Incisional or core biopsies of salivary gland tumours: how far should we go?

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Abstract

Trends in the evaluation of salivary gland masses have changed as imaging studies have improved and sampling techniques have evolved over the past several decades. Whether clinically palpable or detected by imaging studies, salivary gland masses have been readily evaluated by fine needle aspiration. More recently, imaging guided core-needle biopsy has been employed with mixed results. The literature on these techniques is reviewed and analyzed with particular attention to tissue adequacy and diagnostic accuracy. Comparison is made using selected case presentations to highlight the advantages and disadvantages of establishing a diagnosis when core-needle biopsy is utilized. Core-needle biopsy of salivary gland tumours may be a useful first diagnostic approach as long as the limitations of the procedure are well understood and managed. *Diagnostic Histopathology 2012;18(9):358-365.*

Keywords: Core-needle biopsy; fine needle aspiration; incisional biopsy; open biopsy; radiology guidance; salivary gland

Introduction

Salivary gland neoplasms have a remarkably varied range of architectural and cytomorphonuclear features, both within and between tumours. This diversity contributes to the complexity in reaching an accurate diagnosis. Furthermore, assessment of the interface with the capsule or surrounding parenchyma is often essential in yielding the correct diagnosis.[1] The symptoms of benign and malignant salivary gland neoplasm often overlap. Most salivary gland tumours, whether benign or malignant, will require surgery. Immediate and/or complete resections of suspicious lesions of the salivary gland are often not practical nor feasible. Accurate pre-operative determination of a diagnosis, whether fine needle aspiration or core-needle biopsy, allows for prospective surgical planning and for possible neo-adjuvant or adjuvant therapy.[2] There is a major emphasis by clinicians and patients alike, to attain a definitive diagnosis on the most noninvasive and limited samples possible. Fine needle aspiration has been successfully implemented, but in many cases is only able to give a broad category diagnosis, such as “reactive,” “favour neoplasm” or “malignant”, rather than giving a specific diagnosis. Is a core-needle biopsy or limited incisional biopsy of salivary gland tumours able to go further and yield an accurate and definitive diagnosis?[3] How far should we go?

Tissue can be obtained in a variety of ways: fine needle aspiration (FNA), core-needle biopsy, incisional biopsy, excisional biopsy, and resection. Open biopsy includes incisional and excision biopsy, usually reserved for small lesions of the minor salivary glands, while resection is usually used for major salivary gland tumours. Incisional open biopsy has many of the disadvantages of a resection: general anaesthesia, wide excision, possible nerve damage and bleeding. Open biopsy is generally avoided due to tumour spillage or seeding, nerve damage, scarring and possible fistula development.[4,5]

The disadvantages of open biopsies have allowed fine needle aspiration cytology (FNAC) to come into favour as a well accepted means of procuring tissue. The procedure is quick, easy to perform, and safe with little discomfort to the patient. Immediate adequacy assessment and triage is superior to other methods, often times resulting in rapid diagnosis. However, overlapping cytologic features between tumours contributes to difficulty in interpretation,[2] while the diagnostic accuracy is directly proportional to the cytopathologist’s experience. Furthermore, the number and type of immunohistochemical (IHC) studies may be limited. In spite of these limitations, the reported diagnostic accuracy of FNAC can be as high as 98% when adequate material is obtained.[6-10] However, the insufficient or non-diagnostic rate is up to 29%.[7,11,12] Core-needle biopsy is performed with a small cutting needle to harvest tissue; the needle gauge ranges from 12 to 19 gauge, with most in the 16 to 19 gauge range. Diagnostic accuracy is greatly improved when guided by ultrasound or computed tomography imaging.[5] Core-needle samples preserve the tissue architecture. Due to remarkable intra-tumoural variability, the morphology on a core biopsy may be non-representative. IHC can be more easily performed on core-needle biopsy material. However, the larger needle may result in nerve damage, significant bleeding, and potential tumour seeding of the needle tract.[13-16]

The definitive diagnosis of a salivary gland neoplasm is essential to treatment planning, achieved by rigorous microscopic interrogation and review of the sample. Since open biopsy is generally not a viable alternative and FNAC has been well incorporated into the diagnostic armamentarium, is there a role for routine incisional core-needle biopsy of salivary gland tumours—and a return to our original question: how far should we go? It is important to clarify that core-needle biopsy and FNAC are not as useful or reliable in evaluating non-neoplastic lesions of salivary glands. Lesions such as chronic sialadenitis, benign lymphoepithelial lesion, Sjögren disease, oncocytic metaplasia, polycystic disease and sialolithiasis, among others, are not adequately nor accurately assessed by these techniques. We will discuss these issues within the setting of selected case presentations, with a review of the pertinent literature to shed light upon the advantages and disadvantages of core-needle biopsy.

Materials and methods

A review of the English literature based on a PubMed/Medline search from 1960 to 2011 was performed focusing on core-needle biopsy of salivary glands. There are a limited number of articles dedicated to this topic, although salivary gland lesions are included in general reviews of the technique. There were five articles specifically devoted to the topic, all published within the last 12 years.[2-5,17] The five articles included a total of 169 biopsy results, correlated to resection histology findings. All reported cases were performed by ultrasound-guided biopsies, utilizing various gauge cutting needles, most spring-loaded. No specific manufacturer was employed. As each group reported data differently, raw data evaluation could not be performed in a meta analysis. Where stated, the patients ranged in age from 11 to 92 years without a gender predilection.

We selected five cases with both core-needle biopsies followed by resections to highlight the benefits and potential pitfalls. All core-needle samples were obtained with the assistance of ultrasound guidance. Needle size ranged from 12 to 19 gauge (most using a spring-loaded action), but was not consistent since specimens were obtained by different radiologists. All tissue was submitted in 10% formalin solution for routine processing.

In general, no more than two cores were processed per block. The cores were stretched and placed between sponges to prevent them from moving or folding. While embedding only one core would be ideal, two cores were submitted per block, which approaches the maximal surface area to be sectioned. If the plane of section is horizontal to the long axis of the core there is no potential tissue loss due to divergence of the cylinder of tissue from a 0° to the horizontal. Any divergence from horizontal will decrease the represented area available for review by a significant amount. When multiple cores are embedded together, it is difficult to position all cores in the same plane since cores move to different planes and the cut surface of the cylinders substantially decreases.[18,19] Cores ranged from 2 to 14 mm in length.

Case presentations

Case 1

A 29-year-old women presented with a several year swelling in the left tail of the parotid gland, identified in a retroauricular location. She reported a recent increase in size. There was a heterogeneous 1.4 cm mass identified by imaging. An ultrasound-guided coreneedle biopsy was performed on the deep lobe of parotid gland mass. Four cores were taken, ranging from 0.2 up to 0.4 cm in length. The core-needle biopsy was interpreted to represent an acinic cell carcinoma (Figure 1—Left). The irregular distribution of small acini without any intervening ducts or myoepithelial cells confirmed the diagnosis. The wide resection sample confirmed the diagnosis (Figure 1—Right).

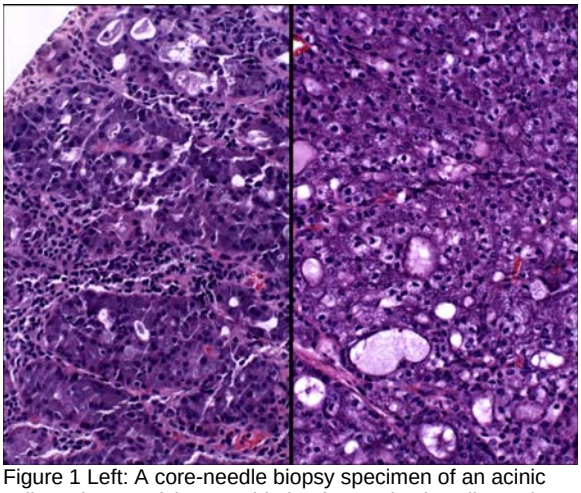

Figure 1 Left: A core-needle biopsy specimen of an acinic cell carcinoma of the parotid gland. Neoplastic cells are large with granular basophilic cytoplasm, nuclei are round and eccentrically placed. There are no ducts. Right: Excision of the same tumour, viewed at a slightly lower power, demonstrates the same characteristics but with the ability to see more the tumour. Acinic cell carcinomas are often homogenous, making them easier to diagnose on core-needle biopsy.

Case 2

A 57-year-old man presented with a recently detected palpable, 2.7 cm right, tail of the parotid gland mass. The mass was rubbery to smooth, non-mobile and well defined. A fine needle aspiration as initially performed, but was interpreted to be “nondiagnostic”. Four cores were obtained, ranging from 0.2 to 0.7 cm in length (Figure 2—Left). The cores were occupied exclusively by oncocytic cells arranged in a biphasic pattern of “light” and “dark” cells surrounded by abundant, granular, oncocytic cytoplasm (Figure 2—Right). The nuclei were round to regular. Mitoses were inconspicuous. There was no mucin production and no myoepithelial component. The core needle and subsequent resection showed oncocytoma.

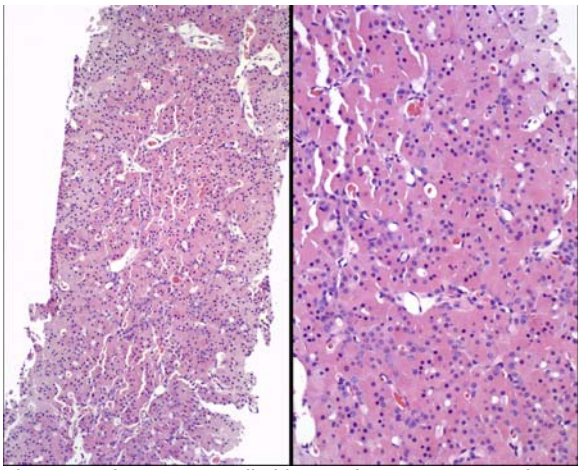

Figure 2 Left: A core-needle biopsy of an oncocytoma shows distinctive large, polygonal epithelial cells with prominently eosinophilic, granular cytoplasm. No other cell type is identified in this small biopsy; therefore it is consistent with an oncocytoma. Right: Higher power shows well developed oncocytic cells with focal dark cells. Oncocytes are found in other tumours so review of several fields is required.

Case 3

A 65-year-old male was found to have a submandibular mass on routine dental examination. Initial imaging suggested a submandibular lymph node. Referral resulted in an ultrasound-guided core-needle biopsy. Two core-needle biopsies were obtained measuring 0.5 and 0.7 cm in length. The tumour showed a spindled cell population set within adipose connective tissue. Isolated tubules were suggested, a feature highlighted by keratin immunohistochemistry. The lesional cells were positive with S100 protein and p63. Cytologic atypia was limited, and there was no necrosis or increased mitoses (Figure 3—Left). The diagnosis of pleomorphic adenoma was rendered, although with a cautionary note about the possibility of a myoepithelial tumour or spindled cell mesenchymal tumour in the differential diagnosis. The resection sample confirmed the diagnosis of pleomorphic adenoma (Figure 3—Right), with many more tubular and glandular profiles noted.

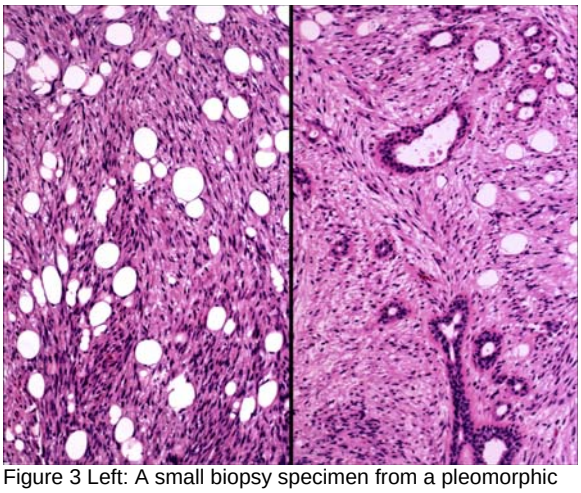

Figure 3 Left: A small biopsy specimen from a pleomorphic adenoma shows areas that are almost schwannoma-like admixed with fat. Right: The resection specimen shows more classic features of a pleomorphic adenoma, especially with the tubular and glandular profiles.

Case 4

An 84-year-old women presented to her doctor with a slowly enlarging mass of the left parotid gland. The patient had experienced pain and some difficulty swallowing. An ultrasoundguided core-needle biopsy was performed on a 3.1 cm mass. The cores ranged from 0.2 to 0.8 cm in length. There was abundant mucinous-type material in the background. Only a couple of fragments contained epithelial cells. There was a hint of transitional epithelium, although no true mucocytes were present. The core-needle biopsy was interpreted to represent a salivary gland neoplasm, with a comment favouring mucoepidermoid carcinoma (Figure 4a). After an excision, the diagnosis was pleomorphic adenoma in which there was extensive mucinous-type degeneration in a tumour that in other foci showed classic features of pleomorphic adenoma (Figure 4b).

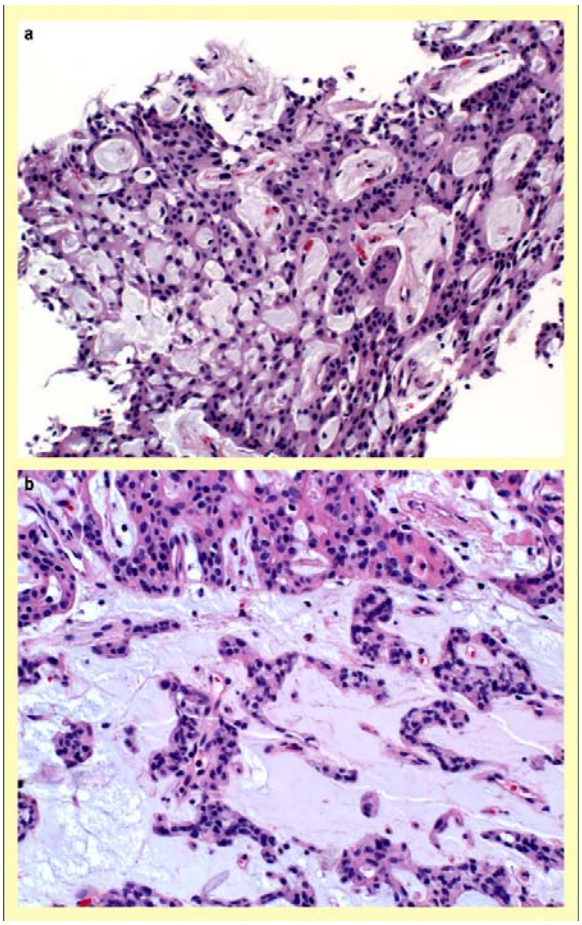

Figure 4 (a) In this core-needle biopsy the case was signed out as: fragments of salivary gland neoplasm, most suggestive of mucoepidermoid carcinoma. This very limited sample appears to mimic the admixture of mucocytes, epidermoid cells and intermediate cells. The open spaces are filled with mucinous-like material and were interpreted as cysts. (b) The excision of this case shows more classic features of a pleomorphic adenoma. The areas in the small biopsy that were interpreted as cysts are more clearly shown as pools of mucinous material with characteristic plasmacytoid epithelial cells of a benign pleomorphic adenoma.

Case 5

A 22-year-old female presented to her doctor with the chief complaint of a firm nodular swelling of the left parotid gland. She reported some numbness. An ultrasound-guided core-needle biopsy was performed. The cores ranged from 0.7 up to 1.4 cm in length. The cores showed glandular to focally cribriform epithelial islands within a hyalinized stroma. The nuclei were small and surrounded a bluish matrix material (Figure 5—Left). The subsequent parotidectomy showed the classic features of adenoid cystic carcinoma (Figure 5—Right).

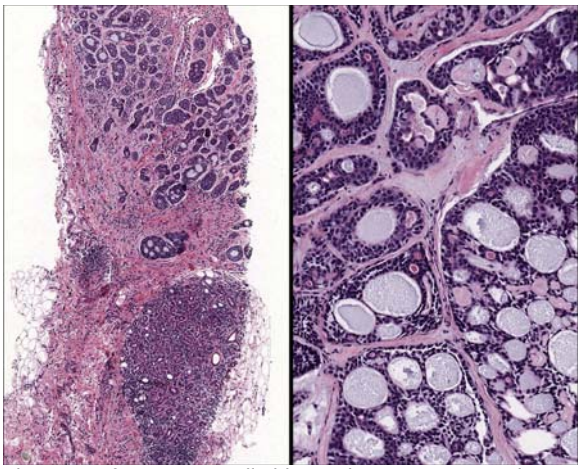

Figure 5 Left: A core-needle biopsy demonstrates an abrupt edge with the uninvolved parenchyma. There is no "infiltration" per se. The cells are small, surrounding glycosaminoglycan material. Right: Resection specimen shows classic areas of adenoid cystic carcinoma.

Evaluation of the published cases[2-5,17] showed a diagnostic accuracy rate for malignant neoplasms from 91.1 to 100%. Specificity and sensitivity was not reported in all the papers, and the lack of raw data made additional calculations unreliable. In the articles that did report sensitivity and specificity for diagnosing a malignant neoplasm, the range was 75–100% and 96.6–100%, respectively. Diagnostic material was obtained in 95.5–100% of cases. Only two immediate complications were reported, both haematomas.

Discussion

Salivary gland neoplasms account for between 2.0 and 6.5% of all neoplasms of the head and neck.[1,20-24] The anatomically complex locations of these tumours combined with their diverse architectural and cellular features generate challenges in establishing an accurate diagnosis, especially if the biopsy is inadequate. With surgical resection the treatment for most neoplasms, establishing whether the neoplasm is benign or malignant aids in developing a surgical treatment plan.[2] What is the best way to get quality material to establish a reproducible, accurate diagnosis?

FNAC is widely used, in spite of problems with nondiagnostic, inadequate, and limited samples. Open biopsies have complications. What is a good middle ground? Do incisional core-needle biopsies fit the bill to get the best quality and quantity of tissue with the fewest patient complications?

Core-needle biopsy sampling has been well established in other organs for decades, providing excellent results which correlate well with subsequent excisions, especially for prostate, breast, liver, and lung.[25-30] The procedure has wended its way into head and neck pathology, although with mixed results. Although the exact technique varies, an automated cutting needle, ranging from 12 to 20 gauge, is employed by a radiologist (or clinician). After injecting local anaesthesia, a small puncture or stab is made, with a number of tissue cores harvested. With a range of 1 to 12 cores obtained, most advocate 2 to 4 cores.[2] Adequacy can be determine by gross inspection, or a touch preparation with pathologist interpretation, the latter similar to a FNA adequacy check. If the sample is non-diagnostic, more cores can be obtained in an attempt to reduce the insufficient rates, which can be as high as 15%.[7,11] Without adequate representative tissue, a diagnosis is nearly impossible. Tissue is usually placed in 10% formalin, although culture, flow, or electron microscopy submissions can be performed before fixation. The patient is observed in a recovery room for a short interval before being discharged.

Ideally, only a single core should be stretched, placed between sponges to prevent the core from moving or folding, and processed. The histotechnologist can embed and cut a "flat" core. This technique provides the maximal surface area for interpretation when a section is made horizontal to the long axis of the core (Figure 6). When multiple cores are processed in the same cassette, they may be in different planes and/or may fragment, making it impossible to get the best possible sections of all submitted cores. There is a significant decrease in surface area examined when the cores are not flat. Specifically, for a 1 x 15 mm core, 15 mm^2 would be reviewed in a single section taken at 0°. This decreases to 9.01 mm^2 and 4.52 mm^2 with a 5° and 10° angle to the cutting blade.[19] Therefore, if one is trying to optimize a limited sample it is imperative to process the tissue correctly.[18] It is our practice to perform a "1, 5, 12" protocol on core-needle samples. This means, after facing off the block, 24 serial sections are cut, placing two sections per slide (total of 12 slides). Then, the 1st, 5th, and 12th slides are stained with haematoxylin and eosin, leaving the other slides available for additional studies, as needed. The unused slides are discarded after 60 days. This technique helps to minimize non-representative sampling. FNA material is often suboptimal for IHC, although cell block material may expand the options for additional studies.[6] Employing the embedding strategy proposed above, targeted, pertinent immunohistochemical stains can be performed. IHC is most helpful in the setting of spindle cell or mesenchymal lesions or metastases, realizing tumour cell spindling is common in epithelial neoplasms.[31,32]

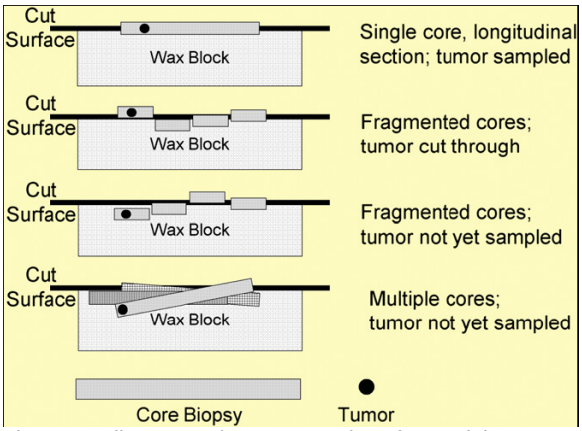

Figure 6 A diagrammatic representation of potential problems when cores are fragmented or multiple cores are processed in a single block. One core, stretched, placed between sponges, and then cut horizontal to the length of the core will yield the highest surface area for evaluation.

There are several advantages and disadvantages for the patient and clinician. Although seldom known to the pathologist, these factors impact the type of sample obtained. The potential advantages of a core-needle biopsy include: (1) Lack of morbidity of an open biopsy; (2) No general anaesthesia, with its attendant additional planning and scheduling; (3) Little to no scarring in a cosmetically sensitive region; (4) Low risk of fistula formation. The potential disadvantages include: (1) Requires radiology coordination and scheduling, different from a FNA; (2) Patient discomfort is

greater than FNA, but less than open excision/resection; (3) Anxiety may increase while the patient waits to have the procedure, potentially lessened with the relatively "instantaneous" performance of a FNA, often by the clinician. The potential complications include haematoma, nerve damage, fistula formation, and tumour seeding: but they are rare.[2-5,17,33,34] Of all the cases reviewed in the literature there were only two haematomas, and no other complications.[4,17] Tumour seeding, particular in parotid gland tumours, is of more concern.[13-15] While rare cases of tumour seeding have been reported after FNA, the risk increases with larger needle bore size, making core-needle biopsies potentially more risky.[5,35] However, this seems to be more a theoretic consideration, not reported in the series reviewed. Admittedly the detection of tumour seeding is difficult, often not specifically sought in the resection sample, and may require long patient follow up to exclude. Again, nerve injury, specifically the facial nerve, is a potential risk, but has not been reported. Finally, fistula formation is detected in other anatomic sites (breast, pancreas, lung),[33,34] but has not been reported in the salivary glands.

Ultrasound alone cannot reliably separate between benign and malignant tumours although it can be used for both palpable and non-palpable lesions. The sensitivity is approximately 40%, specificity about 90%, the positive predictive value of about 30%, although accuracy for malignant tumours is reported at about 20%.[36] Ultrasound cannot show nerves, but does highlight the parotid gland duct, vessels and other landmarks,[4,17,37,38] which can be used to approximate the nerve location. Therefore, to make a definite diagnosis, ultrasound-guided core-needle biopsy or FNA is advocated, specifically to increase the success of getting material from small or non-palpable lesions.[5,6]

One of the significant advantages of core-needle biopsy over FNA is architectural preservation. Many of the most common salivary gland neoplasms show identical cytologic features, while the architecture will make the separation possible; these include basal cell adenoma, basal cell adenocarcinoma, and adenoid cystic carcinoma, to name just one group of tumours with overlapping findings. Beyond the scope of the present discussion, suffice it to say that many lymphomas also require architecture. Furthermore, several non-neoplastic salivary gland also require architectural preservation for diagnosis.[4,39]

Core-needle biopsy is most diagnostic in homogenous or monotonous neoplasms, although axiomatic, this is not really known until the excision. Therefore, sampling is critical. The surface area examined is very limited in comparison to the size of the lesion. Therefore, several cores, directed or targeted to different parts of the tumour by ultrasound guidance will help to reduce this potential limitation. Needless to say, most salivary gland tumours show a wide diversity both within and between tumours.[1] A few examples will be used to highlight these issues.

Cases 1 and 2 illustrate tumours that are relatively homogenous and monotonous throughout. Acinic cell carcinoma shows a classic serous acinar differentiation. This "blue-dot" tumour could be considered an "Aunt Minnie," a diagnosis based on seeing similar images and patterns previously.[40] Quite simply, its core biopsy is characteristic and simply looks like its excision. Likewise, oncocytoma shows large polygonal epithelial cells with prominently eosinophilic, granular cytoplasm. Oncocytic cytoplasm can be seen in other lesions, such as nodular oncocytic hyperplasia or metaplasia, papillary cystadenoma lymphomatosum, mucoepidermoid carcinoma and salivary duct carcinoma, among others.[1] Therefore, there is a possibility the area sampled does not reflect the true nature of the tumour. This particular concept is perhaps even more challenging for clear cell lesions. Nearly all salivary gland neoplasms have a "clear cell" variant, while metastatic renal cell carcinoma and other tumours are also in the differential diagnosis. Therefore, for "oncocytic" and "clear cell" lesions, a more conservative interpretation should be used unless there is compelling support to the contrary.

Cases 3 and 4 highlight the problems with non-homogenous tumours as the name "pleomorphic" implies.[1] Small samples of tumours with diverse architectural and cytologic features can be challenging, perhaps even more so as it is the most common salivary gland neoplasm encountered. Case 3 illustrates the startling variation in pleomorphic adenoma. The core-needle biopsy did not sample any of the ductal or epithelial component, instead showing only a spindled population. While IHC may have helped, there is often differential staining of the various components of a PA, that may not be seen in a core-needle sample. The "myxoid" to mucinous material in case 4, along with a transitional appearance was incorrectly interpreted to represent mucoepidermoid carcinoma. Foci of squamous differentiation and mucous cells in pleomorphic adenomas occasionally resemble mucoepidermoid carcinoma. This pitfall can be avoided if a more generalized "salivary gland neoplasm" diagnosis is made, perhaps favouring a benign or malignant category when working with tumours that have mucocytes and/or epidermoid features.[1]

Adenoid cystic carcinoma (ACC) is diagnosed based on cytology and pattern of growth. However, in small samples, polymorphous low-grade carcinoma (PLGA), epithelialmyoepithelial carcinoma (EMC), canalicular adenoma, basal cell adenoma, basal cell adenocarcinoma, and pleomorphic adenoma can all show overlapping features. Many of these tumours will have similar IHC reactivity patterns, since they are all epithelial-myoepithelial composite tumours. In classic form, ACC shows small cells with scant pale cytoplasm and hyperchromatic, angular (peg-shaped) nuclei.[1] ACC may show an epithelial-myoepithelial carcinoma-like pattern in areas, but EMC may show adenoid cystic pattern also.[41] EMC tends to be a tumour that shows an exaggerated myoepithelial component, often with cleared cytoplasm. But, in small samples, this will be very challenging.

By contrast, PLGA is comprised of cells with delicate, vesicular nuclear chromatin with a syncytial cytoplasmic appearance. [42] Canalicular adenoma develops almost exclusively in minor salivary glands, but a core-needle biopsy of an upper lip lesion may not include the "beaded" or canalicular appearance. The cytologic appearance may overlap.[43]

Conclusion

Incisional core-needle biopsies, if obtained by targeted, ultrasound guided, 18–19 gauge cutting needles, processed correctly as recommended herein, allow for architectural preservation and cytologic evaluation of salivary gland lesions. Tumour heterogeneity and diversity must be taken into consideration when rendering a diagnosis, especially when immunohistochemistry separation is not discerning. Potential complications are limited to haematoma, although imaging guidance may require more coordination. Fine needle aspiration must not be abandoned in favour of core-needle biopsy, but the techniques can be viewed as complimentary and could be employed sequentially in selected cases.

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Practice points

- Salivary gland neoplasms have remarkably varied architectural and cytomorphonuclear features, both within and between tumours. However, a few selected tumours show sufficient homogeneity as to be diagnostic on core-needle biopsy samples.
- The accurate classification of salivary gland neoplasms is essential to treatment planning.
- Fine needle aspiration and incisional core-needle biopsies of salivary gland tumours, when appropriately processed and interpreted can significantly aid in treatment planning. However, both techniques are unreliable in many nonneoplastic salivary gland lesions.
- Tumour heterogeneity and diversity must be included in diagnosis, especially when immunohistochemistry studies are equivocal.
- One core-needle biopsy per cassette should be serial sectioned, with staining selected slides to allow for potential additional studies to be performed on the intervening unstained slides, thereby yielding the greatest surface area for interpretation.

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