Fine-needle aspiration cytology as diagnostic tool of parotid tumors and associated pitfalls in correlation with histopathology

Bhawana Pant¹, Sanjay Gaur², Prabhat Pant³

¹Department of ENT, Government Medical College, Haldwani, Uttarakhand, India, ²Department of Pharmacology, Government Doon Medical College, Dehradun, Uttarakhand, India, ³Department of Pathology, Government Medical College, Haldwani, Uttarakhand, India

Introduction: Fine-needle aspiration cytology (FNAC) has been used for ages as a safe and economical tool for fast pre-operative diagnosis of parotid tumors. It has certain pitfalls which sometimes lead to misdiagnosis and consequently, it may have affect on the treatment of the tumors. Keeping in view of the diverse classification of parotid tumors’ information from cytology should be combined with radiology as well as a clinical diagnosis. Aim: The aim of the study was to discuss some cases where there was a discrepancy between cytological diagnosis and histopathological results and also suggest measures to improve the efficacy of FNAC. Materials and Methods: The study includes 50 cases of parotid tumors who presented to the Department of Ear, Nose, and Throat (ENT) at Government Medical College Haldwani which is a tertiary referral center during 2009–2016. Only adult patients were included and inflammatory swelling was excluded from the study. All patients evaluated contrast-enhanced computerized tomography and magnetic resonance imaging followed by FNAC. Pre-operative diagnosis was made on the findings of the above investigations and different types of parotid surgeries were done. The final diagnosis was made on the histopathological examination. Results: The most common tumor came out to be pleomorphic adenoma (23 cases – 46%) followed by mucoepidermoid carcinoma (12 cases – 24%). In ten cases, there was no clear cut association between cytological diagnosis and final histopathological diagnosis. Conclusion: FNAC is a highly sensitive and specific technique for the diagnosis of many salivary gland swellings. FNAC can be used preoperatively to avoid unnecessary surgery and biopsy. Details of clinical information and radiologic features may help the pathologist to arrive at the appropriate diagnosis and reduce false interpretation. Pitfalls may also occur with the improper technique of FNAC which can be overcome by proper caution.

KEY WORDS: FNAC, histopathology, parotid tumor

INTRODUCTION

Parotid gland tumors are interesting in a way because of variable clinical presentation, radiological dilemma at times, and variable cytological pictures. These factors are very important for a surgeon when pre-operative workup is being done. Fine-needle aspiration cytology (FNAC) plays an important role through at times controversial in cases of benign tumors like pleomorphic adenoma. The problem can be on both levels, i.e., sampling error as well as interpretation at the level of cytopathologists. There are several benign malignant look-alike tumors such as basal cell adenoma and adenocystic carcinoma that can be confused on FNAC.¹ These cases can finally be addressed by the histopathology report of the entire specimen. This study included parotid tumors over a period of 5 years which were studied for clinical presentation, cytology picture, and histopathological report.

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histopathological profile. Pitfalls and shortcomings of FNAC in pre-operative diagnosis of parotid tumors are also discussed.

MATERIALS AND METHODS

The study includes 50 cases of parotid tumors who presented to the Department of ENT at Government Medical College Haldwani which is a tertiary referral center. The duration of the study includes patients presenting from 2009 to 2016. Only adult patients were included and inflammatory swelling was excluded from the study. All patients who were suspected to have tumors were evaluated with radiological tools such as contrast-enhanced computerized tomography and magnetic resonance imaging (MRI). It was followed by FNAC. Pre-operative diagnosis was made on the findings of the above investigations and different types of parotid surgeries were done. The nature of surgery was also changed according to the intraoperative findings. The final diagnosis was made on the histopathological examination. Post-operative radiotherapy or chemotherapy was decided on the basis of the final histopathological diagnosis. Association between pre-operative FNAC finding and final histopathological diagnosis was seen. Cases in which there was no association between cytological and histopathological diagnoses were discussed.

RESULTS AND OBSERVATION

Out of 50 patients included in the study male to female ratio was 2:3. FNAC was performed in all cases and repeat procedure was done in ten patients. FNAC results were divided into the following categories, for example, pleomorphic adenoma, mucoepidermoid carcinoma, Warthin’s tumor, adenoid cystic carcinoma, and lymphoma, as shown in Table 1.

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>No. of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleomorphic adenoma</td>
<td>23 (46)</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Warthin’s tumor</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Basal cell adenoma</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Acinic cell carcinoma</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Lymphoepithelial cyst</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Metastatic from other site</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Case (1)

A case of Warthin’s tumor was diagnosed as low-grade mucoepidermoid carcinoma on cytology. A 63 years old male patient presented with the right parotid gland mass. On cytology, smears were paucicellular and showed few groups and clusters as well as singly dispersed mucinophages along with very occasional small groups, clusters, small sheets of squamous epithelial cells, and intermediate cells against a background containing abundant mucoid/proteinaceous material with numerous singly dispersed lymphoid cells. This patient was diagnosed as low-grade mucoepidermoid carcinoma on cytology [Figure 1]. However, histopathological examination revealed features of Warthin’s tumor. This case seems to be a case of selective sampling on cytology. Multiple sampling is important to overcome the problem of misdiagnosis due to selective sampling. Improper diagnosis may lead to a dilemma as treatment of Warthin tumor is entirely different from mucoepidermoid carcinoma [Figure 2].

Case (2)

A case of high-grade mucoepidermoid carcinoma was diagnosed as poorly differentiated carcinoma on cytology. A 41 years old female patient presented with the right parotid gland mass. On cytology, smears were cellular and showed numerous groups,
clusters, and syncytial aggregates as well as singly dispersed atypical epithelial cells displaying high N: C ratio, moderate amount of dense basophilic cytoplasm, moderate to high nuclear pleomorphism, and against hemorrhagic background suggestive of poorly differentiated carcinoma [Figure 3]. On histopathological examination, sections showed tubule, papillary and cribriform islands, and solid sheets lined by central cuboidal to low columnar epithelial cells and outer myoepithelial cells. Perineural and lymphovascular invasion was present confirming the diagnosis of epithelial myoepithelial carcinoma.

Case (4)
A case of malignant epithelial tumor carcinoma ex pleomorphic adenoma was diagnosed as high-grade mucoepidermoid carcinoma on cytology. A 59 years old male patient presented with the nodular, painless, firm to hard mass over the right parotid gland for the past 6 years. Cytology smears showed numerous atypical epithelial cells on a mucohemorrhagic background displaying high N: C ratio, moderate amount of dense basophilic cytoplasm, moderate to high nuclear pleomorphism, etc. Few cells having finely vacuolated cytoplasm, mucinophages lead to the diagnosis of high-grade mucoepidermoid carcinoma. On histology sections showed singly scattered and few small to large islands and sheets of atypical pleomorphic epithelial cells displaying squamoid differentiation infiltrated in stroma, at places showing areas of necrosis. Adjacent parenchyma showed features of pleomorphic adenoma.

Case (5)
A case of chronic sialadenitis was diagnosed as pleomorphic adenoma with cystic changes on cytology. A 53 years old male patient presented with the nodular, painless, firm to hard mass over the right parotid gland from the past 1 year. On cytology, smears showed few small cohesive groups, clusters, and sheets of benign ductal epithelial cells and acinar cells along with few fibromyxoid and dirty fibrocollagenous stromal tissue fragments against a hemorrhagic background containing scattered small lymphocytes, polymorphs, and cystic macrophages leading to this diagnosis. On histology sections showed diffuse infiltration of salivary gland parenchyma by mononuclear and reactive lymphoid cells with acinar cell atrophy. At places, focal areas of fibrosis, hyalinization, and myxoid degeneration were also seen.

Case (6)
A 19 years old male patient who was a case of acinic cell carcinoma was diagnosed as benign cystic lesion on cytology. On histology tumor mass composed of neoplastic acinar cells forming solid cystic pattern with few large cystic spaces containing eosinophilic material and interspersed lymphoid aggregates. This case was under-diagnosed as benign cystic lesion due to selective sampling, age of the patient, history of short duration, paucity of cellular component, and presence of background mucoid material on cytology.

Case (7)
A case of low-grade mucoepidermoid carcinoma in a 63 years old female was diagnosed as mucous retention cyst on cytology. On aspiration, 2.0 ml fluid was aspirated and swelling slightly regressed in size after aspiration. On cytology, numerous groups/clusters and singly scattered mucinophages were seen
against a mucoid background containing few sheets of squamous epithelial cells. No atypical or malignant cells were seen leading to the diagnosis of mucous retention test. On histology, tumor comprises mucin filled small to large cystic spaces and glandular structures lined by a single layer of mucous cells with pale basophilic cytoplasm along with solid epithelial nests. This case was misdiagnosed due to selective sampling on cytology, so multiple sampling is important to overcome this problem.

**Case (8)**

A case of adenoid cystic carcinoma was diagnosed as basal cell adenoma on cytology because of the presence of hyaline globules in a 56 years old male who presented with an asymptomatic lump over the right parotid region for past 3 years. On cytology few small groups, clusters of small uniform ductal epithelial cells, basaloid cell with scant cytoplasm. On histology sections showed solid sheets, cribriform nests or islands and tubules comprising of small bland myoepithelial cells with scant cytoplasm and round to oval angular nuclei surrounded by hyalinized stroma.

**Case (9)**

A case of salivary duct carcinoma was diagnosed as poorly differentiated carcinoma, possibly adenocarcinoma on cytology. A 65 years male patient with the left parotid gland mass for the past 6 months revealed moderately cellular smears showing groups, clusters, papillaroid fragments, and small sheets as well as singly scattered atypical epithelial cells displaying high N:C ratio, coarse granular chromatin, etc. The histopathological picture showed infiltrative tumor mass composed of neoplastic cells displaying abundant eosinophilic cytoplasm, large pleomorphic vesicular nuclei, and prominent multiple nucleoli arranged in solid, cribriform, and papillary cystic pattern with vascular and perineural invasion.

**Case (10)**

A 52 years old male patient of non-Hodgkin’s lymphoma was diagnosed as chronic sialadenitis on cytology. He had asymptomatic right submandibular gland mass for the past 2 years, now gradually increasing in size. Smears were cellular and showed very occasional small groups and clusters of benign ductal epithelial cells against a background containing a polymorphous population of mature and transformed reactive lymphoid cells. Histopathological examination revealed extensive heterogeneous proliferation of atypical lymphoid cells with the formation of germinal centers at places, replacing the lobular architecture of the salivary gland leading to the diagnosis of non-Hodgkin’s lymphoma.

**DISCUSSION**

Among all human organs, salivary glands offer the largest variety of different histologic types and subtypes of primary neoplasms, most of them arising in the parotid glands. Therefore, it becomes more important to know detailed anatomy and pathologic processes affecting these glands while considering the management of these tumors. The most important factor for choosing the appropriate surgical approach for the primary tumor of the salivary glands is not only the pre-operative differentiation between a benign or malignant lesion but also the determination of the exact histologic subtype among benign or malignant lesions. Histopathologic grading of malignancies is also useful in the assessment of biologic aggressiveness, response to therapy, and prognosis; the grade of a neoplasm is usually expressed in either numeric terms (1, 2, 3) or descriptively (well, moderately, or poorly differentiated). The distinction of some low-grade carcinomas from an inflammatory-based sialadenitis may rely on the finding of daughter cyst proliferations from a seemingly hyperplastic duct.

Poorten et al. concluded that while all mucoepidermoid carcinoma were locally invasive and could recur after surgical removal but it was seen that distant metastasis and death were unlikely in patients with Grade 1 and Grade 2 while Grade 3 carcinomas were fatal in the majority of the cases. Goode et al. concluded in his study that features associated with metastasis or death were more advanced age, tumor size, and pre-operative symptoms. Histopathologic features that correlated with poor outcome were cystic component ~20%, four or more mitotic figures per ten high-power fields, neural involvement, necrosis, and anaplasia. FNAC proved to be a useful and reliable tool in the pre-operative diagnosis of salivary gland masses when performed by a radiologist or a clinician.

In contrast, Das et al. reported, in a study of 712 patients, a diagnostic accuracy reaching only from 80% to 91.1%.

Some researchers also believe that a risk of FNAC might be a possible spread of tumor cells, which can lead to a higher likelihood of local recurrence, especially in pleomorphic adenomas and malignant lesions. Basim et al. had a 10-year experience of dealing with fine-needle aspiration of 154 parotid masses and doing histologic correlation while working at the University of Texas M.D Anderson Cancer Center. A place like this where the majority of patients had either a previous history of malignancy or a high clinical likelihood of malignancy, the use of FNA may be approached from a different perspective. They suggested five major indications for obtaining an FNA of the parotid gland as part of the diagnostic workup: (1) To rule out inflammatory lesions; (2) to identify systemic diseases such as reticuloendothelial tumors; (3) to rule out direct invasion of the gland or metastases (although resection of metastases may be performed when the primary tumor was in the head and neck region); (4) to evaluate unreactsectable lesions and tumors in patients who present as poor surgical candidates; and (5) to evaluate lesions when the probability of a neoplasm is low, such as in children.

Habermann et al. performed a study of primary parotid gland tumors using diffusion-weighted echo-planar MRI and concluded that pleomorphic adenomas were also distinguishable from all other entities, except for myoepithelial adenomas. Although both are benign in nature but from surgery point of view pleomorphic adenomas have a risk of malignant transformation (carcinoma ex pleomorphic adenoma) and the surgical approach has to be much more aggressive due to the high risk of recurrence (e.g., lateral or complete parotid resection) with a higher risk of facial nerve injury. Otherwise, myoepithelial adenomas have an
explicitly lower risk of malignant transformation or recurrences and can, therefore, be resected more conservatively. The use of a combined clinical/radiologic/cytologic “triple test” approach is advocated to minimize false-negative and false-positive FNA diagnoses of parotid masses.[13-15]

CONCLUSION

Finally, we can say that knowledge of cytological overlaps and pitfalls of salivary glands FNAC should always be considered. Details of clinical information and radiologic features may help the pathologist to arrive at the appropriate diagnosis and reduce false interpretation. FNAC is a highly sensitive and specific technique for the diagnosis of many salivary gland swellings. FNAC can be used preoperatively to avoid unnecessary surgery and biopsy. Caution should be taken in the reporting of cystic and inflammatory lesions. Selective sampling, poor differentiation of cells, low cellularity of smears due to mucoid material (in cystic lesions) or hemorrhagic aspirate (in vascular tumors), and squamous metaplasia which may be over diagnosed may lead to a disparity between cytology and histopathological finding. Multiple sampling from different parts of swelling enhances diagnostic accuracy. It is compulsory and wise in conjunction with thorough clinical history, physical examination and other radiological tools such as ultrasonography and MRI if required. Some lesions are well-known sources of false-positive or false-negative diagnoses.

REFERENCES