Parenchymatous thyroid nodules: a histocytological study of 31 cases from a goitrous area

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Abstract

Aims: To analyse the benefits and limitations of fine needle aspiration in the cytological differentiation of parenchymatous nodular goitres from follicular tumours in an endemic area.

Methods: Cytological smears of fine needle aspirates from 31 parenchymatous nodular goitres were studied. A sample from the punctured nodules was fixed in formalin and stained with haematoxylin and eosin for histological analysis.

Results: All nodules occurred in a multinodular gland, were well circumscribed, did not compress surrounding thyroid tissue, and for the most part, were unencapsulated. Two cases showed cytological features of nodular goitre, two of colloid cysts; the remaining 27 were cytologically indistinguishable from follicular lesions.

Conclusions: Most of the parenchymatous nodules studied had features suggestive of follicular lesions or neoplasia, but surgical treatment should only be considered after hormone treatment has proved unsuccessful, and when they are not suspected as malignant clinically. Fine needle aspiration is useful as a diagnostic and screening aid, but the results should be interpreted with caution to prevent unnecessary surgery.

varied appearance. It is often morphologically referred to as colloid nodule when large colloid-rich follicles predominate; as parenchymatous (hyperplastic, adenomatous) nodule when it shows hypercellularity, pseudopapillae, normofollicular, microfollicular and trabecular structures; and as mixed when it shows an admixture.^{1,2} Parenchymatous nodular goitres are architecturally indistinguishable from follicular adenomas and occur more frequently in endemic areas than in iodine-rich regions.^{1,3,4} In a previous study on colloid and mixed nodular goitres we found that cytological interpretation can be difficult.⁵ The aim of this study was to analyse the benefits and limitations of fine needle aspiration (FNA) cytology from parenchymatous nodules.

Methods

Cytological smears from 31 parenchymatous nodular goitres with histological correlation were compiled from 1758 consecutive thyroid FNAs performed in our hospital between November 1984 and December 1989. All patients presented with a multinodular goitre that showed cold nodules on a thyroid scintigram. Large or clinically suspicious nodules were aspirated. FNA was carried out on the parenchymatous nodule, as assessed clinicopathologically on resected thyroid tissue. FNA was mainly based on the technique used at the Karolinska Hospital in Stockholm; the pathologist performs the FNA as well as makes and interprets the smears using mainly the May-Grünwald-Giemsa/(MGG) staining tech-

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Nodular goitre is a lesion of wide ranging and

Figure 1 Well circumscribed unencapsulated parenchymatous nodules with intervening uncompressed thyroid tissue. Note central oedematous stroma (left) and haemorrhage (right) in the nodules (haematoxylin and eosin).

nique.⁶ The description of cell nuclei was based primarily on the Papanicolaou (PAP) stain that was also used in most of the cases. The same pathologist (HRH) processed the formalin fixed specimen and a representative sample from the punctured nodule was selected, embedded in paraffin wax, and stained with haematoxylin and eosin for histological analysis. The histological diagnosis of parenchymatous nodular goitre was based on that of previous studies.^{1,2,7}

Results

HISTOLOGICAL FINDINGS

All nodules studied occurred in a multinodular gland, were well circumscribed, did not compress the surrounding thyroid tissue, and most of them were unencapsulated (fig 1). Histologically, these were hypercellular nodule(s) composed of microfollicles (seven cases), medium sized follicles (two cases), or an admixture (21 cases) that also contained a minor proportion of large follicles (eight cases), trabeculae (four cases), and solid areas (one case). One nodule with a mixed architectural pattern was exclusively composed of oxyphilic (Hürthle) cells (fig 2). About a third of the cases showed large areas of oedematous stroma tissue

(figs 1 and 2). Degenerative changes in the stroma such as fibrosis, haemorrhage, cholesterol deposits with foreign body giant cell reaction, and calcification, were present in about one fifth of the cases.

CYTOLOGICAL FINDINGS

Percentages of cytological findings are shown in the table. The smears in general showed tissue fragments harbouring follicles (fig 3). Trabecular structures were seen in four cases (fig 4). Epithelial cells also occurred individually, in sheets, and clusters that often showed nuclear overlapping (figs 5–7). An occasional sheet of cells arranged in a honeycomb pattern and a large follicle were present in one case each, respectively. Small and medium sized follicles occurred in most cases, about one fourth of which contained intraluminal colloid material (fig 1). The epithelial cells (conventionally regarded as NOS) showed a nuclear cytoplasmic ratio of 1 : 1.5–2, pale cytoplasm with ill defined boundaries, round to oval, central to eccentric nuclei that often showed a diffuse chromatin pattern and a small or prominent single nucleolus (figs 5–6). Transitional cells in a wide range of nuclear

Figure 2 Thyroid nodules showing: (A) small and medium sized follicles, (B) medium sized and large follicles, (C) thick trabeculae with microfollicular component, and (D) follicles lined by oxyphilic cells (haematoxylin and eosin).

Figure 3 Tissue fragment showing micro- and medium-sized follicular structures. Some follicles contain intraluminal colloid (arrows) (May-Grünwald-Giemsa).

Figure 5 Clusters and sheets of epithelial cells with ill defined pale cytoplasm and regular nuclei that overlap slightly (May-Grünwald-Giemsa).

sizes were also observed (fig 10). Occasional nuclear grooving occurred in about one fourth of the cases, and a few nuclear cytoplasmic inclusions were present in two cases (fig 8). Pleomorphic cells with large bizarre nuclei were observed in three cases (fig 9). Background colloid material occurred as dense amorphous masses (seven cases) or was diffusely distributed (five cases) (figs 10–11). Two smears were acellular and showed only diffuse background colloid material. Macrophages, usually few in number, occurred in some cases.

Oxyphilic cells were characterised by abundant, well demarcated, polyhedral cytoplasm containing fine dark (MGG) or eosinophilic (PAP) granules, and one or two round to oval, central to eccentric nuclei with a fine granular chromatin pattern and prominent single or double nucleoli. Nuclei were often of varying sizes and were sometimes irregular and pleomorphic. These cells occurred either in combination with NOS cells (three cases) (fig 10) or as the only cellular element in one case

(fig 7) in which histology showed an oxyphilic cell nodule. Two other cases with oxyphilic cells also showed clusters and sheets of small

Percentage of cytological findings* in 31 parenchymatous nodules compared with 49 colloid/mixed thyroid nodules

	Parenchymatous nodules	Colloid/mixed ⁵ nodules
Microfollicles	74 (1/4+)	19 (1/3+)
Normofollicles	71 (1/4+)	62 (1/4+)
Large follicles	3 (1+)	48 (1/2+)
Trabeculae	13 (1/3+)	
Honeycomb pattern	6 (1/2+)	42 (1/3+)
Small cells	3 (2+)	52 (2/5+)
NOS cells	84 (3/5+)	96 (2/5+)
Nuclear grooving	26 (1/2+)	17 (1/2+)
Nuclear inclusions	6 (1/2+)	6 (1+)
Oxyphilic cells	19 (2/5+)	42 (2/5+)
Pleomorphic cells	6 (1/2+)	4 (1/2+)
Colloid material	55 (1/5+)	83 (1/5+)
Diffuse	22 (2/5+)	73 (1/5+)
Masses	22 (1/5+)	23 (1/4+)
Intraluminal†	18 (1/3+)	20 (1/2+)
Macrophages	6 (3/5+)	37 (3/5+)

* 1+: occasional, 2+: few, 3+: moderate, 4+: many, 5+: abundant.

†Recorded only from 28 and 39 smears, respectively, with follicular structures.

Figure 4 Trabecular structure from case shown in fig 2C (May-Grünwald-Giemsa).

Figure 6 Sheet of cells with pale cytoplasm and regular nuclei with small nucleolus (Papanicolaou stain).

Figure 7 Sheet of oxyphilic cells with abundant cytoplasm and round to oval nuclei of various sizes (May-Grünwald-Giemsa).

Figure 9 Sheet of cells showing pleomorphism (May-Grünwald-Giemsa).

cells with hyperchromatic round nuclei without a nucleolus, medium sized NOS cells in a honeycomb pattern, abundant colloid, and macrophages, suggesting a diagnosis of nodular goitre (fig 11).

Our findings showed two cases (6%) with feature of nodular goitre, and another two smears (6%) with acellular background colloid material suggesting a diagnosis of colloid cysts. The other 27 cases (87%) were cytologically indistinguishable from follicular lesions, four of them could even be regarded as being of oxyphilic cell type either in a pure (one case) or combined (three cases) form.

Discussion

The table shows that parenchymatous nodules differ cytologically from colloid or mixed nodules. The former show a predominance of cells with small to prominent nucleoli, microfollicles, and trabeculae; colloid or mixed nodules show cells with small or inconspicuous nucleoli, a predominance of large follicles, honeycomb pattern, small typical cells, and abundant colloid material and macrophages.⁵

Kini *et al*⁸ described hyperplastic nodular goitre as showing follicular structures, honeycomb pattern, cells with regular small nuclei usually without nucleoli, and very occasionally macrophages and Hürthle cell metaplasia. We confirmed some of their findings, although in the nodules we studied the honeycomb pattern was virtually absent and the epithelial cells were usually of medium size with nuclei showing small to prominent nucleoli. These divergent results might have been due to differences in tissue sampling or histological criteria for diagnosing parenchymatous (hyperplastic) nodules.

Our findings indicate that most parenchymatous nodular goitres have cytological features suggestive of follicular lesions or neoplasia according to current criteria.^{6,8,9} In a previous study we suggested a practical division of follicular lesions into type I (benign, with no cellular atypia, honeycomb pattern, abundant colloid), type III (suspicious, with moderate cellular atypia, nuclear overlapping, prominent nucleoli, scanty or non-existent colloid), and type II (intermediate to the

Figure 8 Nuclear grooving (arrow) and cytoplasmic inclusion (May-Grünwald-Giemsa).

Figure 10 Sheets of oxyphilic cells adjacent to smaller NOS epithelial cells. Background amorphous colloid mass is arrowed (May-Grünwald-Giemsa).

Figure 11 Oxyphilic cells with abundant cytoplasm intermingled with smaller epithelial cells. Note foamy and pigmented macrophages and colloid masses in the background (May-Grünwald-Giemsa).

others).¹⁰ Our findings show that most of the aspirates studied would have been diagnosed as type III follicular lesions and that surgical treatment would have been indicated. Some cases—that is, those showing in addition typical small cells, honeycomb pattern, or abundant colloid—would have fallen into the type II category. In these hormone treatment would have been given and surgery would have been considered if there had been no reduction of the nodule size.¹⁰ In fact, in our experience type II follicular lesions were either nodules or adenomas, but type III follicular lesions also included carcinomas.¹⁰

The cytological diagnosis of follicular lesion or neoplasia should be expected in these cases because parenchymatous nodules are also difficult to differentiate histologically from follicular adenomas, but only as far as conventional morphological criteria are concerned: absence of capsule; occurrence in a multinodular gland; and lack of compression of surrounding tissue.¹⁷ A solitary nodule may not be encapsulated nor be compressed by adjacent thyroid parenchyma, and in this case a diagnosis of adenoma will be justified. Further confusion may arise because perinodular fibrosis may resemble a capsule,¹¹ and some authors regard encapsulated (adenoma-like) nodules as parenchymatous nodules if they occur in a multinodular goitre.¹ Whether these nodules are true adenomas has not been agreed and their differentiation is mostly of academic interest.

Oxyphilic cells not only occurred in the smears from the pure oxyphil nodule but also in five other cases. Two of them showed cytological features of classic nodular goitre and three of follicular lesion.

Oxyphilic cells may occur in combination with other epithelial elements in both nodular goitre and follicular adenomas.^{5,7,8} Their presence in the aspirates and their absence in the parenchymatous nodule studied can be explained by tissue sampling of a different area

from that of the nodule for histological study.

In a few cases a cytological diagnosis of classic nodular goitre (two cases) and colloid cyst (two cases) could not be excluded. The cytological features present in these cases could be attributable to needle pass through a neighbouring colloid/mixed nodule or colloid cyst, respectively, or to tissue sampling from a cytologically non-representative area of the nodule (possibly a mixed nodule) for pathological study. A cytological diagnosis of nodular goitre will probably lead to a clinical trial, while the diagnosis of a cystic lesion may lead to surgical treatment due to the inaccuracy of FNA to exclude the presence of neoplasia in a cyst.¹²

Nuclear grooving and nuclear cytoplasmic inclusions occurred in some of the cases studied. These features may occur in nodular goitre,⁵ follicular neoplasms,¹³⁻¹⁵ and, to a greater extent, in papillary carcinoma that may also have papillary fronds, psammoma bodies, and the ropy appearance of colloid.^{6,14} Pleomorphic cells occurred in two cases. These may occur in nodular goitre,⁵ follicular neoplasms^{15,16} and, to a greater extent, undifferentiated carcinomas. The latter may also have a neoplastic spindle cell component, mitoses, and necrosis.⁶

Our findings suggest that surgical treatment in follicular lesions should be considered only after hormone treatment to reduce the tumour mass has proved unsuccessful, and when they are not suspected as malignant clinically. FNA yields very useful results both as a diagnostic and screening tool if analysed carefully and critically from a clinico-cytological approach that aims at conservative treatment. This avoids unnecessary surgery with its potential attendant risks for the patient and is therefore more cost effective.

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