Virchows Archiv A Pathol Anat (1990) 417:273–276

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Lipid-rich cell thyroid adenoma: histopathology with comparative lipid analysis*

K. Tóth[1], I. Péter[1], T. Kremmer[2], and J. Sugár[1]

Departments of [1] Human and Experimental Tumorpathology and [2] Biochemistry, National Oncological Institute, 1122.Budapest, Ráth György street 7–9, Hungary

Summary. A second case of the unique lipid-rich cell thyroid adenoma is described complemented by detailed lipid analysis. New observations were made. The cytoplasm of the tumour cells contained scattered, aggregated sudanophil crystals; under polarized light the frozen, unstained sections exhibited numerous birefringent lipid crystals; electron microscopy provided further evidence that the clear cell appearance was due to intracellular lipid droplets with scanty glycogen particles. Comparative lipid analysis by thin layer chromatography and high-pressure liquid chromatography (HPLC) revealed quantitative and qualitative differences in lipid composition of tumour cells when compared with goitre cells from normal thyroid gland and subcutane fat. Qualitative differences in triglyceride composition (by HPLC) between tumour cells and subcutaneous fat indicated that the fat accumulation in the follicle cells was not a result of simple storage, but an expression of altered intracellular lipid metabolism.

Key words: Thyroid – Lipid-rich cell adenoma – Crystals – Lipid analysis – Subcutaneous fat

Introduction

Schröder et al. (1984) first reported the lipid-rich follicle cell thyroid adenoma. We report a further case where the histopathology of the tumour was complemented by polarization, electron microscopy and comprehensive chromatographic analysis of lipids. The lipid composition of the tumour cells has been compared with that of goitre, normal thyroid gland and subcutaneous fat in order to determine whether the fat accumulation in the cells was simple storage or the consequence of altered lipid metabolism (Tóth et al. 1989).

Offprint requests to: J. Sugár

* Preliminary results presented at the XII European Congress of Pathology, Porto, Portugal, 1989

Case report

The left thyroid lobe of a male, 62-year-old patient was removed for nodular goitre. On its cut surface there was a well-circumscribed, encapsulated, yellowish-red area (20 mm diameter) clearly distinguishable from the other nodules. Histologically, a tumour consisting of clear cells (Fig. 1 A) was surrounded by a thin capsule. The signet-ring cell appearance of the tumour cells was visible at high power magnification. There was no evidence of capsular or vascular invasion. The cytoplasm of tumour cells showed negative periodic acid-Schiff (PAS) reaction and strong positive staining with Sudan III dye due to the high amount of fat (Fig. 1 B). Some parts of the tumour contained numerous sudanophil crystals. Some follicular structures were still recognizable and their colloid content gave a positive PAS reaction. Under polarized light the frozen, unstained sections exhibited numerous birefringent lipid crystals in the cytoplasm (Fig. 2 A). They were stable at 37° C but removable with lipid solvents (ether-ethanol mixture). The follicle cell origin of the tumour was confirmed by the intraluminal and marginal cytoplasmic positivity for thyroglobulin (Fig. 2 B) and thyroxine using immunoperoxidase techniques. Electron microscopy also confirmed that the clear cell appearance was due to the cytoplasmic accumulation of lipid vacuoles (Fig. 3).

Results

Results of lipid analyses of lipid-rich adenoma, goitre, normal thyroid gland and subcutaneous fat tissue carried out by thin layer chromatography (TLC) are demonstrated in Fig. 4. The quantitative lipid compositions are summarized in Table 1. High-performance liquid chromatographic (HPLC) separation of triglycerides extracted from (a) lipid-rich adenoma and (b) from subcutaneous fat tissue was performed according to Smith et al. (1980) (Fig. 5).

As a result of the lipid analysis by TLC and HPLC, quantitative and qualitative differences were revealed mainly in the triglyceride fraction of the lipid composition of tumour cells when compared with those of goitre, normal thyroid gland and subcutaneous fat. Qualitative differences in triglyceride composition between tumour cells and subcutaneous fat (Fig. 5) indicate that the extreme fat accumulation in the follicle cells is not a result

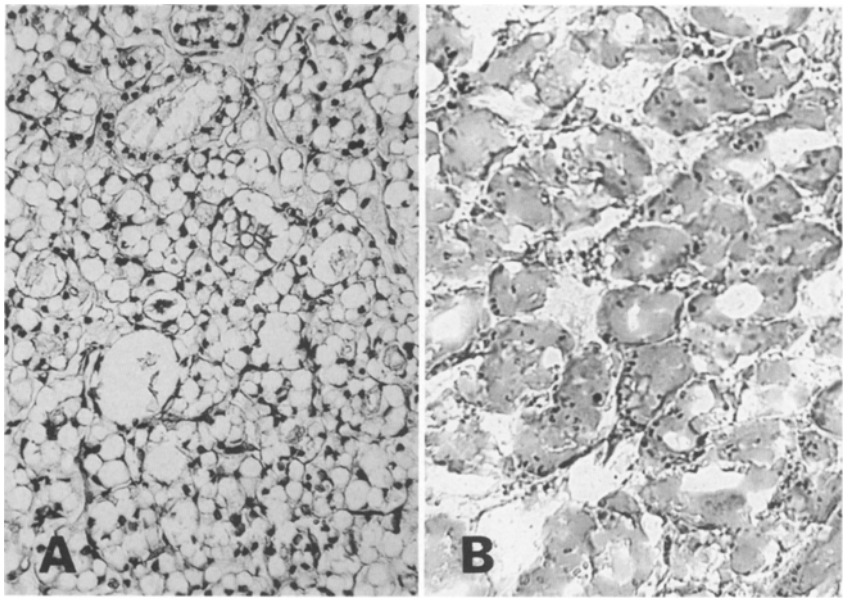

Fig. 1. A Lipid-rich cell thyroid adenoma. The tumour consists of clear cells. H & E ×175 **B** The cytoplasm of tumour cells shows strong positive staining with Sudan III. ×175

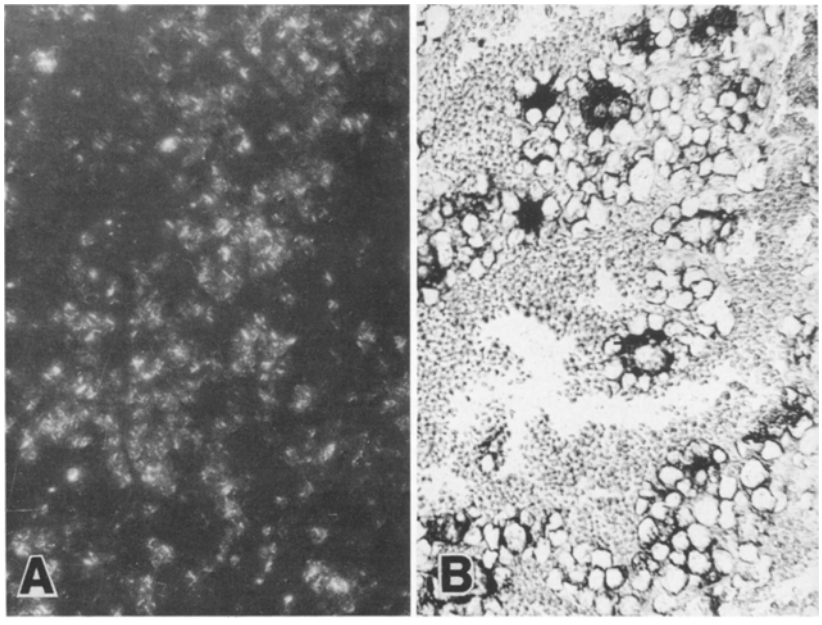

Fig. 2. A Under polarized light the frozen, unstained sections exhibited numerous birefringent lipid crystals in the cytoplasm. ×175. **B** The follicular origin of the adenoma is confirmed by intraluminal and marginal cytoplasmic positivity for thyroglobulin using immunoperoxidase technique. PAP reaction, ×175

of simple storage, but the expression of the altered intracellular lipid metabolism.

Discussion

Morphological features found in clear cells of the thyroid are the formation of vesicles, mitochondrial swelling, accumulation of glycogen and/or fat, and deposition of intracellular thyroglobulin (Carcangiu et al. 1985; Schröder and Böcker 1986; Péter et al. 1989). The presence of neutral mucin in tumour cells in a rare type of thyroid adenoma has been reported (Mendelsohn 1984). Mature interstitial adipose tissue can be observed in a wide range of benign and malignant thyroid lesions as documented in a recent comprehensive study and review (Gnepp et al. 1989). Our study, however, deals with the extreme accumulation of intracellular lipid in the neoplastic follicular cells of the tumour. In follicular adenoma the clear cell phenotype was attributed to the accumulation of lipids in the cytoplasm of the tumour cells detected after Sudan III staining by light microscopy. Sudanophilic, probably aggregated lipid, crystals in the cytoplasm of the cells appeared in some parts of the tumour. Though they might be interpreted as artefacts of the staining procedure, it was not possible to reproduce the same phenomenon in other fat-containing tissues.

It seems reasonable to presume that the sudanophilic lipid crystals in the cytoplasm consisted mainly of trigly-

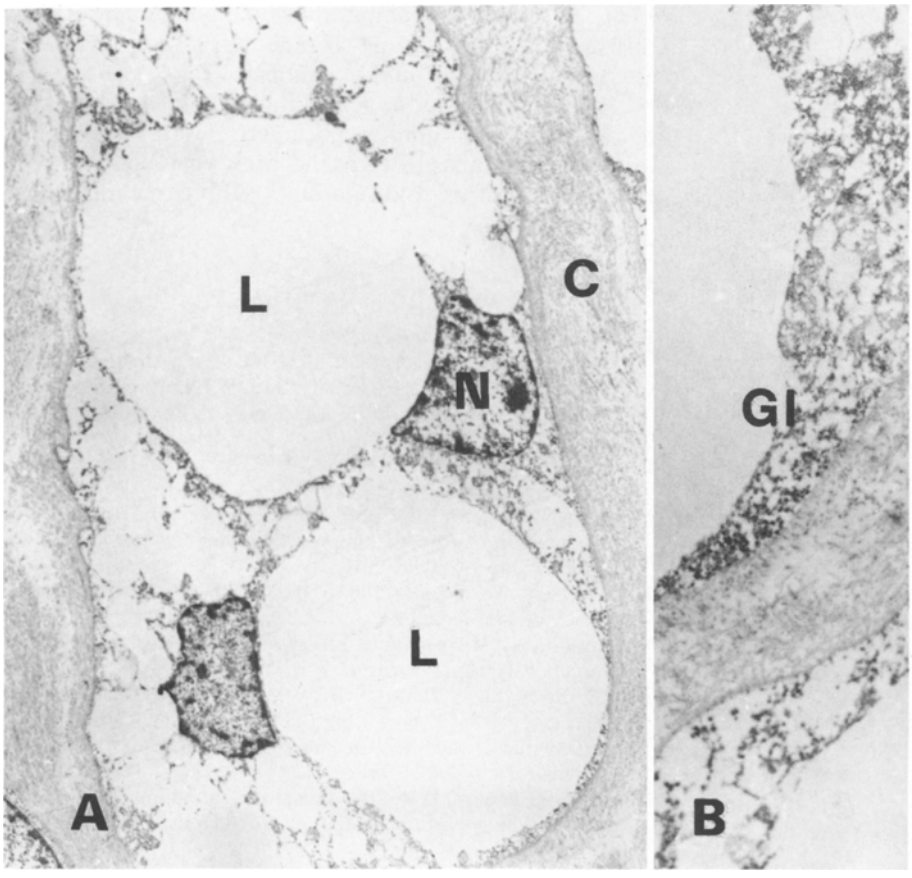

Fig. 3A. Electron microscopy demonstrates that the clear cell appearance is due to cytoplasmic accumulation of lipid vacuoles (*L*). *GL*, Glycogen particles of beta type; *N*, nucleus; *C*, connective tissue fibres. ×1460

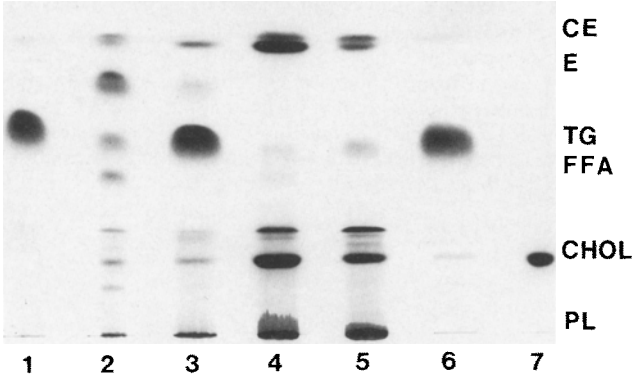

Fig. 4. Thin layer chromatography (TLC) of tissue lipids, on Silica gel pre-coated plate (Merck, Darmstadt) using a solvent system of petrol ether:diethylether:acetic acid (85:15:3, v/v) and developed by charring technique. *CE*, Cholesterol esters; *E*, ether and plasminogen lipids; *TG*, triglycerides; *FFA*, free fatty acids; *CHOL*, cholesterol; *PL*, polar (phospho) lipids. Lines: *1*, TG; *2*, reference mixture of lipids; *3*, lipid-rich adenoma; *4*, goitre; *5*, normal thyroid gland; *6*, subcutaneous fat tissue; *7*, CHOL

Table 1. Lipid composition of normal human thyroid gland, goitre, lipid-rich thyroid adenoma and subcutaneous fat tissue

Tissues	Lipid content of wet tissue (rel. %)	Lipid composition in rel.%[a]					
		TG	E	PL[b]	CHOL	CE	FFA
Normal human thyroid gland	7.2	13.0	–	26.8	15.3	16.7	22.2
Goitre	6.9	11.0	4.0	22.2	19.1	19.7	16.0
Lipid-rich adenoma	78.8	53.1	10.0	1.6	8.8	12.1	13.9
Human subcutaneous fat tissue	96.5	77.2	3.6	3.2	6.1	7.3	2.3

[a] Determined by photodensitometry on thin-layer chromatograms. For abbreviations, see Fig. 4

[b] Calculated from the organic phosphorous content measured in the lipid extracts

cerides because these were the main fraction determined by TLC and HPLC and their individual triglyceride species differed from that in the normal subcutaneous fat tissue detected by HPLC. The change in triglyceride composition may play a role in the crystal formation.

The birefringence of lipid crystals in the tumour is equivalent to the birefringence of different lipid crystals found in frozen mature adipose tissue. Lipids can form crystals in other pathological conditions, such as subcutaneous fat necrosis of the newborn (Balázs 1987). Trig-

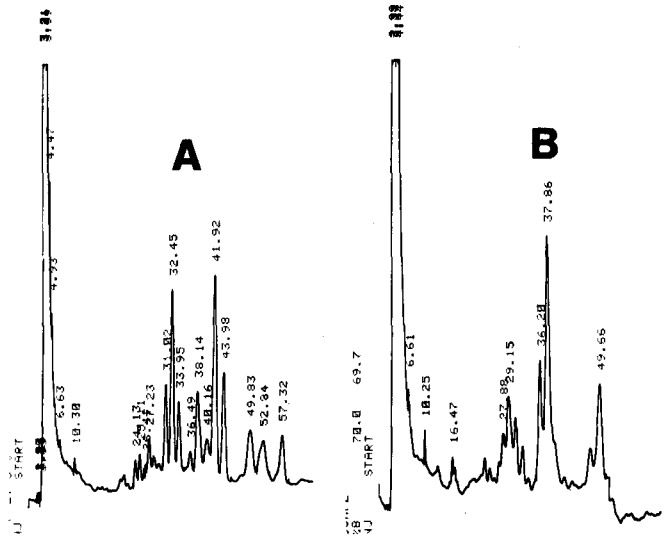

Fig. 5. High-performance liquid chromatographic separation of triglycerides extracted from (**A**) lipid-rich adenoma and (**B**) from subcutaneous fat tissue

lycerides may also occur in crystalline form as shown by X-ray diffraction analysis (Horsfield and Yardley 1965) and may show birefringence under polarized light (Silverberg 1983). In our electron micrographs these crystals were not visible, due to the dissolution of lipids by alcohol during the preparation of the specimen. In the fine structure of the tumour, however, the large empty intracytoplasmic vacuoles were dominant, suggesting a lipid-vacuole nature. The glycogen particles of beta-type were arranged in groups among the vacuoles, but their number was not considerable and we consider that glycogen is not really essential in shaping the clear cell character of the tumour.

The lipid-rich follicle cell is most likely to be seen as a result of metaplastic transformation (Schröder et al. 1984). Based on our comparative lipid analysis by HPLC this process is not simple storage, but an expression of altered intracellular lipid metabolism.

This unique, lipid-rich cell thyroid adenoma should be added to the other well-known variants of benign follicular adenomas listed in the latest WHO histological classification of thyroid tumours (Hedinger et al. 1989).

References

Balázs M (1987) Subcutaneous fat necrosis of the newborn with emphasis on ultrastructural studies. Int J Dermatol 26:227–230

Carcangiu ML, Sibley RK, Rosai J (1985) Clear cell change in primary thyroid tumours. A study of 38 cases. Am J Surg Pathol 9:705–722

Gnepp DR, Ogorzalek JM, Heffes CS (1989) Fat-containing lesions of the thyroid gland. Am J Surg Pathol 13:605–612

Hedinger C, Williams ED, Sobin LH (1989) The WHO histological classification of thyroid tumors: a commentary on the second edition. Cancer 63:908–911

Horsfield GI, Yardley H (1965) Sclerema neonatorum. J Invest Dermatol 44:326

Mendelsohn G (1984) Signet-cell-simulating microfollicular adenoma of the thyroid. Am J Surg Pathol 8:705–708

Péter I, Besznyák I, Szántó J, Füzy M, Bodó M, Sugár J (1989) Clear cell thyroid cancer – undifferentiated type – an immunohistochemical and electron microscopical study. Arch Geschwulstforsch 59:121–128

Schröder S, Böcker W (1986) Clear-cell carcinomas of thyroid gland: a clinicopathological study of 13 cases. Histopathology 10:75–89

Schröder S, Hüsselmann H, Böcker W (1984) Lipid-rich cell adenoma of the thyroid gland. Report of a peculiar thyroid tumour. Virchows Arch [A] 404:1050–1089

Silverberg SG (1983) Principles and practice of surgical pathology. Wiley, New York

Smith SL, Novotny M, Moore SA, Felten DL (1980) Studies of hyperlipidemia in drug induced diabetic rats by high performance liquid chromatography. J Chromatogr 222/1:19–26

Tóth K, Péter I, Kremmer T, Sugár J (1989) Lipid-rich cell thyroid adenoma: detailed histopathologic study with lipid analysis. Pathol Res Pract 185:162