ROLE OF FINE NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS OF SALIVARY GLAND LESIONS

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ABSTRACT

BACKGROUND

Salivary glands are affected by a variety lesions which may be non-neoplastic such as inflammation (Sialadenitis), cysts or neoplastic which includes both benign and malignant tumours. Except for acute infections which are usually painful, salivary gland diseases rarely present with any symptoms during the early stages[1]

MATERIALS AND METHODS

A cross sectional study to evaluate the role of fine needle aspiration cytology in the diagnosis of salivary gland lesions in Department of Pathology, Government Medical College Jammu, Jammu & Kashmir was done. All cases diagnosed in Department of Pathology as salivary gland lesions in cytopathology and histopathology sections from March 2015 to March 2016 were included in the study. Papanicolaou and May-Grunwald Giemsa stained slides of all these cases were reviewed and categorized/diagnosed. Of 156 FNAC cases, 102 had their corresponding histopathology reports. All these cases were retrieved from the histopathology section. H & E slides of all cases were reviewed, where required new H & E slides from paraffin blocks were also made. All these were categorized and diagnosed as per latest guidelines. Clinical features and follow up data was obtained from the consult files of referring surgeon.

RESULTS

The age of patients ranged from 11 years to 80 years with the mean age being 42.7 years. Majority of the patients i.e. 94 out of 156 (60.25 %) were in the age group of 21-50 years. Male to female ratio was 1.3:1. Most of the patients presented with swelling in parotid region i.e. 104 (66.66 %) followed by submandibular region 40 (25.64%) and oral cavity 12 (7.69%). Of the 156 cases, 38 (24.35%) were diagnosed as inflammatory lesions and 114 (73.07%) as neoplastic. Of the 38 inflammatory salivary gland lesions, sialadenitis was the most common lesion 18 cases (47.36%), followed by sialadenosis, 8 cases (21.05%). A total of 114 neoplastic lesions were diagnosed on fine needle aspiration cytology. Out of 114 cases, 92 (80.70%) cases were benign tumours and 22 (19.30%) cases were malignant tumours. 102 of 156 patients had their corresponding histopathological report. Histopathology of biopsy/ surgical specimen revealed that 68 (66.6 %) patients had benign lesions, 20 (19.60%) had malignant lesions while 14 (13.72%) patients had non-neoplastic lesions. FNA cytology findings were correlated with histopathology in cases where histopathology reports were available. In our study, sensitivity and specificity of FNAC is 99.02% and 99.20%. Positive and negative predictive values are 96.6% and 98.14%. Percentage of false negative is 1.01% and accuracy of FNAC is 98.68%.

CONCLUSION

FNAC is a rapid, convenient and accurate method of tissue diagnosis that can be performed on outpatient basis. It is highly sensitive and specific technique for diagnosis of most salivary gland swellings.

KEY WORDS

Salivary Gland, FNAC, Neoplastic, Inflammatory.

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BACKGROUND

The salivary glands are affected by a variety of lesions which may be non-neoplastic such as inflammation (Sialadenitis), cysts or neoplastic which includes both benign and malignant tumours. Except for acute infections which are usually painful, salivary gland diseases rarely present any symptoms during the early stages.[1] Due to this, there is generally a long interval before the patient reports to hospital. Infections of the salivary glands are usually viral in origin, only a minority of cases are due to bacterial infection. Initiation and progression of salivary gland infections depends on the decrease in host resistance to infection and may be encountered secondary to a variety of predisposing conditions including trauma, immunosuppression, debilitation and local conditions such as duct obstruction by sialolithiasis, stricture or other pathology.[2] Sialolithiasis is the main cause of unilateral diffuse parotid or submandibular swelling.[2] Sialoliths are calcified organic matters that form within the secretory system of the major salivary glands. The sialoadenitis do occur whenever there is reduced salivary flow which results into retrograde infection of the glandular tissue via the salivary duct. Sialoadenitis can also be due to

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obstruction of the duct due to stone, common in submandibular glands.[1] Other reactive lesions of salivary gland include mucocele, mucous retention cyst and extravasation cyst that commonly arises from the minor salivary glands.[3] Mucocele have been reported in varying ages, but young age is more favoured from 10 – 20 years with a slight male predilection.[4] Favoured sites are the lower lip (60–70%) and floor (6–15%) of mouth.[4,5] They usually present as painless swellings with bluish hue when mucin is near the surface, however when deep in the tissues they may be diffuse and covered by the normal mucosa without change in colour. Diagnosis is based principally on the clinical examination, radiographic findings and histological findings.[4] HIV associated salivary gland disease, hepatitis C virus associated sialadenitis, drug associated salivary gland disease, granulomatous sialadenitis, nonspecific reactive changes, necrotizing sialometaplasia, Sjogren's syndrome and Mikulicz syndrome are other non- neoplastic salivary gland lesions.

Salivary gland tumours elicit considerable medical interest because of their multifaceted clinical presentation, varied histological appearance and the associated difficulties predicting their prognosis.[6] The incidence ranges from 0.4–13.5/lac population.[7,8] Salivary gland tumours arise from the superficial lobe and present as facial swellings. Tumours that occur in the deep lobe often expand through the parapharyngeal space manifesting as oropharyngeal swelling[9]. Although salivary gland tumours are rare, they account for 2–6.5 % of all the head and neck tumours.[8] Benign tumours, occurring most commonly include pleomorphic adenoma, Warthin's tumour, oncocytoma etc. while malignant tumours include mucoepidermoid carcinoma, adenoid cystic carcinoma, and acinic cell carcinoma etc. Pleomorphic adenoma, a benign mixed tumour is the most commonly reported benign tumour of the major and minor salivary glands worldwide.[10] The commonest site for pleomorphic adenoma is the parotid gland followed by the minor salivary glands.[11,12] However this has also been reported in ectopic salivary gland sites, such as neck, nose cervical lymph nodes and the parapharyngeal spaces.[12] Warthin's tumour or papillary cystadenoma lymphomatosum is the most common salivary gland occurring between fifth and eighth decades of life[10] and accounting for approximately 5 – 6 % of epithelial salivary gland neoplasms. It is almost exclusively a tumour of parotid gland and peri parotid lymph nodes.

Malignant tumours comprise 15–30% of all parotid tumours, 40% of submandibular gland tumours, 70–90% of sublingual and over 50% of minor salivary gland tumours. Thus, the likelihood of a salivary gland tumour being malignant is more or less inversely proportional to the size of the gland.[13] Between 64- 80% of all primary epithelial tumours occur in parotid glands, 7–11% occur in the submandibular glands, less than 1% occur in the sublingual glands and 9–23% occur in the minor glands.[14] Mucoepidermoid carcinoma is the most common malignant neoplasm of the major and minor salivary glands in adults and children accounting for 4.06% of tumours. Adenoid cystic carcinoma is the second most common salivary gland tumour, accounting for 1.63% of all salivary gland neoplasms. It is a slow growing but aggressive tumour of the submandibular and minor salivary glands and has tendency for distant metastasis.[15] Lesions mimicking salivary gland tumours can arise in tissues close to the salivary glands such as lymph nodes, soft tissue and skin.[16] Differential diagnosis of these masses on clinical examination are salivary gland tumours, inflammatory process and enlarged lymph nodes. Thus, a mass in the salivary gland region presents as a diagnostic challenge with regard to its site of origin, histological behaviour and tissue diagnosis.[17,18] In routine practice usually a incisional or excisional biopsy is done for which patient has to admitted in hospital, worked up anaesthesia and then taken to operation theatre and then for histopathology it takes 3–4 days. Whereas FNAC is a OPD procedure and patient can be sent back home. Moreover fine needle aspiration cytology has emerged as the most widely accepted diagnostic tool for salivary gland lesions, due to their superficial location and easy accessibility.[19] Fine needle aspiration cytology is accurate, simple, rapid, inexpensive, well tolerated and harmless procedure for the patient.[8] Therefore we planned this study to see whether fine needle aspiration in can be used to type salivary gland lesions as benign and malignant. So that patients are taken up for surgery depending upon the diagnosis of FNAC.

MATERIALS AND METHODS

It is an observational study. All cases of salivary gland lesions diagnosed in FNA cytology and surgical pathology sections of Department of Pathology from January 2016 to Dec. 2017 were retrieved from cytology and consult files of Govt. Medical College, Jammu. In cytology section 156 cases were identified over a period of two years. Papanicolaou and May-Grunwald Giemsa stained slides of all these cases of salivary gland lesions were reviewed and categorized/diagnosed as per the recent guidelines. Of 156 cases, 102 had their corresponding histopathology reports. All these cases were retrieved from the histopathology section. H & E slides of all cases were reviewed, where required new H & E slides from paraffin blocks were also made. All these were categorized and diagnosed as per latest guidelines. Clinical features and follow up data were obtained from the consult files of referring surgeons. Statistical analysis was performed using SPSS 10.0 for windows student version (SPSS Inc. 233 South Wacker Drive, 11th Floor, Chicago, IL 60606-6412). Standard variables of specificity, sensitivity and predictive value were also applied.

RESULTS

The age of patients ranged from 11 year to 80 year with the mean age being 42.7 year. Majority of the patients i.e. 94 out of 156 (60.25 %) were in the age group of 21–50 years. Male female ratio was 1.3: 1. Most of the patients presented with swelling in parotid region i.e. 104 (66.66 %) followed by submandibular region 40 (25.64%) and oral cavity 12 (7.69%). Most of the swellings were non – tender: 132 (88.46 %) were non-tender and 18 (11.53 %) were tender. Parotid gland was the most commonly involved site 106 (67.94 %) followed by submandibular gland 38 (24.35%) sublingual gland 1 (1.28%) and minor salivary glands in 5 (6.41 %). Cytology diagnosis was divided into inflammatory and neoplastic lesions

Inflammatory Lesions

Of the 156 cases, 38 (24.35%) were diagnosed as inflammatory lesions and 114 (73.07%) as neoplastic lesions.

Four cases had inadequate material for evaluation. Of the 38 inflammatory salivary gland lesions, sialadenitis was the most common lesion: 18 cases (47.36%) followed by by sialadenosis: 8 cases (21.05%), chronic non-specific reactive hyperplasia [Intra-parotid lymph node]: 6 cases (15.78 %), non – neoplastic cysts: 4 cases (10.25 %) and two cases of abscess. All cases of sialadenitis were in submandibular gland, sialadenosis was encountered equally in submandibular and parotid gland. Non- neoplastic cysts were seen in parotid gland and minor salivary gland. Chronic reactive hyperplasia was seen in parotid and submandibular glands. Two cases of abscess were seen in parotid gland.

FNAC Diagnosis	Number of Cases	Percentage
Sialadenitis	18	47.36%
Sialadenosis	08	21.05%
Reactive Lymphoid Hyperplasia	06	15.78%
Non- Neoplastic Cysts	04	10.52%
Abscess	02	5.26
Total	**38**	**100%**

Table 1. Table Showing Inflammatory Lesions

Neoplastic Lesions

A total of 114 neoplastic lesions were diagnosed on fine needle aspirate. Out of 114 cases, 92 (80.70%) cases were benign tumours and 22 (19.30%) cases were malignant tumours. Among the benign tumours, pleomorphic adenoma was the most common tumour, accounting for 70 (61.40%) cases followed by Warthin's tumour constituting 20 (17.54 %) cases. Mucoepidermoid carcinoma was the most common malignant tumour constituting 8 (7.01%) cases followed by 6 (5.26 %) cases of adenocarcinoma, 4 (3.50%) cases of acinic cell carcinoma and two case each of adenoid cystic carcinoma and Non-Hodgkin's lymphoma. Pleomorphic adenoma was seen in the 3rd to 5th decade where as Warthin's tumour was seen in 40 – 80 a year age group. In contrast malignant tumours were seen in patients older than 50 years age except for two case each of mucoepidermoid carcinoma and polymorphous low-grade adenocarcinoma which were seen 2nd decade of life. The neoplastic lesions showed male preponderance with a male to female ratio 1.1:1 but in Warthin's tumour more male predominance was observed with ratio of 4:1. Out of 114 neoplastic lesions, parotid gland was most common site observed with 90 (78.94 %) cases followed by 14(12.28%) cases in submandibular glands, 8 (7.01%) cases in minor salivary glands and two cases (1.75%) involving sublingual gland respectively. Out of 92 benign tumours, 70 cases were diagnosed as pleomorphic adenoma accounting for 59.64% cases. Most of them were found to be involving the parotid gland (58 case) followed by submandibular gland (6 cases), minor salivary gland (4 cases) and sublingual gland (2 case). Warthin's tumour accounted for 20 (17.54%) cases, 16 out of 20 were in parotid gland and the remaining 4 cases were seen in submandibular gland. Two cases of basal cell adenoma were seen involving the parotid gland (1.75%). Mucoepidermoid carcinoma, the most common malignant tumour in the present study, was found to involve parotid gland in six cases out of 8 (7.01%) cases and two cases were in minor salivary glands.

Adenocarcinoma was diagnosed in 6 (5.45%) cases involving parotid gland in 4 cases and submandibular gland in two cases. Acinic cell carcinoma was diagnosed in 4 (3.50%) cases, 2 cases each were seen in parotid and submandibular glands. Two cases of adenoid cystic carcinoma were diagnosed involving the minor salivary glands. Two cases of Non- Hodgkin's lymphoma were also diagnosed involving parotid gland.

FNAC Diagnosis	No. of Cases	Percentage
Pleomorphic Adenoma	70	61.40%
Warthin's Tumour	20	17.54%
Basal Cell Adenoma	02	1.75%
Mucoepidermoid Carcinoma	08	7.01%
Adenocarcinoma	06	5.26%
Acinic Cell Carcinoma	04	3.50%
Adenoid Cystic Carcinoma	02	1.75%
NHL	02	1.75&
Total	114	100%

Table 2. Table Showing Neoplastic Lesions of Salivary Gland

Analysis of Result of Histology

102 of 156 patients had their corresponding histopathological report. Histopathology of biopsy/ surgical specimen revealed that 68 (66.6 %) patients had benign lesions, 20 (19.60%) had malignant lesions while 14 (13.72%) patients had non-neoplastic lesions. In non-neoplastic lesions there were 10 cases of sialadenitis and two cases each of mucocele and lymphoepithelial cyst. Results of benign and malignant lesions are shown in tables given below.

Sr. No.	Histology Dx	No. of Cases	Percentage
1.	Pleomorphic Adenoma	48	47.05
2.	Schwannoma	02	1.96
3.	Warthin's Tumour	14	13.72
4.	Basal Cell Adenoma	02	1.96
5.	Papillary Cystadenoma	02	1.96

Table 3. Table Showing Different Benign Lesions on Histopathology

Sr. No.	Histology Dx	No. of Cases	Percentage
1.	Mucoepidermoid Carcinoma	08	7.84
2.	Adenocarcinoma	04	3.92
3.	Acinic Cell Carcinoma	04	3.92
4.	Adenoid Cystic Carcinoma	02	1.96
5.	Non-Hodgkin's Lymphoma	02	1.96

Table 4. Table Showing Different Malignant Lesions on Histopathology

Cytohistological correlation: FNA cytology findings were correlated with histopathology in cases where histopathology reports were available. All 5 cases of sialadenitis correlated with histopathology. Four cases of non-neoplastic cysts reported on FNAC were diagnosed as two cases of each mucocele and lymphoepithelial cyst on histopathology.

Cytohistological correlation of benign and malignant lesions is table 5 & 6.

FNAC Dx	No. of Cases	Histology Dx	No. of Cases	Remarks
Pleomorphic Adenoma	52	Pleomorphic Adenoma Schwannoma Mucoepidermoid Carcinoma	48 02 02	TP TP FN
Warthin's Tumour	14	Warthin's Tumour	14	TP
Basal Cell Adenoma	02	Basal Cell Adenoma	02	TP
Table 5. Cytohistology Correlation of Benign Tumours				
TP: True positive, FN: False negative				

FNAC Dx	No. of Cases	Histology Dx	No. of Cases	Re-marks
Mucoepidermoid Carcinoma	08	Mucoepidermoid Carcinoma Papillary Cystadenoma Squamous Cell Carcinoma	04 02 02	TP TP FN
Polymorphous Low-Grade Adenocarcinoma Adenocarcinoma NOS	04	Polymorphous Low-Grade Adenocarcinoma Mucoepidermoid Carcinoma	02 02	TP TP
Non- Hodgkin's Lymphoma	02	Non- Hodgkin's Lymphoma	02	TP
Adenoid Cystic Carcinoma	02		02	TP
Acinic Cell Carcinoma	04		04	TP
Table 6. Cytohistology Correlation of Malignant Tumours				

Thus, out of 88 neoplastic lesions reported on FNAC, 84 were true positive, 2 false negative and 2 false positive.

Test	Disease	No Disease
Positive	14 (True Positive)	0 (False Positive)
Negative	88 (True Negative)	0 (False Negative)
Table 7. Cytohistological Correlation in Terms of True Positive & False Positive of Non-Neoplastic Lesions		

Test	Disease	No Disease
Positive	66 (True Positive)	0 (False Positive)
Negative	34 (True Negative)	2 (False Negative)
Table 8. Cytohistological Correlation in Terms of True Positive & False Positive of Benign Neoplastic Lesions		

Test	Disease	No Disease
Positive	18 (True Positive)	2 (False Positive)
Negative	82 (True Negative)	0 (False Negative)
Table 9. Cytohistological Correlation in Terms of True Positive & False Positive of Malignant Neoplastic Lesions		

Thus in our study sensitivity and specificity of FNAC is 99.02% and 99.20%. Positive and negative predictive values are 96.6% and 98.14%. Percentage of false negative is 1.01% and accuracy of FNAC is 98.68%.

DISCUSSION

Salivary gland lesions can arise from a number of aetiologies including inflammatory processes, cysts and tumours. Lesions mimicking salivary gland tumours can arise in tissue close to the gland, such as lymph nodes, soft tissue and skin.[16,20] Clinical examination of the salivary glands can be inaccurate in distinguishing between salivary gland tumours and inflammatory processes.[20,21] Thus a mass in the region of the salivary gland presents a diagnostic challenge with regards to its site of origin, histological behaviour and tissue diagnosis.

Fine needle aspiration cytology (FNAC) plays a vital role in the evaluation of the salivary gland lesions, especially in a developing country like India where the cost of hospital stay and medical expenses are often not affordable by the patients. The age of patients in our study ranged from 11 year to 80 year with the mean age being 42.7 year and maximum incidence was in 5th to 7th decade which is comparable with other studies.[8,20,21] The male female ratio in our study was 1.3: 1 which is comparable with other studies[7, 22, 23]. In our study the parotid gland swelling was the most common clinical presentation of salivary gland lesions which is comparable with other studies.[8,22,24] In our study inflammatory lesions were 25% and neoplastic lesions were 75% which is comparable to the study conducted by Khandekar MM et al.[25] But other studies by Singh A et al[21] and Gandhi SH et al[7] showed a higher incidence of non- neoplastic lesions. In our study sialadenitis was the most common non neoplastic lesion, 18 cases (47.36%) involving the submandibular gland mainly and found to be in the age group of 3rd to 8th decade of life which is almost similar to the study by Jain R et al.[26] In our study the ratio of ratio of benign and malignant lesions is similar to other studies.[7,20,25] In our study, the most common site of neoplastic lesions is parotid gland followed by submandibular gland which is similar to the study by Sengupta S et al[27] and Gandhi SH et al.[7] In our study most common benign tumour pleomorphic adenoma accounting for 59.64% cases, and maximum number of cases were seen in 5th to 7th decade, followed by Warthin's tumour which accounted for 20 (17.54%) cases, 16 out of 20 were in parotid gland and the remaining 4 cases were seen in submandibular gland. Two cases of basal cell adenoma were seen involving the parotid gland (1.75%). This corroborated well with other studies.[7,20,21] There has been a variation in the reported occurrence of malignant salivary gland tumours. Mucoepidermoid carcinoma, the most common malignant tumour in the present study, was found in 5th to 7th decade and involved parotid gland in six cases out of 8 (7.01%) cases and two cases were in minor salivary glands. The youngest patient of mucoepidermoid carcinoma was 11-year-old female. The above results are comparable with other studies.[7,20] Adenocarcinoma was diagnosed in 6 (5.45%) cases involving parotid gland in 4 cases and submandibular gland in two cases which is comparable to the study Atarbashi MS et al.[28] Acinic cell carcinoma was diagnosed in 4 (3.50%) cases, 2 cases each were seen in parotid and submandibular glands and was seen in 3rd and 5th decade which is similar to the study conducted by Fernandes GC et al.[15] Two case of adenoid cystic carcinoma were diagnosed involving the minor salivary glands which are also similar to other studies[15]. Two cases of Non- Hodgkin's lymphoma were also diagnosed involving parotid gland. On cytohistopathological correlation mucoepidermoid carcinoma was the most common tumour. These findings are similar to the studies conducted by Vaidya S et. al.[21] And

Singh a et. al.[20] The second most common tumour is adenocarcinoma which correlates with the finding of Stewart FW et. al.[29] On literature review, the sensitivity of salivary gland FNAC ranges from 80 -98% and specificity from 80 – 100 %. In our study sensitivity and specificity of FNAC is 99.02% and 99.20% and accuracy is 98.68% which is close to the study reported by Gandhi SH et. al.[7] Ersoz C et. al.[30] And comparable to other studies. The positive predictive value and negative predictive value in our study are 96.66% and 98.14% respectively which are comparable to other studies.[21,31,32] FNAC is a commonly accepted, sensitive and specific technique in the diagnosis of both neoplastic and non-neoplastic lesions of salivary gland. Hence, cytology can clearly distinguish between salivary and non-salivary gland lesions, benign and malignant tumours, and also specific and non-specific inflammation. Thus, it provides a decisive direction for therapeutic management of the patient. FNAC is a utility tool for subtyping of salivary gland lesions with variable specificity and sensitivity.[25]

CONCLUSION

FNAC is a rapid, convenient and accurate method of tissue diagnosis that can be performed on outpatient basis. It is highly sensitive and specific technique for diagnosis of most salivary gland swellings. Despite its limitations, salivary gland FNAC is simple, safe, reliable and remains a powerful diagnostic tool for salivary lesions.

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