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Salivary Gland FNA: Anatomic, Clinical, and Technical Considerations

Anatomic Considerations

The major salivary glands consist of the parotid, the submandibular, and the sublingual glands. Under the control of the parasympathetic nervous system, the major salivary glands are responsible for the principal portion of saliva produced, which can be as much as 1.5 liters per day. The minor salivary glands of the oral cavity, pharynx, and upper airways contribute only a small percentage of the overall volume of saliva, but they are particularly important for supplying the mucus layer that protects the tissues of the oral cavity and upper respiratory tract.

Embryologically, the major salivary glands develop during the 6th to 8th weeks of gestation. The parotid gland arises first from ingrowth of the oral ectoderm into the surrounding mesenchyme. By the 7th week of development, the parotid gland moves in a dorsal and lateral direction to reside in the preauricular region, and by the 10th week, the facial nerve divides the surrounding parotid gland into anatomic superficial and deep compartments. A majority of parotid gland tumors develop within the superficial lobe, making FNA and clinical management relatively easy. Tumors originating within the deep lobe of the parotid gland usually present as pharyngeal swellings due to expansion into the parapharyngeal space. The parotid gland is unique among the salivary glands in that it incorporates lymphoid tissue during development, sometimes with entrapment of salivary gland epithelial cells. The latter are believed to be the source of lesions such as Warthin tumor and lymphoepithelial cysts. The minor

salivary glands develop after the major glands and derive from the oral ectoderm and the nasopharyngeal endoderm.

The adult parotid gland, which weighs approximately 15 g, is enclosed in a fibroadipose tissue capsule, and has as its anatomic borders the masseter muscle anteriorly, the zygomatic arch superiorly, the external auditory canal posteriorly, and the styloid process, styloid muscle, and great vessels inferiorly (Fig. 2.1). The tail of the parotid extends over the mastoid tip and lies over the sternocleidomastoid muscle. The main excretory duct of the parotid gland is known as Stenson's duct, which courses along the masseter muscle and the buccal fat pad, and then passes through the buccinator muscle before opening into the oral cavity near the second maxillary molar. Accessory parotid gland tissue is found in approximately

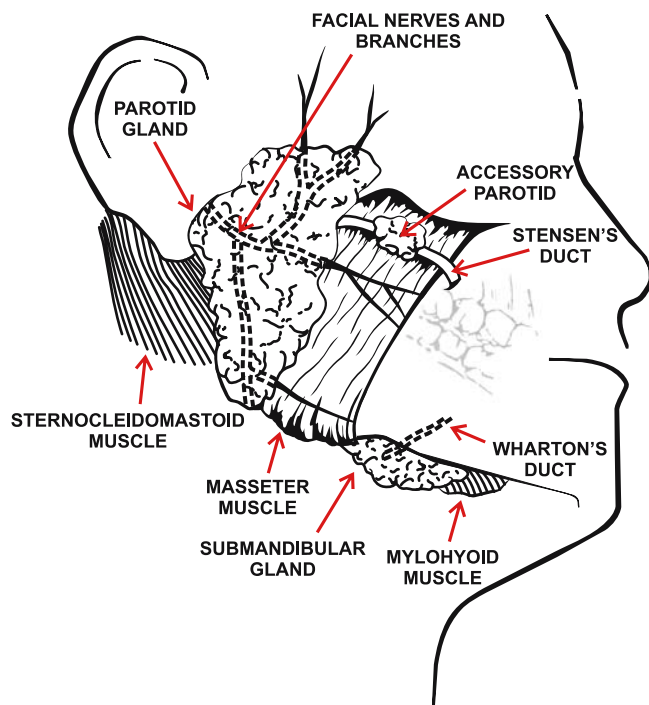


FIG. 2.1. Anatomic relationship of the major salivary glands.

20% of individuals and can occur along the anterior surface of the parotid gland as well as along the length of Stenson's duct. Blood supply to the parotid gland is from branches of the external carotid artery. Lymphatics to the paraparotid lymph nodes derive from the temporal region, scalp, auricle, eyelids and lacrimal glands, while the intraparotid lymph nodes drain the nasopharynx, soft palate, middle ear, and external auditory canal. Parotid gland lymphatics drain into the superficial and deep cervical lymph nodes.

The submandibular gland and the sublingual gland, unlike the parotid gland, are derived from endodermal tissues. The submandibular gland (aka submaxillary gland) weighs 7–8 g, and resides within the submandibular triangle formed by the anterior and posterior bellies of the digastric muscle and the inferior margin of the mandible (Fig. 2.1). The gland is divided into superficial and deep lobes by the mylohyoid muscle, with the deep lobe being the largest. The main excretory duct of the submandibular gland is Wharton's duct, which empties into the oral cavity on the anterior floor of mouth. The blood supply is from submental branches of the facial artery, and lymphatic drainage is to the deep cervical and jugular lymph nodes. The sublingual gland is the smallest of the major glands and weighs only 3 g. It rests in the sublingual fossa of the mandible bounded by the genioglossus and mylohyoid muscles (Fig. 2.1). There are multiple small excretory ducts from the sublingual gland that may connect directly to the oral cavity or join to form Bartholin's duct, which usually empties into Wharton's duct. The vascular supply comes from the sublingual and submental arteries, and lymphatic drainage goes to the submandibular lymph nodes.

Clinical Considerations

Diagnostic Workup and Physical Examination

For a patient presenting with a major salivary gland mass, the clinical workup includes:

- Complete history and physical examination
- Imaging studies (sialography, ultrasound, CT, or MRI)
- FNA
- Summary evaluation and possible presurgical planning

A complete history and focused physical examination is performed to assess the extent of salivary gland disease. Key points to cover include the approximate length of time that the lesion has been present, rate of change in the size of the mass (rapid or slow), associated fever or pain, drug exposures, history of malignancy and chronic illnesses such as rheumatologic disease or sicca syndrome (dry eyes, mouth). Physical examination of a salivary gland lesion is best accomplished with the patient comfortably seated with adequate back and head support. After carefully examining and palpating the mass and its relation to surrounding head and neck structures, particular emphasis is given to evaluating the patient for the presence of trismus, status of facial nerve function, presence of hypesthesia or anesthesia of the skin of the face or neck, and any otologic or oral findings. In addition, the entire neck should be palpated to detect any cervical lymphadenopathy.

Key Physical Exam Findings for a Major Salivary Gland Mass

- Size of mass
- Relationship to surrounding structures (e.g., fixation to skin)
- Trismus
- Facial nerve dysfunction
- Hypesthesia or anesthesia of skin
- Cervical lymphadenopathy

Imaging Studies

When imaging studies are used, they are most often obtained prior to the performance of an FNA since the latter has the potential to introduce traumatic changes in the tissue. A variety of imaging techniques are available for evaluating a major salivary gland mass, including sialography, ultrasonography, computed tomography (CT) scanning, and magnetic resonance imaging (MRI), with the latter two being the most popular. Sialography is applied to a limited extent for evaluation of ductal disease such as calculi, obstruction, and penetrating trauma. Ultrasonography can be used for superficial masses to distinguish extrinsic from intrinsic lesions, and it has also been used to direct FNA for difficult-to-palpate and complex cystic masses. It has the advantage of being inexpensive

and free of complications, but is limited to superficial masses and by its lack of anatomic detail.

High-resolution imaging such as CT or MRI is most commonly used in current practice and is essential for those salivary gland masses with clinical findings suggestive of malignancy, for deep-seated lesions, and for tumors of the submandibular or minor salivary glands. CT scanning is the most cost-effective imaging study for the evaluation of both intrinsic and extrinsic parotid masses; however, it is not very useful for the assessment of general parenchymal disease or ductal architecture. CT can be applied with or without simultaneous sialography and intravenous contrast enhancement (Fig. 2.2). In addition to its value in assessing salivary gland neoplasia, CT is excellent for the detection of salivary gland calculi, and it can also be applied to the evaluation of cystic



FIG. 2.2. Axial CT with intravenous contrast of a superficial left parotid gland tumor. The mass measures 1.2cm, has sharp margins, and shows slight enhancement. Cytologic evaluation of the mass revealed a pleomorphic adenoma.

lesions. In addition, CT is often combined with FNA to sample tumors, particularly those that are deep-seated, and at our institutions this is done in conjunction with a cytopathologist who provides a “rapid interpretation” for assessing sample adequacy and guiding ancillary studies.

MRI is currently the method of choice for the evaluation of salivary gland lesions (Fig. 2.3), especially those involving soft tissues, and with gadolinium-enhancement, MRI is considered equal or superior to contrast-enhanced CT. Contraindications to the use of MRI include patients with pacemakers and

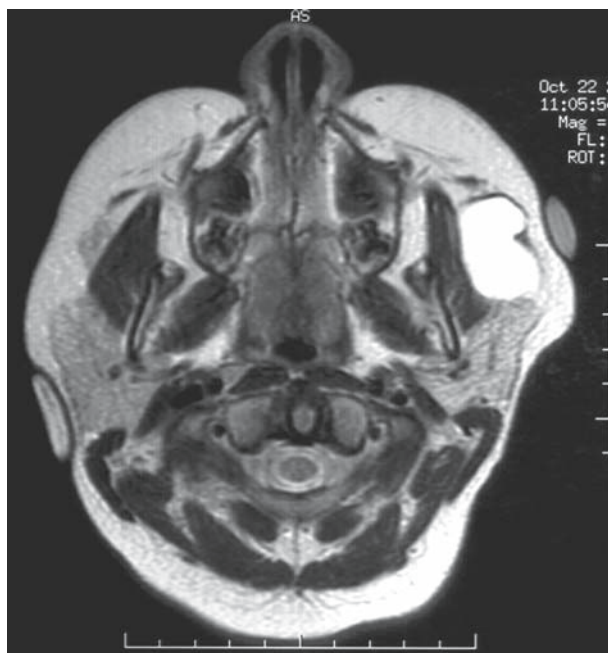


FIG. 2.3. MRI with contrast reveals a 2.8cm well circumscribed, cystic mass superficial to the left masseter muscle and anterior to the left parotid gland along the tract of Stenson's duct. FNA revealed an acinic cell carcinoma that on surgical resection was present within accessory parotid gland tissue of the cheek.

those patients who are agitated or unable to be compliant during the imaging procedure. MRI is considered quite sensitive to the presence of masses within the salivary gland, but less sensitive to inflammatory disorders, and insensitive to calcifications. In addition, MRI is less sensitive to the detection of cystic lesions than is CT. For lesions within or near bone, CT and MRI are complementary.

FNA and the Clinical Management of Salivary Gland Lesions

The role of FNA as a diagnostic test for lesions of the salivary gland is strongly rooted in the clinical management algorithm for salivary gland tumors. While a detailed discussion of the management of salivary gland neoplasia is beyond the scope of this book, some general statements can be made regarding treatment options that have implications for FNA evaluation. For inflammatory and other non-neoplastic causes of salivary gland enlargement, nonsurgical management can often be used. Thus, when properly combined with clinicoradiologic findings and an adequate sample, FNA can, in a subset of cases, obviate the need for surgical intervention. When the mass is malignant, FNA can influence the clinical management by distinguishing between primary and metastatic disease. The most common clinical scenario, however, is a primary mass lesion for which surgery will almost certainly be performed, but the extent of the surgery will depend upon a number of factors, such as the grade and stage of the tumor. For benign and low-grade tumors, surgery alone is usually the treatment of choice. Particularly since a majority of parotid gland tumors arise in the superficial lobe, treatment will usually entail a simple superficial parotidectomy with negative margins. Post-operative radiation therapy is considered for those cases where resection margins are positive. In contrast, high-grade or high-stage tumors are managed by radical surgery that may include sacrifice of the facial nerve and lymph node dissection. Since FNA is highly accurate at distinguishing between low- and high-grade neoplasms, it is very useful for guiding the preoperative planning for such cases.

FNA and the Clinical Management of Salivary Gland Masses

- Primary versus metastatic disease (metastatic workup)
- Non-neoplastic salivary gland enlargement (nonsurgical treatment)
- Benign and low-grade tumors (limited surgery)
- High-grade tumors (radical surgery \pm nerve sacrifice \pm LN dissection)

Technical Aspects of Salivary Gland FNA

Fine-needle aspiration of the salivary gland is similar to FNA of palpable lesions in other anatomic sites. Probably the most important aspect of performing a good salivary gland FNA is adequate sampling and appropriate sample preparation. An adequate sample that includes both air-dried and alcohol-fixed preparations and good clinicoradiologic correlation are the keys to success in salivary gland FNA. In this context, many different “FNA styles” can be used to obtain a similar FNA result, and it will be up to each individual through experience to develop a style that is comfortable.

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FNA Equipment

The standard equipment that we use in the performance of a salivary gland FNA includes 25-gauge sterile needles of either 1” or 1-1/2” length attached to a 10cc syringe and a Cameco syringe pistol or other suitable syringe holder. Of note, some aspirators, including those at our institutions, prefer to use a needle and 10cc syringe without a holder and without applying negative pressure in what we refer to as the “pencil or French technique.” Other materials used during the FNA procedure include 95% ethanol in Coplin jars for slide fixation, normal saline, Hank’s buffered saline, or RPMI in 1.5ml tubes for rinsing the needle, glass “plus” slides with one end frosted for labeling, gauze, alcohol pads, and adhesive bandages. In

general, we do not use local anesthetic prior to performing the FNA except for special circumstances such as very painful lesions.

Performing the FNA

After obtaining informed consent, and using universal precautions against blood contact, the aspirator cleans the skin overlying the nodule to be aspirated with an alcohol pad. Using the first finger and thumb or first and second fingers of the free hand, the nodule is held firmly in place while the other hand is used to smoothly and rapidly insert the needle into the nodule. Pressure on either side of the nodule will help to reduce any pain from the needle stick. The aspirator should then apply a vacuum to the syringe, followed by multiple short, quick back and forth movements with the needle for approximately 5–10 seconds without significantly changing the direction of the needle. In our opinion, a “fanning” movement of the needle during the aspiration could result in more tissue trauma and potential for bruising. The aspirated material (except for cystic lesions) should remain within the barrel of the needle. Once aspirated material or blood appears within the needle hub, the vacuum should be released and the needle withdrawn from the site; this prevents unnecessary dilution of the sample with blood. Upon withdrawal of the needle, a gauze pad is placed over the site and moderate pressure is applied to prevent development of a hematoma. A drop of the aspirated material is expressed onto a glass slide, and 2 smears are made – one for alcohol-fixation and one for air-drying. The needle is then rinsed into a tube containing saline (or other physiologic balanced buffered solution). This aspiration technique is generally repeated 3–5 times (in slightly different areas to maximize sampling) until an adequate sample (based upon rapid assessment) is obtained.

When possible, the salivary gland FNA should be performed by, or in collaboration with, a cytopathologist in order that a preliminary interpretation of the sample can be made before the procedure is completed. This allows for assessment of sample adequacy, but it also permits the triage of the sample for ancillary studies. For example, the needle rinsings from lymphoid lesions can be sent for flow cytometric evaluation for potential lymphoproliferative lesions, a cell block can be made for cases where histochemical and immunohistochemical studies will be needed, microbiologic cultures can be sent for lesions that appear to be inflammatory/

infectious, and a sample can be placed into glutaraldehyde fixative for ultrastructural studies on selected challenging cases.

Summary of Salivary Gland FNA Technique

- Obtain informed consent
- Sterilize skin with alcohol swab
- Immobilize nodule with pressure from 2 fingers of left hand
- Smoothly and rapidly insert needle
- Apply vacuum followed by multiple short, rapid needle strokes
- Release vacuum and withdraw needle
- Obtain an adequate sample by performing 3–5 separate needle sticks
- Prepare both air-dried and alcohol-fixed smears

FNA Specimen Processing

As mentioned previously, a combination of both alcohol-fixed and air-dried smears are essential to maximize the diagnostic evaluation of a salivary gland FNA sample. Because many salivary gland tumors contain a variable combination of cells and matrix material, Diff-Quik and Papanicolaou stains are complementary in the evaluation of salivary gland aspirates. Diff-Quik staining highlights the cytologic features and tinctorial properties of any matrix material that may be present. This is key in distinguishing certain common salivary gland tumors such as pleomorphic adenoma and adenoid cystic carcinoma (see Chapter 6), where the appearance of the matrix rather than the cells is the most important diagnostic feature (Fig. 2.4). Diff-Quik stained smears are also more useful than Papanicolaou-stained preparations for the evaluation of cytoplasmic vacuoles as in acinic cell carcinomas (see Chapter 8). In addition, for the rapid assessment of an FNA specimen, air-dried Diff-Quik preparations are much less time-consuming to prepare. Alcohol-fixation and Papanicolaou staining are useful for better visualizing the nuclear features of the cell, including chromatin pattern, nuclear membrane irregularities, nucleoli, and inclusions. In our opinion, a detailed evaluation of nuclear atypia is best achieved using Papanicolaou staining.

As an adjunct to standard smears, needle rinsings are important since they can be used to produce a thin-layer preparation,

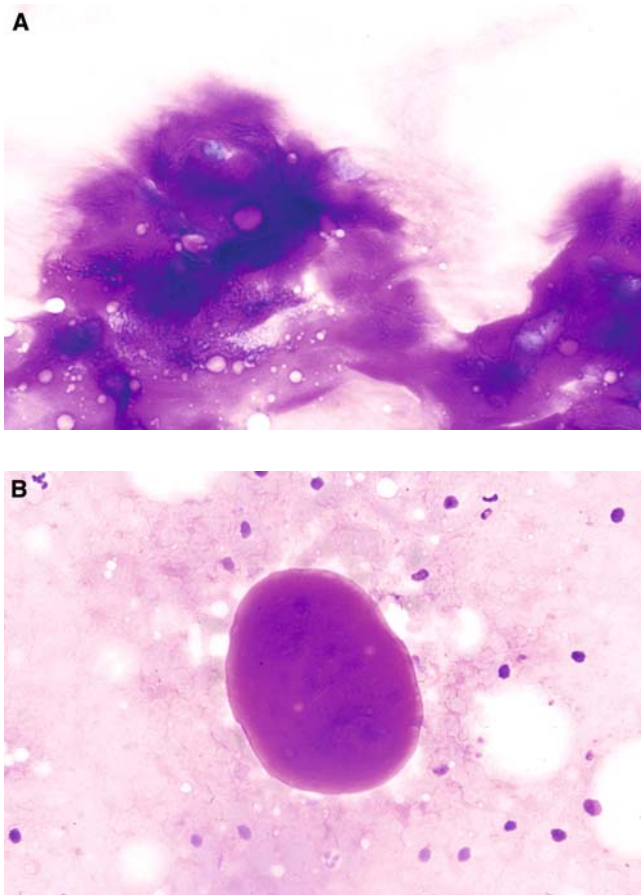


FIG. 2.4. Diff-Quik staining of air-dried smears provides key differential diagnostic information about matrix-containing salivary gland tumors by highlighting characteristic features of the matrix as demonstrated by aspirates of pleomorphic adenoma (A) and adenoid cystic carcinoma (B).

cytospin, and/or cellblock. Thin-layer (TP) or cytospin preparations in our opinion should not be the sole method for evaluating salivary gland lesions, especially those containing matrix material. TPs do have the advantage of concentrating the cells onto a single slide and of removing excess obscuring blood. For cystic lesions where the cellular components are diluted within

a large volume, TP is probably the best preparatory method to use. A cell block can be prepared from the needle rinsings for those cases where histochemical (e.g., mucicarmine, PTAH) or immunohistochemical (e.g., S-100, cytokeratin) stains would be useful in the diagnostic evaluation.

FNA Specimen Processing

- Air-dried, Diff-Quik staining (rapid processing, highlights matrix material and cytoplasmic vacuoles)
- Alcohol-fixed, Papanicolaou staining (highlights nuclear details and atypia)
- Thin-layer preparation (concentration of cells into monolayer, removal of obscuring blood)
- Cell block (histochemical and immunohistochemical stains)
- Needle rinsings (flow cytometric and microbiologic studies)

Suggested Reading

- Allen SM, Boon AP, Brownridge DM, Chadwick CH, Buckley JG. Fine needle cytology of palpable head and neck lesions: a comparison of sampling methods with and without suction. *Cytopathology* 1999;10:97–106.
- David O, Blaney S, Hearp M. Parotid gland fine-needle aspiration cytology: an approach to differential diagnosis. *Diagn Cytopathol* 2007;35:47–56.
- Kontis TC, Johns ME. Anatomy and physiology of the salivary glands. In: Bailey BJ (ed): *Head and neck surgery – Otolaryngology*, 2nd ed. Philadelphia: Lippincott-Raven Publishers, 1998:531–539.
- Martinez-Madrigal F, Micheau C. Major salivary glands. In: Sternberg SS (ed), *Histology for pathologists*. New York: Raven Press, 1992:457–478.
- NCCLS. Fine needle aspiration biopsy (FNAB) techniques: approved guideline. NCCLS document GP20-A. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA, 1986 [www.clsi.org].
- Powers CN and Frable WJ. *Fine Needle Aspiration of the Head and Neck*, Boston: Butterworth-Heinemann, 1996:1–21.
- Stewart B, Kruskal B, Kelly D, Sosna J, Kane RA. Utility and safety of ultrasound-guided fine-needle aspiration of salivary gland masses including a cytologist's review. *Ultrasound Med* 2004;23:777–783.
- Wong DS, Li GK. The role of fine-needle aspiration cytology in the management of parotid tumors: a critical clinical appraisal. *Head Neck* 2000;22:469–473.

Salivary Gland Cytopathology

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2008, X, 268 p. 176 illus., 164 illus. in color., Softcover

ISBN: 978-0-387-76622-5