology, 3rd series. Armed Forces Institute of Pathology, Washington, D.C., pp 27–29
9. Weitaner S, Appenzeller J (1973) Ectopic cartilage in the thyroid. Oral Surg Oral Med Oral Pathol 36:241–242
10. Youngs LA, Scofield HH (1967) Heterotopic salivary gland tissue in the lower neck. Arch Pathol 83:550–556