The role of fine needle aspiration cytology in the diagnosis of thyroid lesions

Grace McKee MB BS MIAC

J R Soc Med 1998;91:(Suppl. 33)28-32

SECTIONS OF ENDOCRINOLOGY, PATHOLOGY AND SURGERY

INTRODUCTION

Fine needle aspiration cytology (FNAC) is a simple, inexpensive, easily performed outpatient procedure which can provide a rapid diagnosis. It has been widely used in Europe for decades, mainly in the Scandinavian countries¹⁻⁴, but is a somewhat under-used technique in the UK. It is eminently suitable for the investigation of superficial palpable lesions in many sites, including the thyroid gland.

The role of cytology in thyroid swellings is twofold: it can be therapeutic, for example aspirating a large cyst can relieve pressure symptoms. Cytology also has a part to play in pre-operative diagnosis by identifying the disease process in both solitary nodules and in diffuse enlargement of the thyroid gland. A specific diagnosis cannot always be arrived at as sampling is variable and not always representative, but the surgeon is provided with information which helps in deciding management options. Cytological examination of aspirated material can detect thyroiditis, toxic hyperplasia and colloid goitres as well as neoplastic processes, epithelial, lymphoid and metastatic.

The equipment required to perform FNAC is minimal; glass slides with frosted ends (to be labelled in pencil), fixative, either alcohol in a Coplin jar or spray fixative, a 10 or 20 cm³ syringe, 23- or 25-gauge needles and a universal container for cyst fluids. A microbiology loop is extremely useful for spreading the aspirate on the glass slide.

The aspiration procedure is extremely simple. The use of local anaesthetic is a matter of personal choice but is usually unnecessary. The mass should be immobilized during insertion of the needle at right angles to the skin surface. A time-saving hint is to draw up 1 ml of air into the syringe before commencing the procedure so that when aspiration is completed the material can be expelled immediately onto the glass slide. If this is not done, the needle should be disconnected after removal, air drawn into the syringe and the needle then reconnected before expelling the aspirate. This prevents cells being sucked into the barrel of the syringe from where they cannot be retrieved. Sampling of the lesion may also be performed using capillary action⁵⁻⁸, whereby the needle is inserted into the lesion and moved up and down rapidly several

times. This method produces a good yield of cells without the large amounts of blood produced by vigorous suction.

The preparation of good quality smears is a technique that requires practice. The well-known blood film type of smear can only be produced after much practice and often results in material flowing off the edge of the slide, particularly in bloody aspirates. Controlled expulsion of aspirate onto the centre of the glass slide should aim to result in a drop of approximately 5 mm diameter which can then be rapidly, but gently spread in a circular fashion with a microbiology loop or by using the length of the needle. Other authors have described an alternative method for dealing with heavily blood stained smears in two stages⁹. Several smears should be prepared, both air dried (necessitating waving the slide in the air or using a hair dryer on a cool setting) and wet fixed by immersion into alcohol or by spray fixation. Cyst fluid should be collected in a clean dry universal container. The cytology request form should state the clinical findings and previous treatment if any.

In the laboratory, the air dried smears are stained with the May-Grünwald-Giemsa stain. Air drying produces artefactual enlargement and flattening of cells, making them easier to find in the smear but occasionally leading to difficulty in the interpretation of thick cell clusters. Colloid is much easier to identify on the air dried smear because it stains a bright purplish-blue, whereas it appears pale yellowish-orange with the Papanicolaou stain. Wet fixed smears are stained using the Papanicolaou stain. Fixation causes cells to retain their normal size and three dimensional structure making clusters of cells easier to visualize. However, it can be difficult to distinguish between bare thyroid epithelial nuclei and lymphocytes on a wet fixed smear alone. Cyst fluids are centrifuged and cytopspin preparations made which are then air dried or wet fixed and stained appropriately.

Thyroid aspiration is generally a safe procedure which is well tolerated. Care must be taken to prevent a haematoma developing. A complication that has been reported is the development of necrosis in lesions after aspiration¹⁰⁻¹⁴.

The adequacy depends not only upon the nature of the lesion but also upon the aspirator. Constant practice is the only way of developing expertise. Trainee aspirators may

Figure 1 Cyst fluid, MGG $\times 100$. This field illustrates the haemosiderin-filled macrophages (siderophages) commonly seen in thyroid cysts. There are a few bare thyroid epithelial nuclei and erythrocytes in the background

Figure 3 Hashimoto's thyroiditis; Hürthle cells, MGG $\times 100$. Hürthle cells have abundant cytoplasm and may appear pleomorphic. They may be seen in colloid goitres and in follicular neoplasms as well as in Hashimoto's disease

Figure 2 Cyst fluid unstained, polarized light $\times 63$. Cholesterol crystals are large, square or rectangular shaped with a corner chipped off. They are indicative of long-standing haemorrhage into the cyst

Figure 4 De Quervain's thyroiditis, MGG $\times 40$. This is characterized by enormous, multinucleated giant cells, debris and inflammatory cells. This field shows a huge multinucleated giant cell and some dense colloid

benefit from aspirating apples or oranges and spreading the juice on glass slides. The minimum number of cell clusters required in an aspirate varies from centre to centre¹⁵. The cellularity expected is related to the type of lesion, for example, cyst fluid may contain no thyroid epithelial cells but would still be considered adequate, whereas an aspirate from a solid nodule would need to contain at least six moderately-sized groups of epithelial cells.

Normal thyroid epithelial cells have small round uniform nuclei and little cytoplasm and may be seen in groups or as single bare nuclei. Colloid may appear as thick blobs, opaque material showing cracks or paving, or as a thin pale wash in the background. Most thyroid abnormalities have features which point to the diagnosis but which have to be searched for carefully, especially in suboptimal aspirates. The cytological features of thyroid lesions have been described in great detail in recent cytology textbooks¹⁶⁻¹⁸.

THYROID CYST

The fluid aspirated from a thyroid cyst is often quite cellular but may not contain epithelial cells. There are usually numerous foamy macrophages, many containing haemosiderin (siderophages), altered blood, colloid and small groups of benign thyroid epithelial cells (Figure 1). A drop of unstained cyst fluid examined under polarized light will show cholesterol crystals (Figure 2) if there has been long-standing haemorrhage into the cyst. It must be borne in mind, however, that papillary carcinoma of the thyroid may present as a cystic lesion and the presence of psammoma bodies (calcific concretions) in otherwise unremarkable cyst fluid is a feature that should cause concern.

THYROIDITIS

Lymphocytic thyroiditis and Hashimoto's disease show common features, namely large numbers of lymphocytes and plasma cells in addition to benign thyroid epithelial

Figure 5 Colloid nodule, pap × 100. This field shows a group of thyroid epithelial cells with pale pinkish-orange colloid in the background

Figure 6 Colloid nodule, MGG × 40. An intact thyroid follicle is illustrated, composed of small uniform thyroid epithelial cells

cells. With Hashimoto's thyroiditis Hürthle cells (HC) (Figure 3), multinucleated and epithelioid histiocytes are common. Lymphoid follicle centre cells may also be noted. De Quervain's thyroiditis is diagnosed by the presence of large multinucleated giant histiocytes, debris, inflammatory cells including lymphocytes and abundant colloid (Figure 4).

Figure 7 Follicular neoplasm, MGG × 100. Two well-developed microfollicular structures are shown, composed of uniform thyroid epithelial cells. A few bare nuclei are also seen

Figure 8 Papillary carcinoma, pap × 100. This papillary group is composed of cells with variably-sized nuclei, a few showing grooves. The intranuclear inclusions are not well defined in this field

Figure 9 Medullary carcinoma, pap × 100. This tumour shows cells with abundant pink granular cytoplasm. There is noticeable variation in nuclear size and occasional cells are binucleate

Figure 10 Anaplastic carcinoma, pap × 40. This field illustrates the marked pleomorphism and giant cells characteristic of anaplastic thyroid carcinoma. There is necrotic cellular debris in the background

MULTINODULAR GOITRE, COLLOID NODULE

These lesions exhibit variable cellularity ranging from barely adequate to extremely cellular, the latter raising the possibility of a neoplastic proliferation. Colloid is usually abundant (Figure 5) and many foamy macrophages are present including siderophages. From a few to many groups of benign epithelial cells may be seen, sometimes as large sheets of cells and intact thyroid follicles noted (Figure 6). These cells are fragile and bare epithelial cell nuclei are seen scattered throughout the background. Occasionally, these may be mistaken for lymphocytes and the lesion misdiagnosed as Hashimoto's thyroiditis or even lymphoma. Enlarged and abnormal oncocyctic cells are often seen—HC or Askanazy cells which, if numerous, may mimic a HC neoplasm.

FOLLICULAR NEOPLASM

On histological sections, the only distinguishing features between a benign follicular adenoma and a malignant follicular carcinoma are the presence of capsular invasion and invasion of blood vessels of lymphatics^{19,20}. The cellular features can be identical in both lesions. Cytology which examines cells out of context has no way of assessing invasion and, therefore, all follicular lesions must be reported as follicular neoplasms with a recommendation for histological examination. Follicular neoplasms usually produce cellular aspirates composed of small (micro-follicular) clusters of uniform epithelial cells (Figure 7) and little colloid with no evidence of foamy macrophages or bare nuclei. HC neoplasms are composed of HC (oncocyctic) with variable numbers of thyroid follicular cells.

PAPILLARY CARCINOMA

These tumours may occasionally present as cystic masses. Aspirates from papillary carcinomas are cellular and contain colloid, many foamy macrophages, siderophages and papillary clusters of epithelial cells. These cells exhibit large pale nuclei, often with grooves and intranuclear inclusions. The epithelial cells are often seen arranged around fibrovascular cores (Figure 8). Psammoma bodies, sometimes showing a laminated structure, are a particular feature of this neoplasm.

MEDULLARY CARCINOMA

This tumour may show a variety of histological patterns which are reflected in the fine needle aspirate. The sample is usually cellular and contains scattered pleomorphic malignant cells with eccentric nuclei, abundant cytoplasm containing granules and bi- or multinucleation (Figure 9). Spindle shaped tumour cells are noted in aspirates from the spindle cell variety of this carcinoma. Amyloid is detectable

on both air dried and wet fixed preparations in some tumours. It is birefringent under polarized light without the use of special stains.

ANAPLASTIC CARCINOMA

These tumours are easily diagnosed on aspirates as they are composed of a mixture of large bizarre malignant cells, giant cells and spindle cells in a necrotic background (Figure 10).

LYMPHOMA

Lymphomas may be primary tumours in the thyroid or part of a systemic disease process. The features are similar to those of lymphoma in other sites, namely a monomorphic population of abnormal lymphoid cells in non-Hodgkin's lymphoma while aspirates from Hodgkin's lymphoma contain Reed–Sternberg or Hodgkin's cells.

Metastatic tumour deposits do occur in thyroid from primary tumours of breast, kidney, lung and the gastrointestinal tract. Squamous carcinoma cells in aspirates are usually metastatic although primary squamous carcinoma of the thyroid can also occur, but is rare.

In conclusion, FNAC has a useful role to play in the pre-operative investigation of thyroid disease although it has its limitations. This technique should be more widely applied as expertise in aspiration and interpretation of aspirates will improve with practice.

REFERENCES

- 1 Soderstrom N. Punctures of goitres for aspiration biopsy. A preliminary report. *Acta Med Scand* 1952;144:23–44
- 2 Einhorn J, Franzen S. Thin-needle biopsy in the diagnosis of thyroid disease. *Acta Radiol* 1962;58:321–36
- 3 Löwhagen T, Willems JS, Lundell G, *et al.* Aspiration biopsy cytology in diagnosis of thyroid cancer. *World J Surg* 1981;5:61–73
- 4 Löwhagen T, Grunberg P, Lundell G, *et al.* Aspiration biopsy cytology (ABC) in nodules of the thyroid gland suspected to be malignant. *Surg Clin N Am* 1979;59:3–18
- 5 Santos JE, Leiman G. Nonaspiration fine needle cytology. Application of a new technique to nodular thyroid disease. *Acta Cytol* 1988;32:353–6
- 6 Ciatto S, Iossa A, Cicchi P, *et al.* Nonaspiration fine needle cytology of thyroid tumours [Letter]. *Acta Cytol* 1989;33:939
- 7 Rajsekhar, Sundaram C, Chowdary T, *et al.* Diagnostic utility of fine-needle sampling without aspiration: a prospective study. *Diagn Cytopathol* 1991;7:473–6
- 8 Mair S, Dunbar F, Becker PJ, Plessis W. Fine needle cytology—is aspiration suction necessary? A study of 100 masses in various sites. *Acta Cytol* 1989;33:809–13
- 9 Abele JS, Miller TR, King EB, Löwhagen T. Smearing techniques for the concentration of particles from fine needle aspiration biopsy. *Diagn Cytopathol* 1985;159:65
- 10 Keyhani-Rofagha S, Kooner DS, Keyhani M, O'Toole RV. Necrosis of a Hürthle cell tumour of the thyroid following fine needle aspiration: a case report and literature review. *Acta Cytol* 1990;34:805–8

- 11 Layfield LJ, Lones MA. Necrosis in thyroid nodules after fine needle aspiration biopsy: report of two cases. *Acta Cytol* 1991;**35**:427-30
- 12 Alejo M, Matias-Guiu X, de las Heras Duran P. Infarction of papillary thyroid carcinoma after fine needle aspiration [Letter]. *Acta Cytol* 1991;**35**:478-9
- 13 Jayaram G, Aggarwal S. Infarction of thyroid nodule: a rare complication following fine needle aspiration [Letter]. *Acta Cytol* 1989;**33**:940-1
- 14 Jones JD, Pittman DL, Sanders LR. Necrosis of thyroid nodules after fine needle aspiration. *Acta Cytol* 1985;**29**:29-32
- 15 Guidelines of the Papanicolaou Society of Cytopathology for the Examination of Fine-needle Aspiration Specimens from Thyroid Nodules. *Papanicolaou Soc Cytopathol Task Force Standards Practice* 1996;**15**:84-8
- 16 McKee G. Thyroid. In: *Cytopathology*, Vol 86. London: Mosby-Wolfe, 1997:111
- 17 Orell SR, Sterrett GF, Walters MNI, Whitaker D, eds. Thyroid. In: *Manual and Atlas of Fine Needle Aspiration Cytology*, 2nd edn. London: Churchill-Livingstone, 1992
- 18 Bibbo E. Thyroid. In: *Comprehensive Cytopathology*, 2nd edn. Philadelphia: WB Saunders, 1997:673-701
- 19 Lang W, Georgii A, Stauch G, Kienzle E. The differentiation of atypical adenomas and encapsulated follicular carcinomas in the thyroid gland. *Virchows Arch Path Anat Histol* 1980;**385**:125-41
- 20 Yamashina M. Follicular neoplasms of the thyroid: total circumferential evaluation of the fibrous capsule. *Am J Surg Pathol* 1992;**16**:392-400