Intraoral and Oropharyngeal Lesions: Role of Fine Needle Aspiration Cytology in the Diagnosis

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Abstract The oral cavity is affected by a wide range of pathologic lesions, for which a morphologic diagnosis is required for proper management. Fine needle aspiration (FNA) is being increasingly used for preliminary diagnoses of such lesions. This is retrospective analysis of intraoral and oropharyngeal lesions diagnosed with FNAC over a period of 7 years. Out of total 55 cases, a definite diagnosis could be made on cytology in 50 cases (90.9 %). These 50 cases were further included in the study. Thirty cases were reported as non-neoplastic and 20 as neoplastic (11 benign and nine malignant). The diagnoses were made taking into account the background material (blood, mucin) and the predominant cells present (neutrophils, lymphoid cells, macrophages, hemosiderin laden macrophages, squamous cells, basaloid cells, spindle cells, giant cells). Histopathological diagnosis was available in 17 cases and corresponded with FNA diagnosis in 16 cases (94.12 %). No significant complications were seen in patients undergoing these FNAs. It can be concluded that FNA is a simple and rapid diagnostic test that can be useful for preliminary assessment of oral and oropharyngeal lesions.

Keywords Oral cavity · Pharyngeal masses · Tongue swelling · Cheek · Fine needle aspiration

Introduction

The oral cavity and oropharynx is affected by a wide range of pathologic lesions that may originate from squamous mucosa, salivary glands, mesenchymal structures, and lymphoid tissue. A variety of lesions including inflammatory, cystic and benign or malignant neoplasms can occur within the oral cavity that requires a morphologic diagnosis for guiding further management. These lesions have been traditionally treated on clinical basis and evaluated by surgical biopsy. Studies of transmucosal needle aspiration of oral cavity lesions are limited [1–10]. The oral cavity and oropharynx are readily accessible to fine needle aspiration (FNA) and it may be a useful technique for preliminary assessment. With use of quick staining methods, a rapid provisional diagnosis can be made in most cases. A series of 50 cases, which highlights the utility of FNA cytology in diagnosis of oral and oropharyngeal lesions, is presented. The emphasis is on discrimination of inflammatory from tumor like lesions and benign from malignant tumors. The diagnostic approach and detailed cytological findings and differential diagnoses are also discussed.

Materials and Methods

The data of patients who underwent intra-oral FNA over a period of last 7 years were retrieved and analyzed. The FNA was performed in the out-patient clinics. Prior to procedure, the patients were asked to gargle with water. The samples were taken with the patients in a supine position. Head lamps, disposable tongue depressors and sterile gauze were used for better visualization. For deep seated lesions in oropharynx and posterior tongue, patients received local anesthesia in the form of lignocaine spray or

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Fig. 1 Clinical photograph showing the procedure of intraoral FNA

lignocaine viscous gargle to avoid gag reflex. Sedation was not required in any of the cases. The approach of FNA in all the cases was transoral and it was performed by aspiration technique with 22–23 G needle attached to 10 ml syringe, mounted on Cameco's handle; 38 mm long needles were used for deep seated lesions (Fig. 1). One to two passes were made per case. Tight closing of the mouth and swallowing achieved hemostasis, although in superficial lesions, compression was also given by dry cotton wad. Procedure time taken was usually 1–2 minutes. The smears were air dried for May-Grunwald Giemsa stain (MGG) and wet fixed in 95 % alcohol for hematoxylin and eosin (H&E) staining. Special stains like mucicarmine and periodic-acid-Schiff (PAS) were done wherever required. The cytological diagnosis was given within 48 h. The cytological diagnoses were compared with the histopathological diagnoses, which was available in 17 cases. The estimation of the sensitivity, specificity and accuracy of the FNAC method was conducted according to the definitions of Trott, where sensitivity is the ability of the test to identify malignant lesions and specificity is the ability to identify benign lesions. Accuracy was calculated as the number of FNAC results that were similar to those of the regular biopsy [10].

Results

Out of a total of 15,205 FNACs performed over a period of 7 years, 55 (0.36 %) cases of intraoral/oropharyngeal lesions could be retrieved. Out of these 55 cases, sufficient material was obtained in 50 cases (90.9 %). Only these cases were further taken into study. Out of 50 cases; there were 27 males and 23 females and the age ranged from 4 to 82 years. The sites of FNA included palate and gingiva (15 cases), tongue (eight cases), oropharynx and tonsil (14

cases), floor of mouth (nine cases), cheek or buccal mucosa (two cases) and lips (two cases) and based on the cells aspirated, the lesions were divided into inflammatory/reactive, benign, and malignant (Table 1). The inflammatory/reactive conditions were seen equally in all age groups; the benign neoplasms were seen in adults (20–70 years) and the malignant lesions were seen in middle aged to older adults (42–69 years; one case 25 years). Table 2 provides the cytologic and final histologic diagnosis.

Cytologic Findings

In nearly all the cases, at one edge of the smear, oral squamous cells, neutrophils and mucin were present and were interpreted as contamination from oral mucosa. Smears that showed dense neutrophilic infiltrates along with macrophages were reported as acute inflammation (Fig. 2). These were treated with antibiotics and did not require histopathological examination. Cases that had mucoid aspirates, and hypocellular smears with scattered macrophages and neutrophils were diagnosed as mucocysts. In a single case of FNA from blue black swelling tongue, smears showed altered blood and hemosiderin laden macrophages and a diagnosis of hematoma was given.

In seven cases, predominantly lymphoid cells were present. In cases that showed all stages of lymphoid maturation i.e. mature lymphocytes, follicle centre cells and lympho-histiocytic tangles, a diagnosis of reactive lymphoid proliferation was given. These patients had symptoms for a long duration (1–3 years) and enlargement of any other lymphnode groups was not present. In two cases smears showed monomorphic lymphoid cells and these were reported as non-Hodgkins lymphoma (NHL). In one case, the patient was 67 years old female and FNA was performed from gingival swelling. Smears showed small to intermediate sized cells, compatible with low grade NHL. Final diagnosis was follicular NHL on preauricular lymphnode biopsy. The other case was a 69 year old male with enlargement of left tonsil and submandibular lymphnode for one month. The lymphoid cells were large with frequent mitoses and tingible body macrophages and diagnosis of NHL-high grade was rendered.

Among the lesions rich in squamous cells; in three cases there were anucleate squamous cells and mature cells without atypia and reported as benign keratinous cyst. In four cases, the smears were less cellular and the squamous cells were pleomorphic with irregular hyperchromatic nuclei and diagnosed as squamous cell carcinoma. Squamous cell carcinoma was found to be the most common malignancy.

Smears with basaloid epithelial cells had varied diagnoses. Cases diagnosed as pleomorphic adenoma (PA)

Table 1 Spectrum of inflammatory and neoplastic lesions (benign and malignant) of oral cavity diagnosed on FNA (n = 50)

	Inflammatory/reactive (30)	Benign (11)	Malignant (9)
Tongue	Mucocele (2) Acute inflammation (2) Hematoma (1)	Benign spindle cell lesion (1) Spindle cell lesion, s/o hemangioma (1)	Squamous cell carcinoma (1)
Oropharynx/Tonsil	Reactive lymphoid proliferation (4) Acute inflammation (3) Keratinous cyst (2)	Benign nerve sheath tumor/pleomorphic adenoma (1)	Squamous cell carcinoma (2) Non Hodgkins lymphoma (1) Adenocarcinoma (1)
Palate & gingiva	Acute inflammation (4) Mucocele (1)	Pleomorphic adenoma (2) Spindle cell tumor (2) Spindle cell proliferative lesion (1) Osteoclastic giant cell rich lesion (1) Odontogenic tumor (1)	Non Hodgkins lymphoma (1) Squamous cell carcinoma (1) Polymorphous low grade adenocarcinoma/pleomorphic adenoma (1)
Floor of mouth	Mucocele (4) Acute inflammation (2) Reactive lymphoid proliferation (1) Keratinous cyst (1)		Adenoid cystic carcinoma (1)
Buccal mucosa cheek	Acute inflammation (1)	s/o Hemangioma (1)	
Lips	Mucocele (2)		

Table 2 Cytological diagnoses according to predominant cells in aspirates with their histopathological correlation

Predominant cells on aspirates	Cytological diagnosis (50)	Histopathological diagnosis (17)
Neutrophilic infiltrate	Acute inflammation (12)	
Lymphoid cells	Reactive lymphoid hyperplasia (5) Non-Hodgkins lymphoma (2)	Non-Hodgkins lymphoma (2)
Macrophages in a mucoid background	Mucocele (9)	Mucus extravasation cyst (3)
Hemosiderin laden macrophages	Hematoma (1)	
Squamous cell rich lesions	Keratinous cyst (3) Squamous cell carcinoma (4)	Squamous cell carcinoma (2)
Basaloid epithelial cell lesions	Pleomorphic adenoma (2) Odontogenic tumor (1) Adenoid cystic carcinoma (1) Polymorphous low grade adenocarcinoma/ Pleomorphic adenoma (1) Adenocarcinoma (1)	Adenoid cystic carcinoma (1) Polymorphous low grade adenocarcinoma (1) Mucoepidermoid carcinoma (1)
Spindle cell lesions	Benign nerve sheath tumour/pleomorphic adenoma (1) Benign nerve sheath tumour (2) Spindle cell proliferative lesion (1) Benign spindle cell lesion (1)	Schwannoma (3) Cement-ossifying fibroma (1) Sarcomatoid SCC (1)
Haemorrhagic lesions with few spindle cells	s/o Hemangioma (2)	Cavernous hemangioma (1)
Osteoclastic giant cell rich lesion	Giant cell rich lesion (1)	Giant cell reparative granuloma (1)

showed chondromyxoid stroma with plasmacytoid and basal epithelial cells with moderate cytoplasm (Fig. 3). Surgical excision was advised in both the cases. In a case of palatal swelling, the basaloid cells were mildly

hyperchromatic with inconspicuous nucleoli and scanty cytoplasm. Metachromatic stromal material was also present. Both possibilities of polymorphous low-grade adenocarcinoma (PLGA; Fig. 4) and PA were given. In a case

Fig. 2 Dense neutrophilic infiltrate along with macrophages seen in a case of acute inflammation. (H&E stain; $\times 400$)

Fig. 3 A case of pleomorphic adenoma shows bland epithelial cells, some with plasmacytoid appearance intermixed with a chondromyxoid stroma. (H&E stain; $\times 200$)

of FNA floor of mouth, there were small tumor cells that surrounded hyaline globules in a cribriform arrangement and a diagnosis of adenoid cystic carcinoma was made (Fig. 5). In another case of FNA tonsil, cells were arranged in glandular pattern; they had uniform eccentrically placed nuclei and moderate cytoplasm. A diagnosis of adenocarcinoma was given. The histopathology revealed low grade muco-epidermoid carcinoma. In one case, there was a lytic lesion in mandible. Smears showed few basaloid cells with preserved polarity and diagnosis of benign odontogenic tumor was given in corroboration with radiological and clinical diagnosis.

Smears rich in spindle cells also had varied diagnoses. In cases diagnosed as benign nerve sheath tumor the cells were present in cohesive clusters in a myxoid stroma and had slender nuclei with pointed ends (Fig. 6). Occasional

Fig. 4 Smear shows clusters of basaloid cells with mild pleomorphism from a case of FNA palate. Histopathology showed polymorphous low-grade adenocarcinoma. (H&E stain; $\times 200$)

Fig. 5 FNA smears from adenoid cystic carcinoma, floor of mouth show small basaloid cells surrounding hyaline matrix spheres in a cribriform pattern. (H&E stain; $\times 200$)

Verocay bodies were appreciated in one case. In a single case of FNA oropharynx of a 15 year old boy, because of presence of abundant metachromatic myxoid stroma, both possibilities of nerve sheath tumor and PA were given. Histopathological diagnosis was schwannoma. In another case, a 70 year old female had firm to hard swelling right gingiva, palate and maxilla. FNA showed clusters of slender spindle cells with bland nuclear chromatin and was diagnosed as spindle cell proliferative lesion. Biopsy showed bony spicules in a fibrous stroma and reported as cemento-ossifying fibroma. In another case, FNA from smooth swelling, posterior tongue in a 60 year male smoker, showed few spindle cells and was reported benign. Histopathology showed sarcomatoid squamous cell carcinoma with spindle cells positive for cytokeratin.

Fig. 6 FNA smears from schwannoma shows cells present in cohesive clusters with slender nuclei with pointed ends. (H&E stain; $\times 400$)

In two cases, one 4 year old child (cheek) and the other 65 year old woman (tongue), the lesions were bluish, soft and compressible on palpation. Smears were haemorrhagic with few small plump spindle cells and possibility of hemangioma was given on FNA. Histopathology of the latter case was cavernous hemangioma. One case of blackish swelling tongue showed hemosiderin laden macrophages and altered blood was diagnosed as haematoma.

There was a single case of FNA of lower gingiva with smears rich in osteoclastic giant cells and mononuclear cells with bland chromatin. Possibilities of epulis, giant cell reparative granuloma and aneurysmal bone cyst were rendered. Histopathological examination confirmed the diagnosis of giant cell reparative granuloma.

Thus, the sensitivity of malignant diagnosis was 90 %; with few differences in typing of tumors. One case diagnosed as benign spindle cell lesion by cytology, was later diagnosed as sarcomatoid squamous cell carcinoma on histology. The diagnostic accuracy of histopathologically proven cases was 94.12 %. The specificity of benign diagnosis was 97.5 %; thirty cases diagnosed with inflammatory or reactive lesions were considered clinically benign and did not require histopathological examination and were managed accordingly. Clinical follow up showed regression of these swelling.

Discussion

FNA is a quick, minimally invasive procedure that can be performed in an outpatient setting. It is a safe technique that has still not been widely utilized in oral lesions. Biopsy from few sites in oral and oropharyngeal region like tonsil and tonsillar fossa is usually difficult. Also there may be situation like trismus and oral submucosal fibrosis which

may make biopsy practically impossible. FNA is cost effective as compared to biopsy which is expensive, may produce unwanted bleeding and requires more time for processing, leading to delay in diagnosis. Moreover an incisional biopsy of an encapsulated tumor is usually contraindicated. The few technical difficulties encountered in oral FNA include the inability to fix the lesions properly and the space available to perform the back and forth movement during aspiration is also less. Head lamps and lignocaine sprays are necessary for deep seated lesions.

In the current series, sufficient material was obtained in 50 out of 55 cases (90.9 %). In these cases it was possible to classify lesions on FNA and to distinguish contaminant squamous cells and mucus from lesional cells. In a study by Gupta et al. smears were inadequate in 7 % cases mostly due to sampling error [11]. Neutrophilic infiltrate that are present in inflammatory conditions, may also be seen in smears from squamous cell carcinomas, mucus extravasation cysts and epidermoid cysts.

A lymphoid cell rich infiltrate can be seen in FNA of lymphoid tissue in Waldeyer's ring. A polymorphic infiltrate is seen in reactive enlargement of tonsils and these patients require only follow-up and biopsy is not required. A high suspicion of NHL should be kept when lymphoid cells are aspirated from unusual locations like cheek, gingiva, etc. or when there is simultaneous enlargement of other lymphnodes as well. In a study it was seen that FNA was superior to biopsy for preliminary diagnosis of NHL, as biopsy may show only superficial tissue whereas the needle reaches the deeper areas and provides more accurate sample [12]. However, flow cytometric analysis or IHC on a deeper biopsy is recommended for optimum diagnosis [13].

Diagnosis of cystic lesions of oral cavity may be less specific due to paucity of specific lesional cells and superimposed infection [9]. The contents must be fully aspirated and then sampled again to obtain material from the capsule. Mucoïd aspirates have a differential diagnosis of benign conditions (mucus extravasation cysts, mucus retention cyst, congenital cyst) and malignant lesions like mucoepidermoid carcinoma. A short history, absence of epithelial cells and presence of muciphages favor diagnosis of mucocele.

Lesions rich in squamous epithelial cells include benign cysts and squamous cell carcinomas. The squamous cells in keratinous cysts are present uniformly throughout the smear and in all the smears. Presence of any nuclear enlargement and irregularity should make one suspicious of a neoplastic etiology. SCC and its variants account for majority of malignancies of the oral cavity as was seen in present series also [14]. False positive diagnosis of SCC may be made in cases of PA with extensive squamous metaplasia and is a potential pitfall [13]. In the current

series a sarcomatoid SCC of base of the tongue was misdiagnosed as benign spindle cell lesion as smears showed spindle cells without nuclear atypia. However on review of slides, fibre cells with hyperchromatic nuclei were observed.

In cases with basaloid epithelial cells (cohesive oval cells with scanty cytoplasm), the differential diagnoses includes benign and malignant salivary gland lesions, odontogenic tumors and basaloid squamous cell carcinoma [9]. In particular distinction between PA, PLGA and adenoid cystic carcinoma may be difficult because they show only mild nuclear pleomorphism and hyaline globules may be present. Diagnosis of PA is favored when cells have a well defined cytoplasm, only few stripped nuclei and a bland finely granular nuclear chromatin [15]. Lee et al. [16] noted that plasmacytoid appearance of tumor cells with abundant cytoplasm is a reliable feature of PA. PLGA occurs most commonly in the palate and its differentiation from other salivary gland tumor remains a challenge (as was seen in one of our cases where differential diagnosis of both PLGA and PA were given). Smears are cellular and tumor cells are arranged in sheets, papillae and around myxoid stroma. The tumor cells display minimal pleomorphism, moderate cytoplasm, round to spindled nuclei, uniform hyperchromasia with inconspicuous nucleoli and absent mitoses and usually no necrosis [17]. In adenoid cystic carcinoma, the cells are arranged around the hyaline globules, have scanty cytoplasm, naked nuclei, nuclear moulding, hyperchromasia and coarse chromatin [15]. Necrosis may be a feature of adenoid cystic carcinoma but is usually not seen with PLGA. Odontogenic tumors require clinico-radiologic correlation.

Among the spindle cell lesions, most common diagnoses were benign nerve sheath tumors. Schwannomas can occur in the oral cavity and smears are cellular and show long slender cells with nuclear kinking embedded in a myxoid stroma [18]. In one case a differential diagnosis of PA was also given because of low cellularity and abundant presence of similar metachromatic ground substance.

Aspirates from hemangioma are frequently acellular and contain sparse groups of small plump spindle endothelial cells with scanty cytoplasm admixed with peripheral blood [19]. Clinical features of compressible mass, in children are highly suggestive of the diagnosis of hemangioma. Deeply situated cellular hemangiomas may pose a difficulty in diagnosis [20]. In hematoma the aspirate is brownish (altered blood) and smears show altered blood with pigment laden macrophages.

For diagnoses of lesions of the jaw a combined clinico-radiological and histological correlation is essential for exact categorization. Fibro-osseous lesions of the jaw comprise of a spectrum of diseases which include osseous

dysplasia, fibrous dysplasia, and ossifying fibroma [21]. FNA smears show clusters of fibroblast-like cells with bland nuclei, and no nuclear atypia or mitotic figures along with some multinucleated giant cells. Calcified material or bony spicules may not be evident [22]. In a case of cement-ossifying fibroma, there was involvement of maxillary bone and only few benign spindle cell clusters were seen in smears.

Differential diagnoses were given on cytology in a case of central giant cell granuloma. Other giant cell rich lesions of the jaws include cherubism, peripheral giant cell granuloma, aneurysmal bone cyst, traumatic bone cyst and jaw tumour of hyperparathyroidism. Their distinction is difficult on cytology due to identical features comprising of many giant cells [23]. Central giant cell granuloma has been postulated to be an inflammatory lesion, a reactive lesion, a true tumor, or an endocrine lesion [24]. It is usually asymptomatic, found predominantly in children and young adult females and accounting for less than 7 % of all benign jaw lesions [24].

Jaw lesions rich in basal cells include ameloblastoma and follicular cysts. The exact location, history and radiological appearances must be considered before a definitive cytological diagnosis of odontogenic tumors is made. The characteristic combination of basaloid, stellate and polygonal squamous cells help in making a specific diagnosis of ameloblastoma [25]. Thus, FNA alone may not be an accurate procedure for definitive diagnosis of osseous lesions, but it can be a useful when used in conjunction with clinical and imaging findings.

The sensitivity, specificity and diagnostic accuracy in our study is similar to other studies [5, 26]. However sensitivity was much higher than a study by Gupta et al. because cases with inadequate aspirates were not taken into study. In cases where FNA was unsatisfactory, the authors emphasize the need of repeating the FNA or recommending biopsies. Of the 50 cases in our series, there was only one false negative case of sarcomatoid squamous cell carcinoma. The remaining cases were accurately classified as reactive versus benign versus malignant/suspicious, thereby guiding further management as further biopsy was not required in 33 cases.

Conclusion

FNA permits rapid and accurate diagnosis of both benign and malignant lesions of the oral cavity and oropharynx. This is very helpful for patient management which may help avoid unnecessary surgery and allow for quicker treatment. Thus it may be used as the first line of investigation in evaluation of oral and oropharyngeal lesions.

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Compliance with Ethical Standards

Conflict of interest There are no financial disclosures or conflict of interest from any authors.

Ethical standards The procedures followed were in accordance with the ethical standards in accord with the Helsinki Declaration of 1975 as revised in 1983.

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