Review

Establishing an accurate diagnosis of a parotid lump: evaluation of the current biopsy methods – fine needle aspiration cytology, ultrasound-guided core biopsy, and intraoperative frozen section

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Abstract

The optimum technique for histological confirmation of the nature of a parotid mass remains controversial. Fine needle aspiration cytology (FNAC), which has traditionally been used, is associated with high non-diagnostic and false negative rates, and ultrasound (US)-guided core biopsy and frozen section have been explored as alternatives. US-guided core biopsy is more invasive than FNAC, but is safe, well-tolerated, and associated with improved diagnostic performance. Although frozen section offers better specificity than FNAC, it has a number of important drawbacks and cannot be considered as a primary diagnostic tool. US-guided core biopsy should be considered as the initial diagnostic technique of choice, and in units where the accuracy of FNAC is good it can be used when FNAC is equivocal or non-diagnostic.

Keywords: Fine needle aspiration cytology; Ultrasound-guided core biopsy; Frozen section; Parotid gland lesion

Introduction

To establish an accurate diagnosis of a parotid lump it is now generally accepted that triple assessment, which comprises clinical examination, imaging, and confirmation by biopsy as appropriate, is necessary. Most centres use high-resolution ultrasound as the initial diagnostic imaging of choice as it is quick, safe, and non-ionising, and in experienced hands is capable of a high degree of accuracy; 93% accuracy has been reported for parotid malignancy. For lesions that are large, complex, or likely to be malignant, it guides the need for further investigation, usually with magnetic resonance imaging, but for most focal, and possibly neoplastic lesions, definitive histological confirmation is necessary.

Accurate diagnosis enables the appropriate timing and type of operation (if indicated) and potentially avoids operation in the elderly or unfit, or for certain neoplasms such as Warthin’s tumour. It also allows patients to be informed about potential injury to the facial nerve when they give their consent.

Definitive and accurate preoperative diagnosis requires cytological or histological analysis, and the best way to obtain specimens remains controversial. Open surgical parotid biopsy originally fell out of favour because of a number of problems, which included operative complications (injury to the facial nerve and wound infection), delayed complications including formation of a fistula or sialocele, and tumour

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recurrence secondary to tumour spillage.\textsuperscript{3} Subsequently, by the early 1980s, open biopsy was largely superseded by fine needle aspiration cytology (FNAC), which was traditionally done blind and usually in the outpatient department.

**Fine needle aspiration cytology**

Although successful results have been reported, it has become increasingly clear that there is considerable variability in the accuracy of FNAC, and high non-diagnostic rates and poor sensitivity or specificity have been reported.\textsuperscript{4–6} The technique is well established, and is commonly used as it is quick, safe, relatively non-invasive, and cheap. However, when done blind and by clinicians with different levels of experience, poor technique or inaccurate or insufficient sampling can result in high rates of non-representative or insufficient aspirates.

The perceived and real problems associated with blind FNAC have led clinicians in different specialities to explore ways to improve the diagnostic yield of parotid biopsy procedures. Broadly, they fall into 3 main categories: use of various techniques to improve the yield of FNAC, use of core biopsy with ultrasound (US) guidance, and finally, publication of data that re-examine the use of intraoperative frozen section. Several systematic reviews with meta-analyses on these techniques, and specifically their performance in the parotid glands, have been published, and we will refer to them in the remainder of this article.

Several techniques that can potentially improve the diagnostic yield of FNAC have been described. US-guidance enables precise sampling of the lesion, selectively avoids cystic areas within tumours, and avoids damage to adjacent (vascular) structures.\textsuperscript{7} When a cytologist or cytology technician assesses cellularity at the time of sampling, its performance is further improved.\textsuperscript{8} Alternatively, clinical models run purely by a cytologist, which allow repeated sampling of a lesion until a diagnostic aspirate is obtained, have also been described.\textsuperscript{9,10} In larger centres, additional ancillary technology may be available such as in situ hybridisation or flow cytometry to further improve diagnostic rates.

A meta-analysis from 2011, which looked at 64 studies published since the late 1980s, included data on FNAC done both blind and under varying levels of optimised conditions.\textsuperscript{11} Overall, it was found to be safe and well-tolerated and had high reported specificity (97%) but lower sensitivity (80%). Diagnoses were found to be reliable, but there was a high false negative rate (20%). Not all the studies included information on non-diagnostic samples, but where available, the rate was found to be around 8%.\textsuperscript{10} The analysis also showed a significantly wide variation in the performance of FNAC across centres.

What are the reasons for these findings? For the most accurate results, FNAC must be done either by an experienced clinician using ultrasound guidance with a cytologist or cytology technician in attendance, or by a cytologist with ancillary backup cytology diagnostic facilities. In reality, and certainly in the UK, cytologists, cytology technicians, and ancillary equipment are in relatively short supply, and in many units, FNAC done blind by clinicians remains the norm.

There are also intrinsic diagnostic problems even when a cellular aspirate is obtained. The diagnosis of lymphoid hyperplasia, namely the differentiation of reactive nodal hyperplasias from low-grade lymphoma, is usually not possible with FNAC alone.\textsuperscript{12} Cytological diagnosis of salivary gland neoplasms can be difficult as they often have low-grade nuclear morphological features that can look similar.\textsuperscript{11} Cellular pleomorphic adenomas, monomorphic adenomas, adenoid cystic carcinomas, low-grade mucoepidermoid and adenocarcinomas, can all have overlapping cytological features.\textsuperscript{10} In addition, specimens do not provide the architectural information necessary to diagnose some lesions, and in largely cystic tumours (such as Warthin’s tumour and mucoepidermoid carcinoma) it is often difficult to aspirate enough material for accurate diagnosis.\textsuperscript{10} In a recent paper about the performance of FNAC in a cytologist-led clinic, Fakhry et al. confirmed the problems associated with the technique even when there was an opportunity for repeated sampling.\textsuperscript{10} They reported correct diagnoses in 116/138 cases (84%) with 8 false negative (6%) and 14 false positive (10%) results. The sensitivity for malignancy was 73% and specificity 87%.

**Ultrasound (US)-guided core biopsy**

US-guided core biopsy was initially established in the diagnosis of breast and abdominal masses, and was first described in the parotid gland in 1999 in a series of 16 patients with parotid lumps. In 13 of them initial FNAC had been non-diagnostic,\textsuperscript{13} but US-guided core biopsy provided diagnostic specimens in them all. It was found to be better than clinical examination alone in 31% of patients, and in all those operated on results correlated completely with final surgical histological findings. Subsequently, further meta-analyses of published papers on the efficacy of the technique in the parotid glands have been done.\textsuperscript{14,15}

The technique is well described.\textsuperscript{16} It is more invasive than FNAC as it involves local anaesthesia and a small incision in the skin. A needle (usually 18 or 20G) is deployed by means of a spring-loaded automated biopsy device to obtain a core or cores of intact tissue. Crucially, the tissue contains architectural details that can be sent for detailed immunohistochemical analysis, which enables confirmation of the type and grade of a tumour and improves the diagnosis of lymphoid hyperplasia. Its ability to diagnose parotid lymphoma is well known, and treatment can now be initiated on the results obtained from core biopsy alone without the need for further investigation.\textsuperscript{16} The ability to provide a core of tissue also means that the technique can be used to make a confident diagnosis of parotid involvement by systemic disease such as
Sjögren syndrome and sarcoidosis, not usually possible with FNAC.

The most recent summary meta-analysis, which incorporated 12 studies (fewer than those on FNAC) from between 1999 and 2012, reported high overall sensitivity (96%) and specificity (100%), and a non-diagnostic rate of only 1.6%.\(^{15}\) It supported the safety of the technique in the outpatient department with only 8 haematomas reported after the procedure (1.6%), and was well-tolerated by patients.

There are concerns about the potential for tumour seeding after US-guided core biopsy. The authors of the meta-analysis acknowledged that the follow-up period for some patients in the studies was low,\(^{15}\) but no seeding was reported and there have been only sporadic reports after parotid needle biopsy.\(^{17,18}\) However, continued surveillance is needed as it can occur up to 20 years after the procedure.\(^{17}\) In a review of seeding after biopsy of salivary gland lesions, only 2 cases were found after large-gauge needle biopsy and 2 after FNAC, noting the larger number of cases and longer follow-up periods for FNAC.\(^{17}\) The risk of seeding seems to be related to the size of the needle, and is rare with 18/20G needles, which are commonly used in the parotids. Some surgeons excise the tract of the needle core biopsy at the time of operation, although there is no evidence that it is routinely required. As well as the high sensitivity and specificity of US-guided core biopsy, the authors of the 2014 meta-analysis found less variability in performance between studies when compared with FNAC.

As with FNAC, diagnosis of a well-differentiated malignancy such as basal cell adenocarcinoma with US-guided core biopsy is difficult, as the entire resected specimen must be reviewed and capsular infiltration observed before malignancy is confirmed.\(^{16}\) Also, as with FNAC, there may be problems with mainly cystic tumours because it can be difficult to obtain enough tissue to make a diagnosis. In this instance, triple assessment is essential in all cases. When clinical findings or imaging, or both, suggest malignancy, core biopsy can be repeated or, in a minority of patients, lesions can be excised for formal diagnosis. Frozen section (see later) could be considered at this stage if clinically appropriate and histological support is available. Intrinsically however, histological diagnosis is often difficult in these cases, and as the entire lesion is usually required for precise confirmation, formal excision may be preferable.

The use of US guidance can improve the diagnostic accuracy of both core biopsy and FNAC. A study published in 2012 retrospectively compared the accuracy of the 2 techniques in the diagnosis of a parotid mass.\(^{19}\) Of the 171 patients included, 107 had US-guided FNAC and 64 US-guided core biopsy. Core biopsy had significantly higher sensitivity than FNAC in the differentiation of benign from malignant lesions (94.1% compared with 55.6%), higher specificity (100% compared with 93.3%), and higher accuracy (98.4% compared with 86.9%). In patients with lymphoma, diagnosis was accurate in all 6 who had core biopsy, but in the 4 who had FNAC it was not definitive. The authors concluded that US-guided core biopsy was to be preferred over US-guided FNAC “when a definitive diagnosis of a parotid solid mass is needed”.\(^{19}\)

Ultrasound uniquely depends on the operator, and sono-graphic examination of the head and neck is recognised as challenging. For US-guided biopsy services to be effective, a pool of trained operators must be available to work across a wide spectrum of institutions. Traditionally, ultrasound has largely been the preserve of radiologists, although this situation is changing, and ultrasound or biopsy examination could be done by interested clinicians with appropriate training and support from radiologists. The Royal College of Radiologists has published useful guidance for training in ultrasound and suggested several levels of experience. We recommend that interested clinicians read them.\(^{20}\)

**Intraoperative frozen section**

The meta-analysis of 2011 on intraoperative frozen section looked at 13 studies published between 1985 and 2010.\(^{21}\) Frozen section in itself has acceptable accuracy (90% sensitivity, 99% specificity) and has been proposed as a confirmatory tool when the results of FNAC are equivocal or non-diagnostic.\(^{10}\) There are, however, concerns that reflect those associated with open biopsy: risk of tumour spillage and seeding with potential disruption of the operative field for malignant lesions. As previously stated, histological diagnosis of salivary tumours can be complex and challenging, and many histopathologists would be not be comfortable providing a definitive diagnosis using this method. An accurate preoperative diagnosis rather than one obtained intraoperatively brings huge potential benefits to the surgeon and to the patient in terms of informed consent and operative planning.

**Conclusion**

Previously, one-stop neck lump clinics based on FNAC with support from cytology technicians or cytologists were proposed by the National Institute for Clinical Excellence (NICE),\(^{22}\) but US-guided core biopsy does not lend itself to this type of setting because of the delays involved in the histological reporting of specimens. Improvements in the adequacy and accuracy of the technique compared with FNAC will ultimately facilitate more timely diagnosis and treatment for most patients. Previous work has suggested that alternative mechanisms for the provision of diagnostic clinics can offer equal or more effective care than the models suggested by NICE,\(^{23}\) and it is likely that over time, as in breast practice, US-guided core biopsy will largely replace FNAC in the diagnosis of parotid neoplasms.

**Conflict of interest**

We have no conflicts of interest.
Ethics statement/confirmation of patient permission

None.

References
