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Original Article

Fascin expression in pleomorphic adenoma and mucoepidermoid carcinoma

Sedigheh Rahrotaban[1], Faezeh Azmoudeh[2], Seyedeh Mahboubeh Kiyani[3]

[1]Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, Tehran, [2]Department of Oral and Maxillofacial Pathology and Dental Caries Research Center, School of Dentistry, Qazvin University of Medical Sciences, Qazvin, [3]Dentist, Iran

ABSTRACT

Background: Salivary gland tumors constitute an important part of oral and maxillofacial pathology. Pleomorphic adenoma (PA) and mucoepidermoid carcinoma (MEC) are the most common benign and malignant salivary gland tumors. Fascin is an actin-bundling protein that increases the motility of normal and transformed epithelial cells. The aims of the study were to determine the expression of fascin in these tumors and to determine its role in their progression.

Materials and Methods: A total of 40 formalin-fixed, paraffin-embedded tissue blocks of PA, and 20 blocks of MEC were included in this study. Diagnostic confirmation was performed through examination of hematoxylin and eosin sections. Both tumors were immunohistochemically analyzed for the presence of fascin using Avidin-Biotin complex method and evaluated via light microscope by 2 independent observers. Statistical analysis was performed using Kruskal-Wallis and Chi-square tests with significant level of $P < 0.05$.

Results: In both the tumors, the percentage of stained cells was significantly correlated with intensity of staining ($P = 0.01$ in PA and $P = 0.00$ in MEC). In PA, statistical analysis showed a significant direct correlation between percentage of stained cells and recurrence ($P = 0.00$).

There was no significant correlation between intensity and percentage of staining with clinicopathologic factors in MEC.

Conclusion: Fascin might be a useful marker for recurrence of PAs and patients with high fascin expression in primary PA should be followed up periodically to detect potential recurrence as soon as possible.

Key Words: Benign, immunohistochemistry, malignant, salivary gland, tumor.

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Address for correspondence:
Dr. Faezeh Azmoudeh, Department of Oral and Maxillofacial Pathology. Qazvin University of Medical Sciences, Qazvin, Iran.
E-mail: fa.azmoodeh@gmail.com

INTRODUCTION

Human fascin is a highly conserved 55-kDa actin-bundling protein that is considered to be involved in the assembly of actin filament bundles present in microspikes as well as in membrane ruffles and stress fibers.[1-3]

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The expression of fascin is highly specific to tissue and cell types. Fascin is plentifully expressed in tissues such as brain and spleen and in specific types of cells such as neuronal and glial cells, microcapillary endothelial cells, and antigen-presenting dendritic cells.[4,5]

The expression of fascin in epithelial neoplasms has been described only recently. In normal epithelial cells, fascin expression is usually absent or very low but is often upregulated in several types of human neoplasms, such as ovarian, breast, pancreatic, colon, lung, and skin tumors.[6,7]

It's overexpression results in decreased cell-to-cell adhesion and increased epithelial cell motility.[8,9]

Salivary gland tumors include a significant part of oral tumors and are the next common neoplasm of the mouth after squamous cell carcinoma.[10] Pleomorphic adenoma (PA) of the parotid gland is the most common salivary gland tumor. Regardless of modern microsurgical techniques, recurrence rates remain at about 5% after operation. Repeated operations increase the risk of facial paralysis and the risk of malignant transformation with time.[11] Brieger *et al*. showed that fascin might be a useful marker for recurrence of PA.[10]

Mucoepidermoid carcinoma (MEC) is one of the most common salivary gland malignancies. MEC is regularly seen in the 35 to 65 year-old age group, but it is also the commonest salivary malignancy in children. MEC is reported to manifest variable biologic aggressiveness, basically showing association with its histological features.[11,12]

Few studies have targeted fascin expression only in one type of salivary gland tumors. Thus, this retrospective study was performed to determine the expression of fascin in PA and MEC and its possible association with the clinic opathologic features of the sample.

MATERIALS AND METHODS

Tissue samples

In this descriptive-analytical study, the achieved tissue samples from 40 cases of PA and 20 cases of MEC specimens were selected. Diagnosis was based on histopathological examination of hematoxylin and eosin-stained sections. The patients with PA consisted of 17 men and 23 women with mean age of 37.52 years and the cases with MEC consisted of 7 men and 13 women with mean age of 48.45 years, who had undergone surgery between 2002 and 2011. Metastatic and recurrent tumors and small samples were excluded. At the time of this study, we recalled the patients, 48 cases of 60 presented for their recall appointment and 10 recurrences of 36 PA were found, and one of the 12 MEC patients expired because of the tumor.

Immunohistochemistry

3 to 4 micron sections from paraffin-embedded specimens were mounted on poly-L-lysine-coated glass slides.

After rinsing with 3 changes of xylol for deparaffinization, the sections were rehydrated with 5 changes of alcohol (100%, 100%, 95%, 85%, and 75%). In order to inactivate endogenous peroxidase, sections were incubated for 5 minutes in 3% H_2O_2, and were then rinsed with phosphate-buffered saline (PBS).

Specimens were stained with the monoclonal anti-fascin (Dako, Denmark) at a dilution of 1:50 by using Avidin-Biotin complex method and evaluated via light microscope (Olympus BX41TF, Tokyo, Japan) by 2 independent observers who were unaware of the diagnosis.

Positive controls consisted of stained endothelial cells as internal control and tissue specimen sections of Hodgkin lymphoma with notorious antigenic reactivity. A negative control was stained by omitting the primary antibody.

Specimen evaluation

Intensity was determined in comparison with endothelial cells with high known reactivity as internal control. Intensity and percentage of staining was scored on the basis of modified semiquantitive Bittinger analysis so that scale of 0 to 4 was used to score relative intensity with 0 corresponding to no detectable immunoreactivity and 1, 2, 3, and 4 for very low, low, moderate, and high staining, respectively. Then, the percentage of positive cells was determined and a scale of 1 to 4 was used; so that 1 showed staining of ≤5% of cells and 2, 3, and 4 showed 5 to 20%, 20 to 50%, >50% staining, respectively (10).

Statistical analysis

Statistical analysis was performed using Kruskal-Wallis and Chi-square tests with significant level of $P < 0.05$.

RESULTS

In this study, we examined fascin expression in PA and MEC. In both the tumors, we didn't have 0 score, it means all the tumors expressed fascin in epithelial tumoral cells. Figure 1 shows fascin expression in PA and MEC.

There was no correlation between PA and MEC intensity and percentage of staining, as shown in Table 1 ($P > 0.05$)

In both the tumors, the percentage of stained cells was significantly correlated with intensity of staining ($P = 0.01$ in PA and $P = 0.00$ in MEC).

In PA, statistical analysis showed a significant direct correlation between percentage of stained cells and recurrence (P = 0.00) [Table 2]. In addition, there was a significant inverse correlation between intensity and patients' age, so that higher intensity was seen in younger patients (P = 0.03).

There was no significant correlation between intensity and percentage of staining with clinicopathologic factors in MEC.

DISCUSSION

The application of immunohistochemical method in pathology has been resulted in marked improvement in microscopic diagnosis of neoplasms and more exact realization of histopathologic features, histogenesis, pathogenesis, and prognosis of those lesions.[13] Fascin is an immunohistochemical marker, the expression of which has been studied in many cancers and most of these studies have shown increase of its level.[14-21] Fascin expression has been shown to be a poor prognostic factor in gastric and esophageal cancer.[22,23] It is also suggested that fascin can be explored as a new therapeutic target for oral and breast cancer.[24,25] In the oral cavity, there are some studies about fascin expression in squamous cell carcinoma.[22-30]

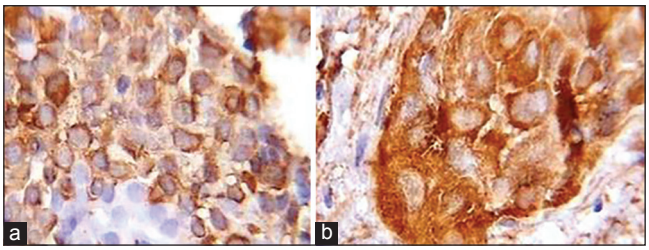

Figure 1: Fascin expression in (a) pleomorphic adenoma (40×) and (b) mucoepidermoid carcinoma (40×)

Table 1: Intensity and percentage of staining

Tumor	Intensity of staining					Percentage of stained cells				
	0	1	2 (%)	3 (%)	4 (%)	0	1 (%)	2 (%)	3 (%)	4 (%)
PA	0	0	17.5	50	32.5	0	10	12.5	35	42.5
MEC	0	0	30	40	30	0	15	10	20	55

Table 2: Percentage of stained cells with fascin in pleomorphic adenoma cell

Percentage of stained cells	<5%	5-20%	20-50%	>50%	
PA with recurrence	10	0	0	90	P=0
PA without recurrence	11.5	19.2	50	19.2	

Salivary gland tumors include a significant part of oral tumors and are the next common neoplasm of the mouth after squamous cell carcinoma. Some prognostic molecular markers such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and Claudin have been related to the prognosis of common salivary gland tumors.[31,32] However, only few studies is published about salivary gland tumors.[10] In this study, although there was no significant difference between fascin expression in PA and MEC, a significant correlation between percent of stained cells and PA recurrence was found. This could be because of fascin's role in the formation of cellular dendrite and pseudopodia that develop beyond the tumor's capsule and help the recurrence of the tumor.[33-35]

These results are consistent with Brieger *et al.*'s study which reported higher expression of fascin in primary PA with recurrence and also in recurred tumors.[10]

In addition, there was an inverse correlation between intensity of staining and patient's age; the younger patients had higher fascin expression. As we know, PA in younger patients is more susceptible to recurrence.

As MEC is a malignant tumor with more invasive behavior and because of fascin role in motility and migration of cells according to previous studies in malignancies,[15,36] we expect to see higher expression of fascin in MEC than PA, but this was not shown in our results. This could be because of limited number of MEC specimens and also impossibility of considering histopathologic grade because most specimens were removed by incisional biopsy.

CONCLUSION

On the basis of our observations, it is suggested that fascin might be a useful marker for recurrence of PA and patients with high fascin expression in primary PA should be followed up periodically to detect potential recurrence as soon as possible.

It is also recommended to analyze fascin expression in higher numbers of patients with MEC, considering different grades of this tumor.

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This research is free of conflict of interest.

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