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Case report

Leiomyoma and neurilemoma: Report of two unusual non-epithelial tumours of the thyroid gland*

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Summary. Two primary spindle cell tumours of the thyroid are described showing light microscopic features of leiomyoma and neurilemoma respectively. The origin from smooth muscle and nerve sheath was confirmed by both immunohistochemical reactions and ultrastructural findings. Review of the literature reveals only one case of leiomyoma and three cases of neurilemoma reported as developing within the thyroid gland. Our observations further support the view that leiomyoma and neurilemoma may occur at this unusual site and are recognizable entities.

Key words: Thyroid neoplasms – Leiomyoma – Neurilemoma – Schwannoma – Spindle cell tumours

Introduction

Non-epithelial tumours of the thyroid gland are infrequently encountered. Among them the benign forms are of such rarity as to merit only brief mention in some pathology textbooks (Meissner and Warren 1968; Rosai 1981). They include teratomas, haemangiomas and paragangliomas. In addition, one case of leiomyoma (Hendrick 1957) and three cases of neurilemoma (schwannoma) (Delaney and Fry 1964; Goldstein et al. 1982; Kneeland-Frantz 1962) are on record.

We report two primary spindle cell tumours of the thyroid showing morphological characteristics of leiomyoma and neurilemoma respectively. Histochemical and ultrastructural information on the two entites is provided and problems in the differential diagnosis are discussed.

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Case report

Case 1. A 45-year-old woman was admitted in July 1981 because of the presence of a firm, painless, palpable nodule localized in the neck. Physical examination revealed a slightly enlarged thyroid and the scan showed a "cold" nodule in the anterior side of the right lobe of the gland. Serum T3, T4 were within normal limits. No cervical lymph nodes were palpable. The patient was taken for sugery and, at operation, the diagnosis on frozen sections was spindle cell tumour of the thyroid, possibly benign. A right hemithyroidectomy was performed without complications. Subsequent pertinent diagnostic procedures excluded possibility of metastasis. The patient is still well, without evidence of recurrent disease, 6 years after surgery.

Case 2. A 33-year-old woman was admitted in October 1986 because of the presence of a nodular firm mass in the right side of her neck. Thyroid scan showed a "cold" nodule in the apical side of the right lobe. T3, T4 serum levels were within normal limits. Ecotomographic study confirmed the presence of a well-demarcated oval mass measuring about 5 cm in diameter. At operation, a specimen of the tumour mass was examined on frozen section and the immediate impression was that of a spindle cell tumour, possibly benign. The surgeon performed an enucleation of the nodule which appeared well encapsulated. No other pathological lesions were noted in the thyroid or regional lymph nodes nor was there any evident connection with peripheral nerves. The postoperative course was uneventful and the patient was doing well when seen at follow-up four and twelve months later.

Materials and methods

Tissue specimens of both tumours were fixed in 10% formalin and embedded in paraffin. Step sections were stained with H.E., Masson's trichrome and Wilder's reticulin. Sections from paraffin-embedded material were used for immunohistochemical studies. They were treated with the avidin-biotinylated peroxidase complexes procedure (Hsu et al. 1981). Antibodies included reagents against alpha actin-smooth muscle (monoclonal, from Dr. G. Gabbiani, Geneva, Switzerland), actin-skeletal

(polyclonal, from Miles, Naperville, IL), desmin (affinity-purified polyclonal, from Dr. G. Gabbiani, Geneva, Switzerland) fetal myosin (monoclonal, from Dr. V. Eusebi, Bologna, Italy), myoglobin (polyclonal, from Immulok, Carpinteria, CA), vimentin (monoclonal, from Dakopatts, Copenhagen, Denmark), F VIII-related antigen, S-100 and myelin basic proteins (polyclonal, from Dakopatts, Copenhagen, Denmark), EMA (polyclonal, from Sera-Lab, Crawley, UK), keratin 55–57 Kd (monoclonal, from Sorin, Saluggia, Italy), thyroglobulin and calcitonin (polyclonal, from Ortho Diagnostic System, Raritan, New Jersey).

For ultrastructural investigation, tissue specimens from both cases were fixed in 2.5% glutaraldehyde in cacodilate buffer pH 7.4, post-fixed in OsO_4, and embedded in epon-araldite. Specimens of Case 2 were obtained from tissue preserved in 10% formalin.

Thin sections from several blocks were stained with uranyl acetate and lead citrate, and examined with a Siemens Elmiskop 102 electron microscope.

Results

The hemithyroidectomy specimen from patient 1 measured 4.2×4.5 cm; the tumour nodule consisted of an apparently encapsulated mass measuring $1.5 \times 1.2 \times 1$ cm. On section, the cut surface was bulging and showed glistening gray tissue (Fig. 1).

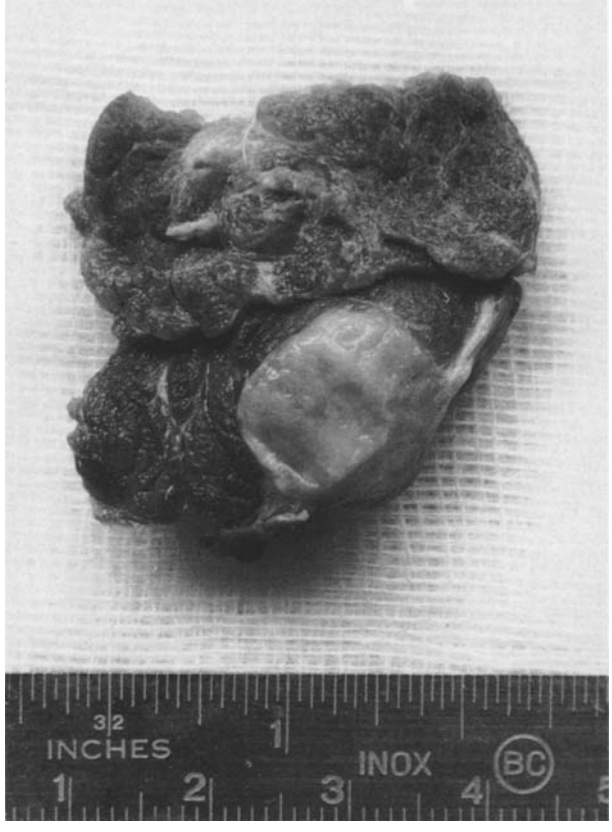

Fig. 1. Case 1, Leiomyoma. The hemithyroidectomy specimen contains a tumour nodule consisting of an apparently encapsulated mass. The cut surface is bulging and shows glistening tissue

The tumour from patient 2 measured $5 \times 2.5 \times 2$ cm and consisted of an oval, firm, translucent, encapsulated mass.

Microscopic examination of histologic sections from Case 1 showed a uniform tumour pattern consisting of intersecting fascicles of deeply acidophilic spindle cells with blunt ended nuclei (Fig. 2). Mitoses were sporadic. An evident fibrotic capsule was seen in peripheral fields; nevertheless, in some areas, the neoplastic tissue appeared to merge into the normal thyroid. At times, the surrounding thyroid tissue showed hyperplastic follicles with sparse foci of lymphocytic infiltration of the intervening stroma. A slight diffuse lymphocytic infiltration was also seen in many fields of the tumour (Fig. 2).

Light microscopic features of Case 2 were characterized predominantly by fusiform cells with moderately abundant eosinophilic cytoplasm arranged in interlacing bundles with some palisading of nuclei (Fig. 3). These patterns closely resembled those of the Antoni A-type neurilemoma. Occasionally, the spindle-shaped cells were widely separated by a watery matrix that stained poorly or not at all with H.E., suggesting the Antoni B type. No axons were found within the tumour.

The results of immunohistochemistry are summarized in Table 1. In Case 1, the neoplastic tissue was strongly labelled by anti-alpha smooth muscle actin (Fig. 2B) and anti-vimentin monoclonals. Focal staining was found when using anti-desmin antibodies. In Case 2, the tumour cells were focally immunoreactive for vimentin, whereas almost all cell population strongly reacted with the antiserum to S-100 protein (Fig. 3B). No positivity for myelin basic protein was seen.

On electron microscopy most tumour cells in Case 1 had abundant cytoplasm surrounded by a large quantity of extracellular collagen (Fig. 4). Cytoplasmic organelles were represented by relatively few mitochondria, rough-surfaced endoplasmic reticulum and aggregates of free ribosomes. Thin actin-like microfilaments arranged in parallel, with focal dense zones, were seen (Fig. 5). The sarcolemma appeared to be well defined and pinocytic vesicles were very few in number and only occasionally found.

Case 2 was almost entirely composed of schwannian cells with complexly entangled processes surrounded by basement membrane substance in a sparse stroma containing scattered collagen fibrils (Fig. 6A). The characteristic feature of these cell processes was their tendency to envelop extracellular material forming pseudomesaxons (Fig. 6B). Peculiar structures, the so called "fibrous long-spacing collagen" were present in the

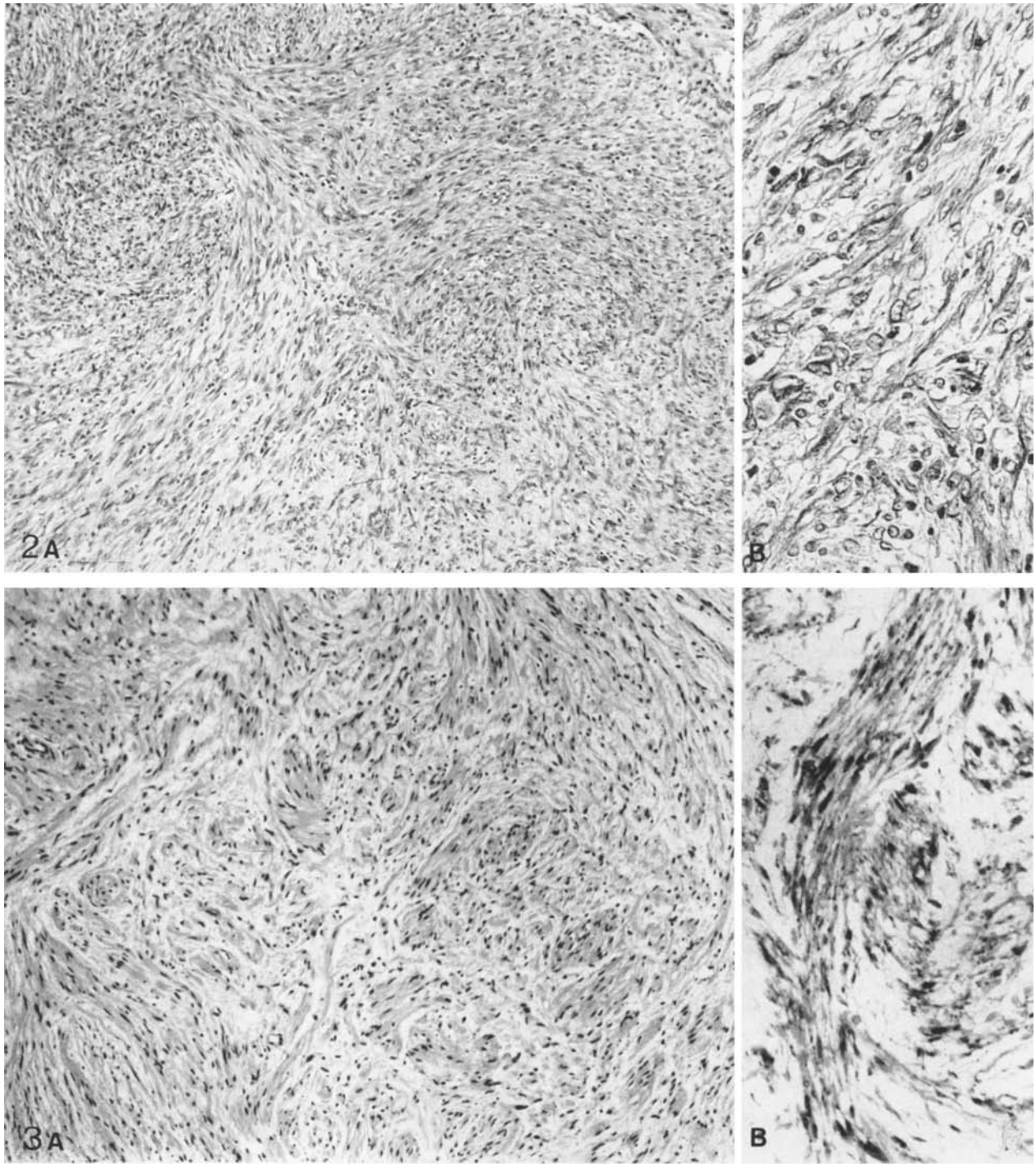

Fig. 2A, B. Case 1, Leiomyoma. **(A)** Tumour pattern showing intersecting fascicles of spindle cells; note the sparse lymphocytic infiltration. **(B)** Immunostain with alpha actin; note intracytoplasmic staining of many tumour cells

Fig. 3A, B. Case 2, Neurilemoma. **(A)** Tumour pattern showing fusiform cells arranged in interlacing or undulating bundles with somehow palisading of nuclei. **(B)** Immunostain with S-100 protein; most of the spindle-cell component is immunoreactive with the antiserum

Table 1. Immunoperoxidase staining profiles of tumour tissue

	ASMA	ASk	Myosin	Myoglobin	Vimentin	Desmin	F VIII-RAg
Case 1	++	+	−	−	++	+	−
Case 2	−	−	−	−	+	−	−
	S-100	MBC	EMA	Keratin/55–57 Kd	Thyroglobulin	Calcitonin	
Case 1	−	−	−	−	−	−	
Case 2	++	−	−	−	−	−	

ASMA = alpha-smooth muscle actin; ASk = actin-skeletal; F VIII-RAg = Factor VIII-related antigen; S-100 = S-100 protein; MBC = myelin basic protein; EMA = epithelial membrane antigen

interstitium and also related to the plasmalemma of the Schwann cells (Fig. 6C). The cytoplasm contained numerous filaments predominantly oriented along the major axis of the cell. No true axons were identified in the tumour tissue.

Discussion

Both the reported tumours were histologically characterized by a tissue prevalently composed of interlacing bundles of spindle cells showing no atypia or increasing mitotic activity. The first impression was that of benign tumours having respectively the appearance of leiomyoma and neurilemoma.

As far as we are aware, the only previously reported case of leiomyoma within the thyroid gland is that of Hendrick (1957). To date, three cases of neurilemoma of the thyroid have been reported in the literature (Delaney and Fry 1964; Goldstein et al. 1982; Kneeland-Frantz 1962).

The diagnoses of the cases from literature were all made by routine histology. Ancillary techniques such as electron microscopy and immunohistochemistry were not employed or, at that time, were not yet available. Thus, since it is widely accepted that every primary thyroid tumour with mesenchymal appearance should be regarded as epithelial in origin unless there is incontrovertible proof to the contrary (Kneeland-Frantz 1962; Rosai and Carcangiu 1987), the true non-epithelial derivation of the cases previously reported might be questioned. In our tumours, the non-epithelial nature was confirmed by immunohistochemical results (Table 1). Indeed, both neoplasms were vimentin positive and showed no reactivity when antibodies specific for epithelial derivation were employed. Furthermore, our immunohistochemical and ultrastructural findings favor the hypothesis of distinct entities as already suggested by light microscopic features. In Case 1, the smooth muscle origin was supported by the strong immunoreactivity for alpha smooth muscle actin and by the presence, at the ultrastructural level, of actin-like micro-filaments. However, the paucity of pinocytic vesicles is not in contrast with this hypothesis, since it has already been reported by others that in some leiomyomas such structures can be incompletely developed (Sobel et al. 1981). In Case 2, a well-expressed immunoreaction against S-100 protein and the ultrastructural finding of schwannian cells strongly suggested nerve-sheath derivation. The negativity of myelin basic protein seems to be partially in conflict with this statement since MBP has been reported as an useful peripheral nerve marker (Du Boulay 1985; Roholl et al. 1985). However, it must be borne in mind that some commercial newly developed marker such as MBP could well be unreactive under unknown circumstances.

S-100 positivity can be found in both neurilemoma and neurofibroma (Nakajima et al. 1982; Weiss et al. 1983); moreover, findings usually seen in neurilemoma such as Verocay's bodies and cystic spaces were absent. Nevertheless, Antoni A and B patterns in a well encapsulated tumour, the presence of "long-spaced collagen", and the absence of axonal structures, all favored the diagnosis of neurilemoma (Dickersin 1987; Erlandsson 1985; Harkin and Reed 1969; Harris 1981; Sobel et al. 1981).

Fig. 4. Case 1, Leiomyoma. The tumour cells show abundant cytoplasm containing dilated mitochondria and an oval blunt ended nucleus. The extracellular collagenous stroma is evident (*C*). (×4000)

Fig. 5. Case 1, Leiomyoma. Thin actin-like filaments are arranged in parallel bundles with focal dense zone (*arrows*). (×16000)

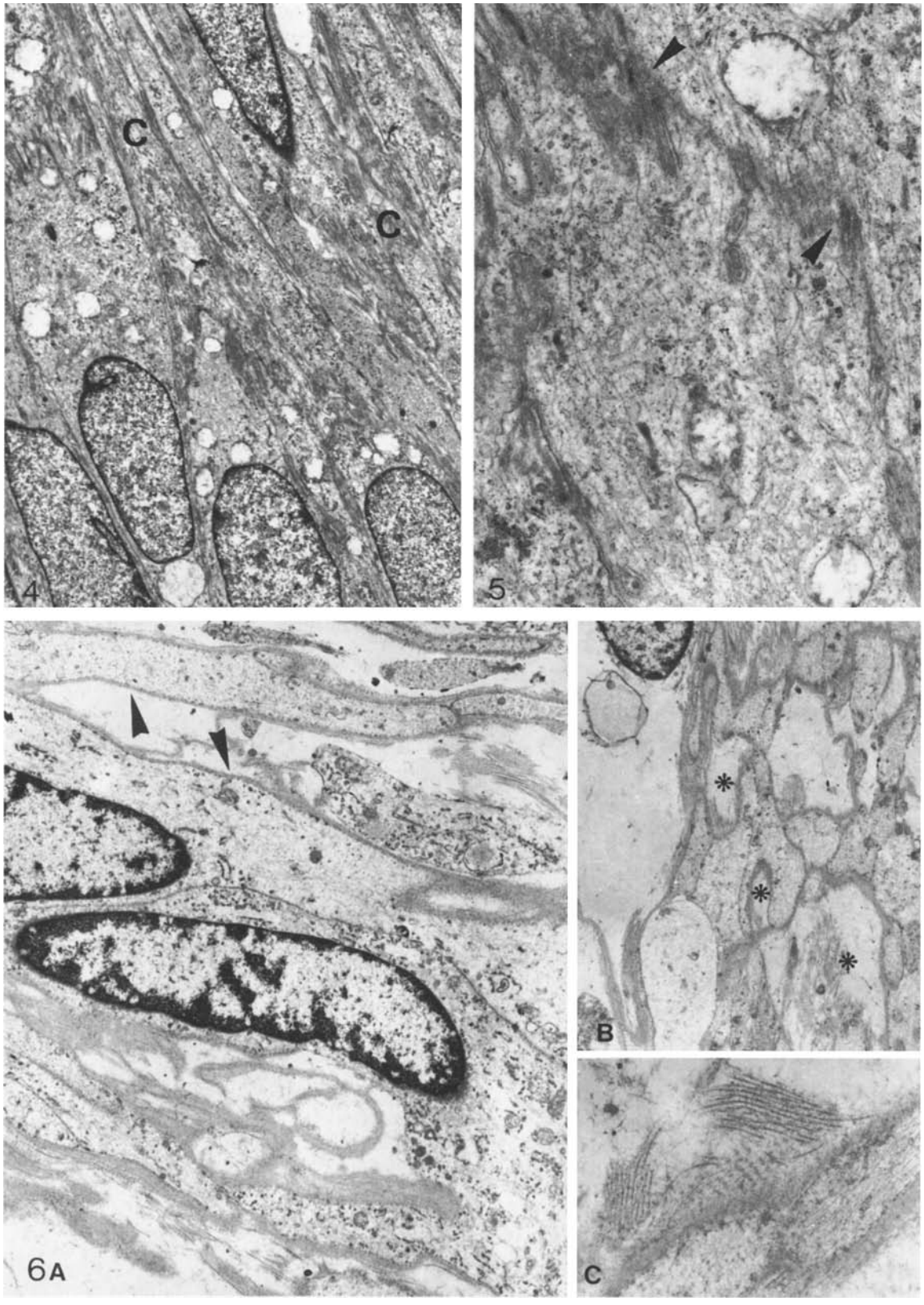

Fig. 6A–C. Case 2, Neurilemoma. (**A**) The cells show thin cytoplasmic processes. These structures and cell bodies are surrounded by basal lamina (*arrows*). (×13600). (**B**) The interwining cell processes wrap around bundles of collagen fibers creating pseudomesaxons (*). (×6600) (**C**). Banded basement material, so called "long-spacing collagen", is present near the plasmalemma of a Schwann cell. (×22000)

Another relevant question deals with the biological behaviour of the tumours we observed. In all previously reported cases but one (Hendrick 1957) follow-up was lacking and the benign nature was inferred on the ground of the morphologic findings only. As to the smooth muscle tumour (Case 1), the possibility of leiomyosarcoma (primary or metastatic) can reasonably be excluded on the basis of the evaluation of the follow-up, together with the absence of both hypercellularity and increased mitotic activity. Nevertheless, the possibility of the so-called metastasizing leiomyoma (Cramer et al. 1980) also seems to be unlikely taking into account, once again, the clinical history and the follow-up. In Case 2, the differential diagnosis involves malignant schwannoma. However, malignant schwannoma is usually found in patients with von Recklinghausen's neurofibromatosis or arises within the perineurium of a sizeable nerve or in direct continuity with a unquestionable neurofibroma (Harkin and Reed 1969; Rosai 1981). None of these conditions were present in our patient and this possibility, in spite of the relatively short follow-up period, also seems to be highly unlikely.

In conclusion, our observations confirm that leiomyoma and neurilemoma may indeed develop in the thyroid and are recognizable entities. Electron microscopy and immunohistochemistry may be regarded as important ancillary techniques in diagnosing these uncommon neoplasms.

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