Virchows Archiv A Pathol Anat (1993) 422:491–497

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Solitary fibrous tumour of the thyroid: clinicopathological, immunohistochemical and ultrastructural study of three cases

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Received August 28, 1992 / Received after revision February 11, 1993 / Accepted February 16, 1993

Abstract. We describe three cases of solitary fibrous tumour (SFT) arising from thyroid stroma. Grossly, the tumours were clearly delimited but only partly encapsulated. The following histomorphological growth patterns were observed: bundles of cells in storiform configuration; non-structured bundles; prevalence of fibrous matrix; highly cellular, non-structured; prevalence of loose, non-structured extracellular substance; cellular proliferation and vascular spaces in a haemangiopericytic configuration and a lipomatous component. Immunohistochemical investigation demonstrated intense, diffuse vimentin positivity and focal, less intense actin positivity in all three cases. At electron microscopy we observed a primitive cell of mesenchymal type, with cytoplasm poor in organelles and rich in filaments; this cell sometimes presented differentiation characteristics. SFT is at present the most correct term for the lesions presented here despite some morphological characteristics which differ from cases reported in the literature.

Key words: Solitary fibrous tumour – Mesenchymal tumour – Thyroid – Immunohistochemistry – Electron microscopy

Introduction

Solitary fibrous tumour (SFT) was first reported as an entity in 1931 by Klemperer and Rabin in the pleura, and for many years it was reported in the literature as a lesion that arose exclusively in that serous membrane. It was known as solitary (or localized) fibrous mesothelioma (Briselli et al. 1981; Dalton et al. 1979; El-Naggar et al. 1989; England et al. 1989; Rayburn and Godwin 1988; Steinetz et al. 1990; Stout and Himadi 1951) although some of these lesions were completely intrapulmonary rather than pleural (Goodland and Fletcher 1991; Yousem and Flynn 1988). There have been less frequent reports of SFT originating from other serous membranes, such as the pericardium (Dalton et al. 1979) and peritoneum (El-Naggar et al. 1989; Goodland and Fletcher 1991; Kim et al. 1992; Young et al. 1990). Recently, SFT have also been described in the mediastinum (Goodland and Fletcher 1991; Witkin and Rosai 1989), nasal cavities and paranasal sinuses (Kim et al. 1992; Witkin and Rosai 1991; Zukerberg et al. 1991) and, exceptionally, in some parenchymal organs, such as the liver (Kottke-Marchant et al. 1989), and in the parotid gland (Miettinen 1991).

We describe three cases of SFT arising in the thyroid: one is also characterized by a lipomatous growth pattern, which has never been described before in this lesion.

The various histomorphological growth patterns and the immunophenotypic and ultrastructural profiles are presented and a possible histogenesis of these cases is proposed.

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Materials and methods

Sections cut from 4–25 paraffin blocks from each case and obtained from material fixed in Bouin's solution (case 1) or 10% formalin (buffered in case 3) were stained with haematoxylin and eosin (H & E). Histochemical staining for periodic acid-Schiff (PAS), PAS digested with diastase, Masson's trichrome, and Gomori's silver impregnation were performed in each case. Immunohistochemical investigation was carried out with a peroxidase-antiperoxidase method and applying primary antibodies against cytokeratins (cocktail of monoclonal antibodies against cytokeratins 8, 18 and 19, Becton-Dickinson, Mountain View, Calif., USA; prediluted), vimentin (Diagnostic Products Corporation, Los Angeles, Calif., USA; prediluted), muscle-specific actin (Biogenex, Dublin, Calif., USA; prediluted), desmin (Dakopatts, Santa Barbara, Calif., USA; 1:50), neurofilament (Biogenex; prediluted), S-100 protein (polyclonal antibody, Dakopatts; 1:300), lysozyme (polyclonal antibody, Ortho Diagnostic System, Raritan, N.J., USA; prediluted), α-1-antitrypsin (polyclonal antibody, Dakopatts; 1:300), α-1-antichymotrypsin (polyclonal antibody, Dakopatts; 1:500), chromo-

granin A (monoclonal antibody, Biogenex; prediluted), and calcitonin (polyclonal antibody, Ortho Diagnostic System; prediluted). Tissue fragments for ultrastructural investigations were retrieved from formalin-fixed material from cases 2 and 3 only. The specimens were rinsed in running water and buffer solution, dehydrated and embedded in epoxy resin. Semi-thin sections were stained with toluidine blue and safranin and checked for light microscopical observation. Ultra-thin sections were stained with uranyl acetate and lead citrate and examined under a Zeiss-CEM 902 electron microscope.

Case reports

Case 1. A 44-year-old woman was hospitalized for an increase in size of a right thyroid nodule that had developed over 10 years and was scintigraphically cold. Ultrasonography demonstrated a solid nodule, apparently encapsulated, which measured $6 \times 3.5 \times 3$ cm and contained small cystic areas. Tri-iodothyronine, thyroxine and thyroid stimulating hormone levels were in the normal range. A right thyroid lobectomy was performed, and at gross examination we observed an encapsulated nodule with a maximum diameter of 6.5 cm, composed of homogeneous, greyish-white tissue of parenchymal-elastic consistency, and containing small areas of cystic degeneration. The patient was disease-free 5 years after surgery.

Case 2. A 61-year-old man admitted to hospital because of rapid growth of a left thyroid nodule which was cold at scintigraphy. The lesion appeared to be clearly circumscribed and solid at ultrasonography, and measured $6 \times 4.5 \times 3.5$ cm. A subtotal thyroidectomy was performed. Grossly, the nodule was well encapsulated, brownish in colour, and of hard consistency. Four years later, the patient was free of disease.

Case 3. A 32-year-old woman who presented with a nodule in the right thyroid lobe that was cold at scintigraphy. Ultrasonography revealed a solid, distinctly circumscribed nodule with a maximum diameter of 3.5 cm. The patient underwent a right lobectomy, and gross examination revealed a well-encapsulated, brownish nodule and focally cystic. Five years after surgery the patient was disease-free.

Results

In all cases the lesion was delimited by a hyaline fibrous capsule on light microscopy. This ranged from thin and almost non-existent to very thick, and was continuous in one case and discontinuous in the other two (Fig. 1).

In the areas not covered by the capsule the proliferating cells infiltrated the thyroid parenchyma, in small fascicles separating the follicles or in nodular structures. Isolated or small aggregates of thyroid follicles were observed immediately under the capsule, with evident resorption vacuoles and thyreocytes presenting signs of activation. Numerous histomorphologic patterns were observed (Table 1) and included bundles in storiform configuration (Fig. 2). Short, interlaced bundles of cells were arranged in whorls around a central axis consisting of a strand of connective tissue or a vessel, or tended to form globular type structures. Non-structured bundels were also seen (Fig. 3). These were always short and poorly organized, straight, curved or coiled, and intermingled in disorderly fashion. This type of cellular proliferation was mixed with varying amounts of extracellular substance and connective tissue matrix. The former was more frequently basophilic, amorphous, finely fibrillary and myxoid. The connective tissue matrix usually consisted of large collagen fibre aggregations that sometimes had a hyaline aspect and were coiled, and more rarely took the form of fine fibrils.

A fibrous pattern occurred (Fig. 4). A connective tissue matrix was prevalent with compact collagen bundles that tended to overwhelm the proliferating cells. The extracellular substance and stromal matrix contained extravasated erythrocytes, and inflammatory material including lymphocytes, monocytes and mast cells, particularly numerous in case 1. In some areas a compact, highly cellular, non-structured pattern was also evident (Fig. 5). In a varying percentage in all three cases and as the prevalent pattern in case 2, the bundle configuration of the cellular proliferation was lost and a completely non-structured growth was seen, with cells compactly and irregularly arranged with little or no extracellular substance and/or connective tissue matrix. A loose, non-structured pattern was seen (Fig. 6) where the proliferation consisted of isolated cells or small cell aggregates enmeshed in abundant extracellular substance. An haemangiopericytic pattern (Fig. 7) was observed in a fair percentage of the lesion in all three cases, and was characterized by cellular proliferation mixed with numerous vascular spaces of varying morphology and diameter. The latter structures frequently appeared as small tortuous clefts with an indistinguishable lumen or larger vascular spaces having a wavy or branched outline delimited by a more or less evident endothelial lining; more rarely the spaces were roundish with regular contours. The smaller and thinner vascular structures were seen in highly cellular areas of the lesion; the larger or pseudocystic structures were associated with poorly cellular areas rich in extracellular substance.

Case 2 presented several lipomatous areas (Fig. 8) with a lobular or cord-like pattern poorly delimited from the surrounding proliferation. These areas were characterized by cells with cytoplasm containing lipid vacuoles, multiple and small, less numerous and larger, occasionally occupying all the cytoplasm.

The proliferating cells, monomorphic and cytomorphologically similar in two of the three lesions, were spindle-shaped with roundish, oval or elongated nuclei, regular or moderately indented profile, finely and regularly dispersed chromatin, and sometimes a small, roundish central nucleolus; the cytoplasm, from scanty to moderate in amount, was weakly eosinophilic and had a fibrillary aspect and generally indistinct margins (Fig. 9). In case 3 the cells had more polymorphic nuclei, with more clumped chromatin and irregular nucleoli.

Mitotic figures were rare in two cases and absent in the other (case 2).

Gomori's silver impregnation revealed considerable numbers of reticulin fibres, thick and fragmented or thinner and continuous, completely delimiting individual cells. PAS staining was focally positive in the cytoplasm as fine granules which were sensitive to diastase.

The proliferating cells were diffusely positive for vimentin in all three lesions, with intensity varying according to the cell type and histomorphological pattern. In general, the cells presented a uniform, moderate positi-

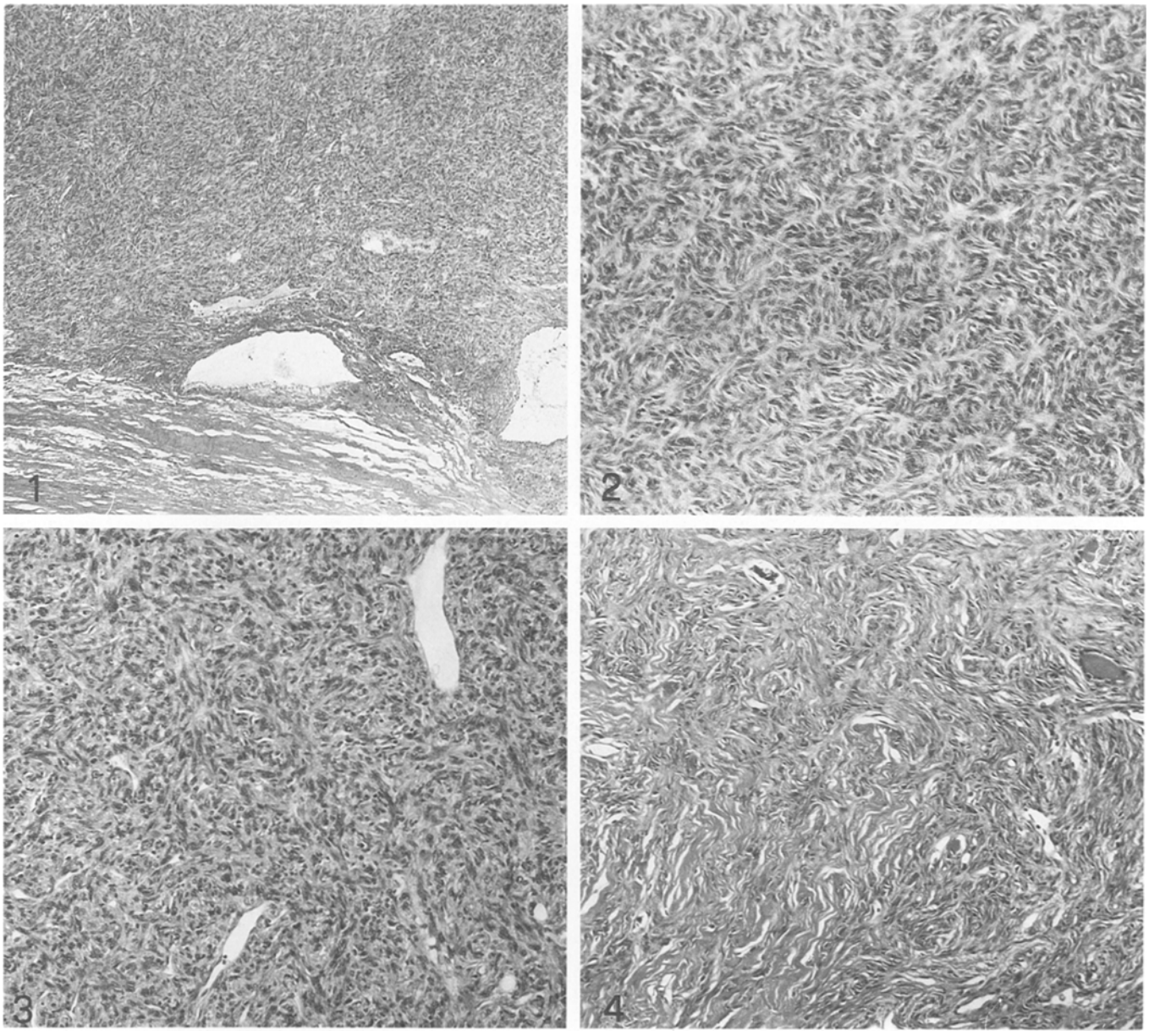


Fig. 1. The lesion is delimited by a thick but sometimes discontinous fibrous capsule and contains entrapped thyroid follicles. Haematoxylin and eosin, ×62.5

Fig. 2. Short, coiled, interlaced bundles of cells, centered on an axis of connective tissue or on a poorly evident vascular cleft (bundles in storiform configuration). Haematoxylin and eosin, ×125

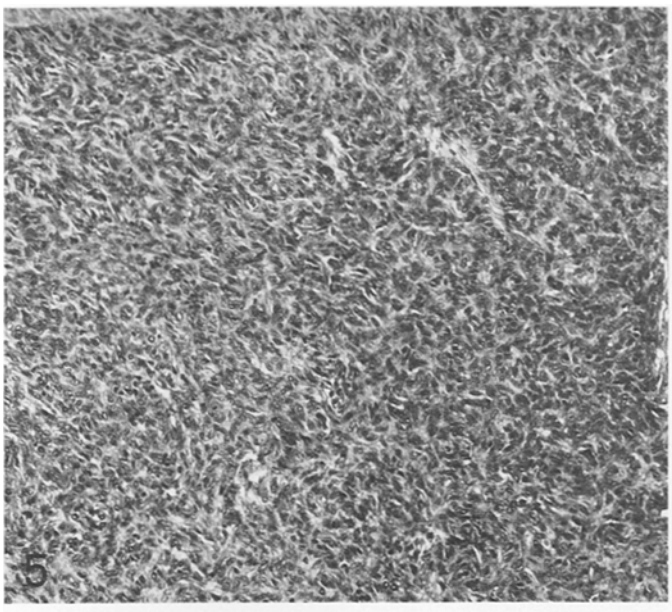
Fig. 3. Short, coiled, irregularly intertwined bundles of cells mixed with a moderate amount of connective tissue matrix and irregular vascular lumina (non-structured bundles). Haematoxylin and eosin, ×125

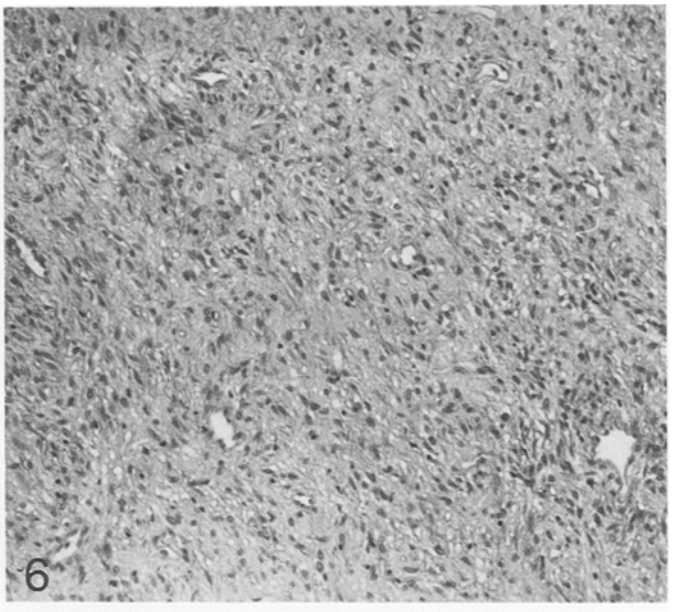
Fig. 4. Short, irregular bundles of cells separated by abundant extracellular substance and connective tissue matrix tending to isolate the individual cells (fibrous pattern). Haematoxylin and eosin, ×125

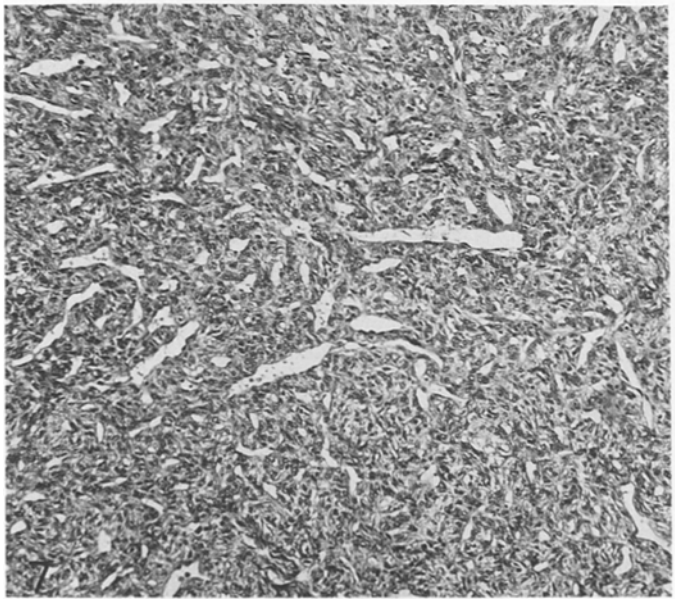
Table 1. Histomorphological patterns of solitary fibrous tumour of the thyroid

Case number	Bundles in storiform configuration	Non-structured bundles	Fibrous	Highly cellular, non-structured	Loose, non-structured	Haemangio-pericytic	Lipomatous
1	+++	+/−	+	+	++	++	−
2	+	++	+/−	+++	−	++	++
3	+++	+	++	+/−	++	+	−

−, Not present; +/−, 5–10%; +, 15–25%; ++, 25–40%; +++, >40%







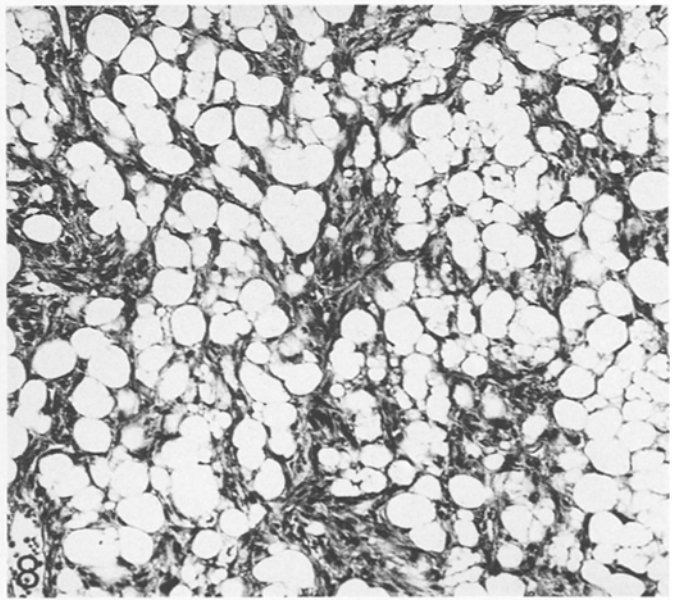


Fig. 5. Highly cellular area characterized by proliferating elements not organized to form recognizable morphological structures (compact, highly cellular, non-structured pattern). Haematoxylin and eosin, ×125

Fig. 6. Cell isolated or organized in abortive bundles and scattered in abundant extracellular substance of myxoid type (loose, non-structured pattern). Haematoxylin and eosin, ×125

Fig. 7. Irregular bundles of cells and numerous vascular spaces of varying morphology from thin clefts to wide lacunae, sometimes irregular in profile and delimited by flattened endothelial cells (haemangiopericytic pattern). Haematoxylin and eosin, ×125

Fig. 8. Irregular cords and lobules of lipid cells, crossed by bundles of proliferating cells and vascular structures (lipomatous pattern). Haematoxylin and eosin, ×125

vity, especially in the cytoplasmic projections, in a coarsely fibrillary pattern or in the form of a large perinuclear globule (Fig. 10). In all three cases we observed isolated spindle-shaped cells scattered in the proliferation with fibrillary positivity for actin in the cytoplasmic projections (*inset*).

Immunostaining for cytokeratins, desmin, neurofilaments, S-100 protein, lysozyme, α-1-antitrypsin, α-1-antichymotrypsin, chromogranin A and calcitonin was negative.

On ultrastructural examination, the cytoplasm of the proliferating cells contained a few cisternae of rough endoplasmic reticulum, more abundant, dilated and tortuous in some cells of case 2. There was smooth endoplasmic reticulum, one or more small Golgi complexes, numerous micropinocytotic vesicles, a fair number of mitochondria, glycogen aggregates in variable quantity from cell to cell and scattered roundish or oval primary lysosomes; in a few cells in both cases ciliated bodies and abortive cilia were seen projecting into the extracel-

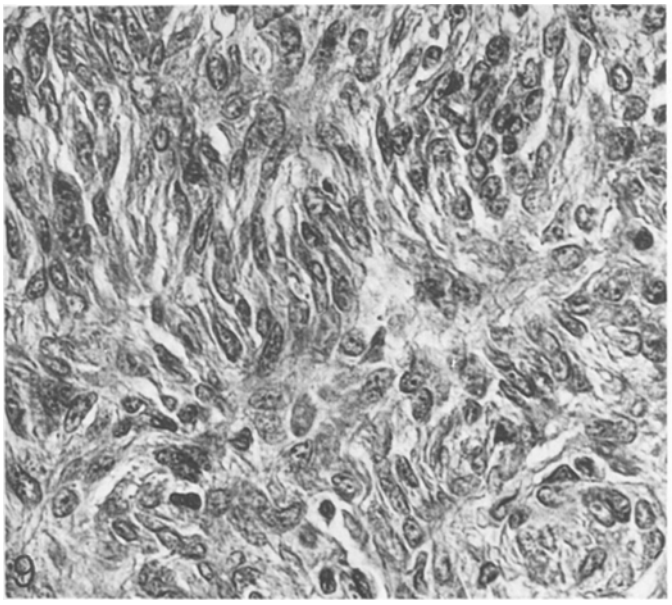


Fig. 9. Spindle-shaped cells of case 1, characterized by monomorphic, roundish or oval nuclei, moderately clumped and peripheral chromatin and sometimes one or more small and irregular nucleoli; the cytoplasm is scanty and finely fibrillary and the cells have poorly defined membranes. Haematoxylin and eosin, ×425

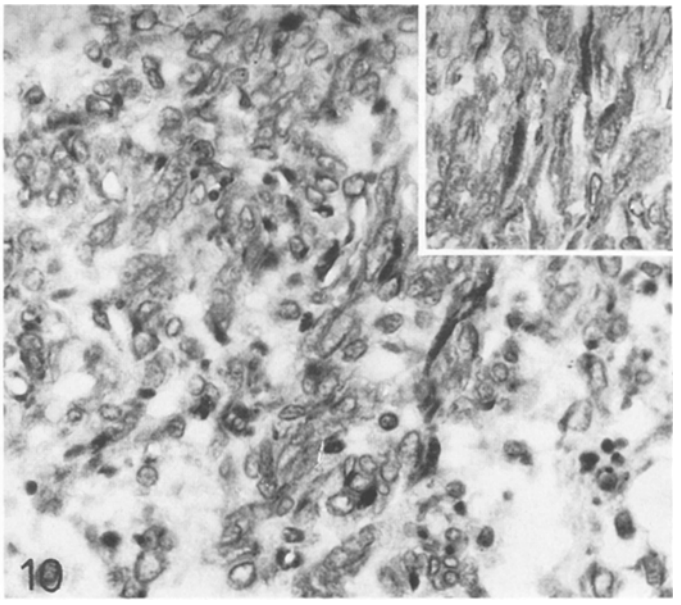


Fig. 10. The cells present diffuse, finely fibrillary positivity for vimentin, more evident in the cytoplasmic projections and sometimes in the form of one or more perinuclear dots. Antivimentin, ×125. *Inset:* A small percentage of the proliferating cells show an intense, uniform reactivity also to actin. Antimuscle-specific actin, ×275

lular space. In the cytoplasm of cells from case 2 we found a large number of roundish lipid vacuoles (Fig. 11).

The cytoskeleton was composed of abundant intermediate filaments generally arranged in large, loose, curved bundles, most often evident in cytoplasmic projections, sometimes interlaced and whorled, even forming globular-filamentous bodies (Fig. 12). In some cells, most numerous in case 3, long straight bundles of microfilaments were observed close to the cytoplasmic membrane and in the projections, with one or more dense bodies (Fig. 13).

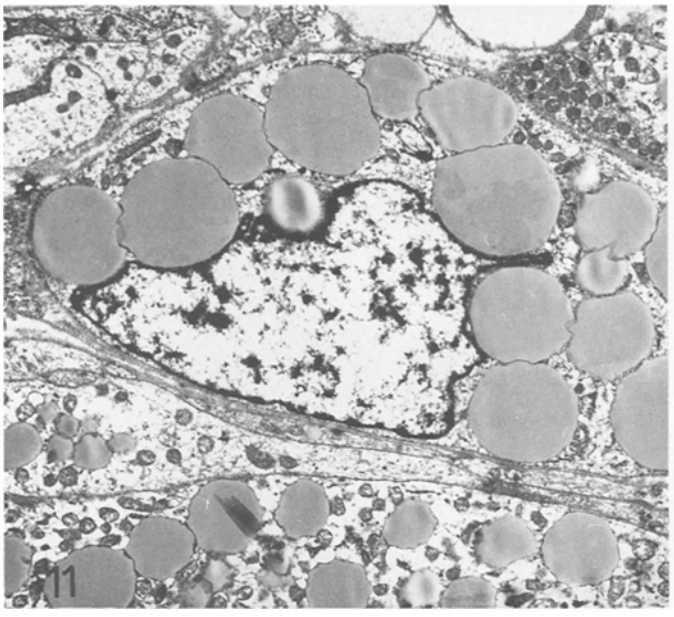
All the cells had large, thick, sometimes intertwined and less frequently longer and thinner cytoplasmic projections. The cytoplasmic membrane presented numerous junctions; hemidesmosomes, mature and immature desmosomes and rare tight and undifferentiated junctions. The extracellular space close to the cytoplasmic membrane presented one or more layer of basal lamina material of varying thickness.

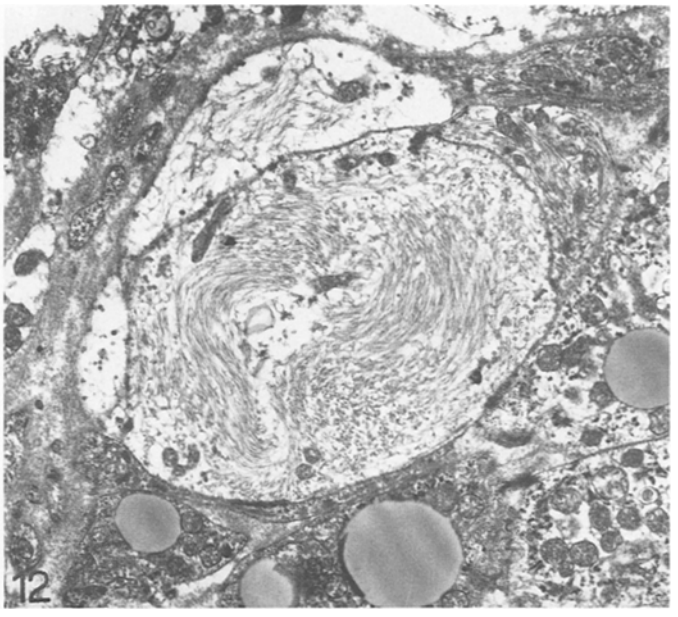
Discussion

Benign thyroid mesenchymal tumours are rare. Four cases of haemangiopericytoma (Justrabo et al. 1989; Kallenberg and Anagnostaki 1979; Proks 1961; Tano Assini et al. 1968), two leiomyomas (Andrion et al. 1988; Hendrick 1957) and four schwannomas (Andrion et al. 1988; Delaney and Fry 1964; Goldstein et al. 1982; Kneeland-Frantz 1962) are reported.

The present cases of SFT of the thyroid are the first to be described. They probably arose in the stroma of the gland; none of them seemed to be attached to the capsule. Based on their histomorphological features, some primary mesenchymal thyroid tumours described in the literature, namely a case of haemangiopericytoma (Justrabo et al. 1989), a schwannoma (Goldstein et al. 1982), and a liposarcoma (Nielsen et al. 1986) could be classified as SFT.

In our cases the range of age at onset (32–61 years) and the gross findings were similar to those of SFT in other primary locations; there were two women and one man and the biological behaviour was benign. These characteristics are those of SFT in general. Histomorphologically, the lesions were extremely polymorphic; the various growth patterns described by us were present in different percentages in the three cases (Table 1). We observed a lipomatous pattern not previously reported; in the normal thyroid scant adipose tissue can be observed near the capsule and around the vessels (Meissner and Warren 1968). Furthermore, aggregates of lipocytes have been described in thyroid lesions and in benign follicular neoplasms such as adenolipoma (Hjorth et al. 1986; Schröder et al. 1984a), hamartomatous adiposity (Asirwatham et al. 1979), diffuse lipomatosis (Plaut 1951), lipid-rich cell adenoma (Schröder et al. 1984b), thyro-lipome (Pages and Tiraskis 1985) and amyloid goitre with infiltration of adipose cells (von Bettendorf et al. 1980). Initially the presence of adipose tissue was interpreted as a degenerative phenomenon and thus related to the age of the thyroid tissue and/or the lesion (Arndt 1924; Gossmann 1927). Subsequent studies have suggested a metaplastic origin from fibroblasts of thyroid stroma (von Bettendorf et al. 1980; Pages and Tiraskis 1985; Schröder and Böcker 1985). An exuberant





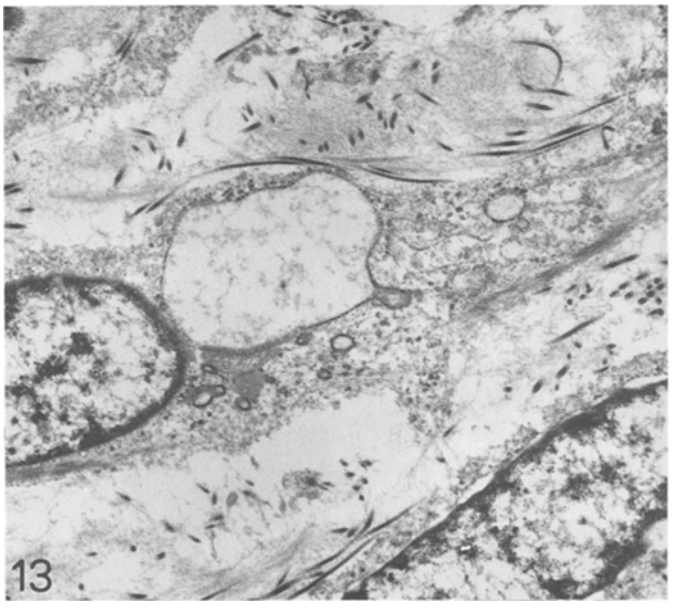


Fig. 11. The cells of case 2 contain cytoplasm that is almost entirely occupied by lipid vacuoles compressing the cytoplasmic organelles and indenting the nuclear membrane; the remaining cytoplasm contains mono- or pluriparticulate glycogen aggregates. Uranyl acetate-lead citrate, ×4,700

Fig. 12. The cells have long, wide cytoplasmic projections of non-structured type, containing mainly intermediate filaments organized in loose bundles or in a whorled pattern and tending to form large globular-filamentous bodies. Uranyl acetate-lead citrate, ×7,400

Fig. 13. Some cells are characterized by straight cytoplasmic projections containing abundant rough endoplasmic reticulum in dilated and sometimes cyst-like cisternae and, close to the cytoplasmic membrane, short bundles of microfilaments with more dense bodies. Uranyl acetate-lead citrate, ×14,300

reactive proliferation of pseudosarcomatous thyroid stromal cells has been described in malignant follicular neoplasms, e.g. papillary carcinoma (Chan et al. 1991; Ostrowski et al. 1989).

Thyroid stromal cells are apparently able to react exuberantly to various stimuli, to proliferate variably, and to differentiate along various mesenchymal lines.

Our immunohistochemical results agree with the immunophenotypic pattern described by some authors (England et al. 1989; Goodland and Fletcher 1991; Steinetz et al. 1990; Witkin and Rosai 1989); we observed a diffuse immunoreactivity for vimentin in all cases and a focal positivity for actin. The latter finding was probably confirmed by ultrastructural examination which demonstrated myofibroblast-like cells.

Electron microscopy in our cases revealed prevalently immature mesenchymal cells characterized by abundant intermediate filaments in large bundles and globular structures, abortive or relatively well-structured cilia and abundant basal lamina material. In addition to this type of cell various differentiation characteristics were expressed: cells with adipose and myofibroblastic differentiation (case 1) and fibroblastic and myofibroblastic (case 2). Thus, in the course of the natural history of the lesion, a variable proportion of the proliferating cell population, starting from a non-committed mesenchymal cell, may undergo differentiation towards one or more mature mesenchymal lines.

The histogenesis of SFT is still controversial. In recent reports the authors propose a purely mesenchymal origin for the lesion from an undifferentiated cell or a cell with fibroblastic characteristics without a clear mesothelial differentiation (Dervan et al. 1986; El-Naggar et al. 1989; Kim et al. 1992; Witkin and Rosai 1989, 1991).

Our cases therefore represent a new primitive mesen-

chymal lesion of the thyroid, which should be included in differential diagnosis of the following neoplastic entities: medullary carcinoma (spindle cell variety), haemangiopericytoma, schwannoma, fibroma and fibrosarcoma, pleomorphic lipoma, spindle cell lipoma and liposarcoma, fibromatosis, fasciitis, benign and malignant fibrous histiocytoma, an exaggerated stromal response in a malignant thyroid neoplasm, and finally peculiar stromal features related to involution of a benign follicular lesion.

We consider SFT the most correct designation for the tumours reported even though they presented some histomorphological and ultrastructural characteristics different from those of other reported cases. SFT is not a well-defined pathological entity; it should probably be considered as a stromal neoplasm arising in visceral, parenchymal organs and serous membranes or, at least in some cases, a mesenchymal proliferation of pseudotumoral type.

Acknowledgements. The authors are grateful to Paola Preti for technical assistance and Michele Masullo for secretarial collaboration.

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