P63 EXPRESSION IN PLEOMORPHIC ADENOMA AND MUCOEPIDERMOID CARCINOMA

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ABSTRACT

Tumors of salivary gland have diverse histological forms and unpredictable clinical behavior. The main application of immunochemistry in salivary gland tumors is to demonstrate the existence of myoepithelial/basal cells or luminal cells. Our objective is to evaluate the myoepithelial marker p63 in pleomorphic adenoma and mucoepidermoid carcinoma. The total number of specimens were 92, of which 41 were neoplastic. Pleomorphic adenoma was the commonest benign tumor accounting for 73.17%, Mucoepidermoid carcinoma was the most common malignant tumor accounting for 52.18%. In this study expression of p63 in pleomorphic adenoma have confirmed the role of myoepithelial cells in the histogenesis of this tumor and lack or minimal expression of p63 in mucoepidermoid indicates minimal myoepithelial cell differentiation in this tumors. IHC enhance the accuracy and be a helpful tool when the diagnosis cannot be assessed by histological examination such as cell of origin, cell proliferation and tumor protein expression.

KEYWORDS: salivary gland, pleomorphic adenoma, mucoepidermoid carcinoma, immunohistochemistry.
INTRODUCTION

The salivary gland gives rise to different types of pathologic processes that contribute to a variety of inflammatory to neoplastic lesions. Their remarkable morphologic variation makes these tumors difficult to diagnose. The overall incidence of salivary gland tumors is approximately 0.4 to 13.5 cases per 100,000 populations. It constitutes 3-6% of all head and neck tumors. Immunohistochemistry enhances the accuracy of diagnosis of cases that cannot be assessed by histological examination. In spite of this, Hematoxylin-Eosin staining is the golden method of diagnosis. Immunohistochemistry detects the nature of cell differentiation, cell proliferation, and tumor protein expression. Main application of immunohistochemistry, p63, in this study is to demonstrate the existence of luminal or myoepithelial/basal component when the diagnosis of pleomorphic adenoma and mucoepidermoid carcinoma is uncertain. In this study, all cases of pleomorphic adenoma p63 is expressed in myoepithelial cells and in mucoepidermoid carcinoma p63 is expressed by the intermediate cells. Thus, p63 expression confirmed the role of myoepithelial cells in the histogenesis of pleomorphic adenoma. Lack or less expression of p63 in mucoepidermoid carcinoma suggests that it originates from excretory or striated duct of salivary gland.

MATERIALS AND METHODS

Patients presenting with signs and symptoms of salivary gland enlargement in Thanjavur Medical College Hospital during the period from September 2011-August 2014 after getting approval from the institutional ethical committee (approval no 022) were included in this study, irrespective of the age group and sex. Grossing of the specimens were done with utmost care, noting the size of the lesion, whether they have circumscribed or infiltrative borders and presence of cystic changes were noted with special attention to the number of cysts, single or multiple, appearance of the surface, color of the walls, presence of papillary projections into the lumen of the cyst wall. All the suspicious were grossly sectioned and subjected to histopathological examination. Sections were processed as small sections of 2-3mm in thickness in the automatic tissue processor and processed in a routine way. Immunohistochemistry of p63 was done on deparaffinized 5µ sections after antigen retrieval by heat using microwave oven.

OBSERVATION AND RESULTS

During the study period out of 92 cases, 29 cases were diagnosed as non-neoplastic and 64 cases as neoplastic lesions of which 41 cases were benign and 23 cases were malignant. Out of 41 benign cases, 30 cases were pleomorphic adenoma, 6 cases of basal cell adenoma, 4 cases of Warthin's tumor, and 1 case of myoepithelioma. The incidence of benign tumors was 64.06%. 23 Cases are diagnosed as malignant. Among this, 12 were mucoepidermoid carcinoma, 5 were Adenoid Cystic Carcinoma, Salivary duct carcinoma, carcinoma ex Pleomorphic Adenoma, and basal cell adenocarcinoma constitutes about 2 cases each. Incidence of malignant tumors among neoplastic tumors was 35.94%.

<table>
<thead>
<tr>
<th>LESIONS</th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleomorphic Adenoma</td>
<td>30</td>
<td>46.87%</td>
</tr>
<tr>
<td>Mucoepidermoid CA</td>
<td>12</td>
<td>18.75%</td>
</tr>
</tbody>
</table>

p63: p63 gene, a member of p53 gene family play an essential role in epithelial development, stem cell identity cell and cellular differentiation. Weber et al. [2002] stated that in normal parotid tissue the expression of p63 was restricted to few basal and myoepithelial cells. Ductal, luminal, and acinus cells were completely negative. In salivary gland tumors shows strong nuclear staining for p63.

**p63 expression pleomorphic adenoma**

<table>
<thead>
<tr>
<th>PLEOMORPHIC ADENOMA</th>
<th>P63[ABLUMINAL CELLS]</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASES-1</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>CASES-2</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>CASES-3</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>CASES-4</td>
<td>POSITIVE</td>
</tr>
</tbody>
</table>

In our study p63 myoepithelial marker was studied in 4 cases of pleomorphic adenoma and all the abluminal cells [myoepithelial cells] were positive for p63. Immunohistochemical positivity of myoepithelial cell marker in pleomorphic edenoma indicates the origin of this tumors from intercalated duct of salivary gland.

**p63 expression in mucoepidermoid carcinoma**

<table>
<thead>
<tr>
<th>MUCOEPIDERMOID CARCINOMA</th>
<th>P63[INTERMEDIATE CELLS]</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW GRADE</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>INTERMEDIATE GRADE</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>HIGH GRADE</td>
<td>POSITIVE</td>
</tr>
</tbody>
</table>

In mucoepidermoid carcinoma, the intermediate cells shows positive for p63 and mucocytes are positive for CK-7. Limited or lack of myoepithelial cell in mucoepidermoid carcinoma indicates the minimal...
myoepithelial differentiation in histogenesis of mucoepidermoid carcinoma. The absence of myoepithelial cells in excretory or striated ducts of salivary gland and negative staining for myoepithelial markers in MEC suggests that it originates from excretory or striated duct component of salivary glands.

DISCUSSION

In the present study out of 92 cases the male to female ratio was 1:2.56. Pleomorphic adenoma shows a slight female preponderance, similar to other studies. However MohbAyub have observed a male preponderance. In our study 12 cases of mucoepidermoid carcinoma were seen comprising 7.9% of all salivary gland tumors and 52.17% of all malignant tumors. Vargas et al. in their study of 124 tumors mucoepidermoid carcinoma constitutes 10.48% of all tumors. Hadi Bilal et al. studied 68 cases of salivary gland tumors of these 15 were pleomorphic adenoma and 9 were mucoepidermoid tumors. All cases of pleomorphicadenoma shows p63 nuclear staining in myoepithelial cells similar to this study. in mucoepidermoid carcinoma p63 is expressed in intermediate cells similar to this study.

IMMUNOHISTOCHEMISTRY IN SALIVARY GLAND TUMOURS

Figure 1

*p63 in nuclei of both myoepithelial and basal cells that surrounds the secretory ductal units (10x)* in normal salivary gland.

Figure 2

*p63 in Pleomorphic adenoma myoepithelial cells are positive (10x).*

Figure 3

*p63 in Pleomorphic adenomas- the myoepithelial cells surrounding the luminal cells are positive (40x).*

Figure 4

*Mucoepidermoid carcinoma. p63 is expressed only in the intermediate epidermoid cells, shows absence of myoepithelial cells (10x).*
Histological grading of mec

<table>
<thead>
<tr>
<th>SERIES</th>
<th>NO OF MEC</th>
<th>LOW</th>
<th>INTERMEDIATE</th>
<th>HIGH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renehan et al</td>
<td>38</td>
<td>87.4%</td>
<td>2.6%</td>
<td></td>
</tr>
<tr>
<td>Goode et al</td>
<td>234</td>
<td>76.06%</td>
<td>7.69%</td>
<td>13.24%</td>
</tr>
<tr>
<td>Present study</td>
<td>12</td>
<td>83.34%</td>
<td>8.33%</td>
<td>8.33%</td>
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</table>

The present study showed a preponderance of low grade mucoepidermoid carcinoma, similar to results of Renehan et al.

p63 in PLEOMORPHIC ADENOMA AND MUCOEPIDERMOID CARCINOMA

In our study five cases of pleomorphic adenoma were selected for myoepithelial marker p63 in all the cases the abluminal cells have taken p63. This implies the origin of pleomorphic adenoma from inter calated duct component In mucoepidermoid carcinoma IHC was done with p63. All the five cases intermediate epidermoid cells have taken p63, but not the myoepithelial cells. This confirms the origin of MEC from excretory or striated duct component of salivary gland. Similar results were observed by Batsakis et al.9, Loyala and souse et al.10, Hadi Bilal et al.12.

CONCLUSION

Out of 13,916 general biopsies received in Thanjavur medical college during September 2012- August 2014, 92 cases were salivary gland lesion accounting for an incidence of 0.6%. Expression of p63 in pleomorphic adenoma have confirmed the role of myoepithelial cells in the histiogenesis of this tumor and lack or minimal expression of p63 in mucoepidermoid indicates minimal myoepithelial cell differentiation in this tumors.

CONFLICT OF INTEREST

Conflict of interest declared None.

REFERENCES