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ORIGINAL RESEARCH

Expression of Extracellular Matrix—Laminin in Oral Squamous Cell Carcinoma: An Immunohistochemical Study

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ABSTRACT

Aim: To evaluate the expression of laminin in various grades of oral squamous cell carcinoma (OSCC) in order to determine whether this protein can be used as a marker for early detection and elucidation of oral cancer.

Materials and methods: Immunohistochemical staining for laminin was done on 60 selected archival blocks of histopathologically diagnosed cases of primary OSCC and the laminin expression was compared between the different histopathological grades of primary OSCC. The statistical analysis was performed by using Chi-square (χ square) test and Gaussian-test with a probability of $p < 0.05$ was considered as significant.

Results: It was observed that laminin expression decreased with tumor progression which may be correlated to the tumor aggressiveness.

Conclusion: There was a gradual decrease of laminin staining with decreasing cellular differentiation, with differentiated lesions showing a more conspicuous staining of basement membrane glycoprotein than less differentiated lesions.

Clinical significance: An understanding of how the extracellular matrix influences tumor development and invasion is fundamental in the development of new prognostic indicators and treatment strategies for oral squamous cell carcinoma.

Keywords: Oral squamous cell carcinoma, Laminin, Immunohistochemistry, Prognosis.

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INTRODUCTION

Oral cancer is one of the most formidable health problems, in terms of morbidity and mortality, facing mankind today. In India and most South-East Asian countries it is the most common neoplasm. The high incidence of this disease is attributed to tobacco chewing and smoking habits, highly prevalent in these populations.

The most common type of oral cancer is squamous cell carcinoma, a malignant tumor of keratinocytes, which accounts for approximately 91% of all malignancies.These malignancies are epithelial in origin and therefore the possibility of early recognition and increased survival exists.

According to the histological typing of oral and oropharyngeal tumors WHO 1971, squamous cell carcinoma is described as a tumor consisting of irregular nests, columns or strands of malignant epithelial cells infiltrating subepithelially. These epithelial tumor cells traverse in different tissue compartments during the process of invasion. One may view these tissue compartments as being divided by basement membranes. There are sound experimental evidences that tumor cells elaborate degenerative enzymes have specificities directed against basement membrane components.[1]

However, basement membranes are thought normally to be synthesized by endothelial, smooth muscle and certain mesenchymal and of course epithelial cells, in fact this synthesizing capability has been demonstrated in cell culture experiments.[2] Basement membrane is ubiquitous extracellular structures that consist mainly of collagenous and noncollagenous protein.[3,4] Chung AE et al[5] were the first to indentify the laminin. However, Timpl R and Rohde H isolated the first isoform of laminin from murine Engelbreth-Holm-Swarm (EHS) sarcoma and characterized it as a major noncollagenous basement membrane glycoprotein of molecular weight 8,500,00 to 1,000,000 consisting of two major types of polypeptides chains in a ratio 1:2 held together by disulfide bonds.[6] Laminin, a basement membrane associated glycoprotein, distributed exclusively on the epithelial portion of basement membrane

in the lamina lucida, is chemically and immunologically distinct and function as an adhesive glycoprotein binding epithelial cell to type IV collagen and basement membrane.[7,8]

Although majority of invasive tumors totally lack extracellular immunoreactivity for laminin, some invasive tumor especially the OSCC exhibits focal extracellular immunoreactivity for laminin, which has been suggested to be due a defect in the incorporation rather than in the production of laminin, since such cells as well as normal cells can secrete laminin in culture medium.[9]

In the present study, an attempt has been made to evaluate the expression of laminin in various grades of oral squamous cell carcinoma (OSCC). In order to determine whether this protein can be used as a marker for early detection and elucidation of oral cancer.

AIMS AND OBJECTIVES

1. To demonstrate laminin staining, immunohistochemically, in different grades of oral squamous cell carcinoma.
2. To study immunostaining pattern of laminin (presence/absence) around the tumor cells in different grades of oral squamous cell carcinoma.
3. To compare the laminin staining pattern (presence/absence) between different grades of oral squamous cell carcinoma.

MATERIALS AND METHODS

The materials for the study include 60 formalin-fixed paraffin-embedded tissue blocks, retrieved for the Department of Oral Pathology and Microbiology, College of Dental Surgery, Manipal. Among these 60 blocks, 20 blocks from each histologically diagnosed well, moderately and poorly differentiated primary oral squamous cell carcinomas were considered for immunohistochemically staining for laminin.

The laminin immunohistochemically kit IMMH-7 was obtained from Sigma Chemically Company (USA) consisted of:

Vial I: Primary antibody—rabbit antilaminin in buffered saline.

Vial II: Biotinylated secondary antibody—goat antirabbit IgG in buffered saline.

Vial III: Peroxidase reagent—ExtrAvidine conjugated peroxidase in buffered saline.

Vial IVA: Acetate buffer 2.5 mol/L PH 5.0.

Vial IVB: 3-amino 9-ethylcarbazole (AEC) in N, N-dimethylformamide.

Vial V: Three percent hydrogen peroxide in deionized water.

Vial VI: Mixing vial.

Two consecutive 5 microns thick sections were taken from each block. One section was used for routine hematoxylin and eosin stain and the other was subjected to immunohistochemical staining for laminin.

Hematoxylin and Eosin Staining

Routine hematoxylin and eosin stain sections of the 60 formalin-fixed paraffin-embedded tissue blocks were made to confirm microscopically the histopathological grades of primary SCC.

Immunohistochemical Staining

For immunohistochemical staining, the five micron thick sections were taken onto microslides on which chrome alum gelatin adhesive was applied and incubated for 1 hour at 50°C over a slide warmer for proper adhesion for section to the slide. The sections were dewaxed in xylene and hydrated through graded alcohol and placed in 0.05 M Tris-HCL-buffered saline of pH 7.6 (TBS) for 5 minutes and then digested with a freshly prepared solution of pepsin in TBS (0.1%) for 30 minutes at 37°C in a moist chamber. This final step was done to increase the immunoreactivity of antigens in the formalin-fixed paraffin-embedded tissue.

Section were then washed in TBS for 5 minutes, dried and placed in 0.3% hydrogen peroxide in methanol for 10 minutes, so as to block endogenous peroxidase activity, following they were washed in TBS for 5 minutes, air dried, treated with rabbit antilaminin in buffered saline for 60 minutes, followed by goat antirabbit immunoglobulin G for 20 minutes and finally with peroxidase antiperoxidase complex for 20 minutes. Between each of the above steps the sections were washed thoroughly with TBS. Bond peroxidase was then visualized with 3-amino-9-ethylcarbazole (AEC) in N, N-dimethyl formamide reagent (that is 4 ml deionized water, 2 drops acetated buffer, 1 AEC chromogen and 1 drop 3% hydrogen peroxide dissolved together) till brown reaction product was seen. The reactions were then lightly counter stained by using Mayer's hematoxylin for 10 seconds, after which they gently washed under running tap water for 1 minute; the sections were then mounted with aqueous media (glycerol in TBS pH 7.6)

In each slide, evaluation for presence or absence of laminin around tumor cells was done by using light microscope.

The statistical analysis was performed by using Chi-square (χ-square) test and Gaussian-test with a probability of $p < 0.05$ was considered as significant.

RESULTS AND OBSERVATION

For the present study, 60 formalin-fixed unstained paraffin tissue sections were retrieved from the files of the Department

of Oral Pathology and Microbiology, College of Dental Surgery, Manipal, for the evaluation of laminin immunostaining pattern, 20 were well-differentiated, 20 moderately-differentiated and 20 poorly-differentiated oral squamous cell carcinoma (Table 4). Age, sex, habit and site of lesion were recorded for all these cases (Tables 1 to 3).

Immunohistochemical staining was carried out on these 60 tissue sections, using the laminin immunohistochemical kit purchased from Sigma Chemical Company (USA). On light microscopic examination a brown reaction product was seen surrounding tumor islands, consistent with basement membrane retention or synthesis, assessment of laminin staining pattern was done around tumor islands, cords and individual dysplastic epithelial cells by attributing the presence or absence of laminin as the parameter for the study.

In the present study, among these 60 tissue sections, presence of laminin was attributed to 34 sections and complete absence recorded in 26 sections (Table 4). Among the 20 cases of well-differentiated SCCs, 16 sections (80%) exhibited presence of laminin whereas 4 sections (20%) exhibited absence of laminin around the tumor islands (Table 4 and Graph 1). The 20 cases of moderately-differentiated SCCs exhibited presence of laminin in 10 sections (50%) and complete absence of laminin in the remaining 10 sections (50%) around the epithelial tumor islands and cords (Table 4 and Graph 1). However, in 20 cases of poorly-differentiated SCCs 8 sections (40%) exhibited presence of laminin whereas

Table 1: Age, sex, habit and site of lesion in 20 cases of well-differentiated primary oral squamous cell carcinoma

Sr. no		*Age*	*Sex*	*Habit*	*Site*
1	38	M	Beedi 1 packet/day for 15 years and alcohol occasional for 15 years	Floor of the mouth	
2	65	M	Pan and tobacco chewing for 35 years	Left buccal mucosa	
3	52	M	Pan and tobacco chewing 2-3/day and beedi smoking for 20 years	Lateral border of tongue	
4	45	F	Pan chewing 4/day for 20 years	Lower alveolar mucosa	
5	74	M	Smoking, chewing tobacco and alcohol	Right buccal mucosa	
6	72	F	Tobacco chewing 5-6/day for 20 years	Right buccal mucosa	
7	41	M	Pan chewing 4/day for 3 years	Lower alveolar ridge	
8	49	M	Tobacco chewing 2/day for 3 years	Left buccal mucosa	
9	65	F	Pan chewing 6-7/day for 30 years	Lateral border of tongue	
10	67	M	Beedi smoking 5-6/day for 25-30 years	Tongue	
11	59	F	Pan chewing 4-5/day for 20 years	Buccal mucosa	
12	50	M	Beedi smoking and pan chewing for the past 35 years	Lower alveolar mucosa	
13	40	F	Tobacco chewing for 15 years	Left buccal mucosa	
14	45	F	Pan chewing 5-6/day for 4 years	Right buccal mucosa	
15	28	M	Beedi smoking 25/day for 15-20 years and pan chewing 1/day for 2-3 years	Tongue	
16	60	M	Pan and tobacco chewing for 30 years	Left buccal mucosa	
17	42	M	Beedi smoking 5/day for 10-15 years	Floor of the mouth	
18	77	F	Tobacco chewing for 15 years	Left buccal mucosa	
19	60	M	Smoking, tobacco chewing and alcohol	Right upper alveolar mucosa	
20	72	M	Beedi smoking 3-4/day for 52 years and betel nut chewing 3-4/day for 52 years	Lower alveolar mucosa	

Table 2: Age, sex, habit and site of lesion in 20 cases of moderately-differentiated primary oral squamous cell carcinoma

Sr. no	*Age*	*Sex*	*Habit*	*Site*
1	60	M	Tobacco chewing for 20 years and alcohol for 20 years	Buccal mucosa
2	70	M	Beedi smoking 1/day for 30 years and tobacco chewing for 20 years	Tongue and floor of the mouth
3	50	M	Betel nut and tobacco chewing and snuff	Buccal mucosa
4	40	M	Tobacco chewing for 15 years and beedi smoking 1 pack/day for 27 years	Lower right alveolus
5	65	M	Beedi smoking 3 packs/day for 40 years	Palate
6	59	F	Pan chewing with tobacco 5 times/day for 30 years	Right buccal mucosa
7	64	M	Tobacco chewing for 40 years	Labial sulcus
8	56	M	Beedi 1 packet/day	Soft palate
9	55	F	No oral habits	Right buccal mucosa
10	65	F	Pan chewing with tobacco 5 times a day for 35 years	Right buccal mucosa
11		M	Pan chewing 2/day for 10 years	Right buccal mucosa
12	72	M	Pan chewing for 40 years	Buccal sulcus
13	43	F	Pan chewing for 30 years	Buccal mucosa
14	64	M	Pan chewing for 35 years	Buccal sulcus
15	78	F	Tobacco chewing 5/day for 30 years	Tongue
16	51	F	Tobacco chewing 4/day for 25 years	Left retromolar region
17	58	M	Pan chewing for 30 years and smoking 1 pack beedi/day 25 years	Buccal mucosa
18	60	F	Pan chewing for 30 years	Buccal mucosa
19	50	F	Pan chewing for 30 years	Buccal mucosa
20	65	F	Pan chewing for 35 years	Left buccal mucosa

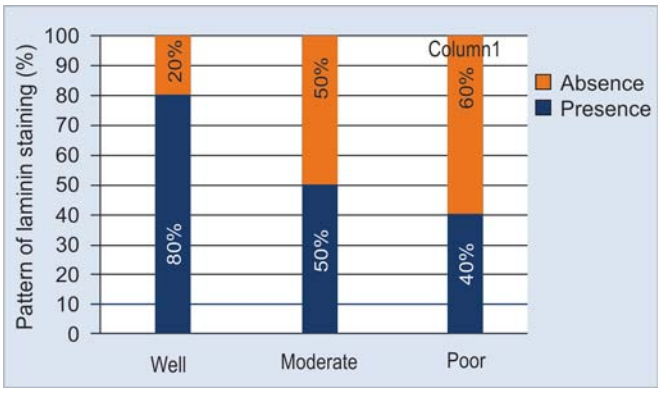
Table 3: Age, sex, habit and site of lesion in 20 cases of poorly-differentiated primary oral squamous cell carcinoma

Sr. no	*Age*	*Sex*	*Habit*	*Site*
1.	80	M	Tobacco chewing 5/day for 40 years	Tongue (right ventral)
2.	44	M	Pan chewing 6 times a day for 20 years	Right buccal mucosa
3.	48	M	Pan chewing 10 times a day for 20 years	Right buccal mucosa and palate
4.	63	M	Tobacco chewing 5/day for 20 years	Tongue (right ventral)
5.	55	M	Smoking beedi and alcohol	Upper right alveolus
6.	60	M	Smoking beedi, chewing tobacco, alcohol	Soft palate
7.	38	M	Beedi smoking for 7 years, tobacco chewing for 5 years	Tongue
8.	45	M	Beedi frequently for 20 years	Buccal mucosa
9.	46	M	Cigarette smoking 25/day for 20 years alcohol frequently for 20 years	Soft palate
10.	68	M	Beedi or cigarette 2-3/day for 10 years, alcohol occasionally	Left alveolus
11.	82	M	Pan chewing 6/day for 40 years	Tongue (right ventral)
12.	45	M	Tobacco chewing/day for 40 years	Tongue (right ventral)
13.	50	M	Pan chewing 8/day for 10 years	Buccal mucosa
14.	45	M	Beedi 3 packets/day for 20 years	Upper and lower alveolus
15.	46	F	Pan chewing with tobacco 5/day for 20 years	Tongue
16.	66	M	Pan chewing 6/day for 30 years	Right buccal mucosa
17.	30	M	Tobacco chewing with beetal nut, beetal leaf and lime	Lateral border of the tongue
18.	53	M	Pan chewing 6/day for 20 years alcohol for 15 years	Buccal mucosa
19.	50	M	Pan chewing 6/day for 25 years alcohol occasionally	Tongue
20.	53	M	Beedi 20/day for 20 years alcohol daily	Palate

Table 4: Immunohistochemical staining pattern of laminin in different grades of primary OSCC

Histopathologic grading	*Number of paraffin-embedded tissue blocks*	*Pattern of laminin staining*			
		Presence		*Absence*	
Well	20	16	80%	04	20%
Moderate	20	10	50%	10	50%
Poor	20	08	40%	12	60%
Total	60	34		26	

$\chi^2 = 8.696$, $p < 0.01$ highly significant



Graph 1: Laminin staining pattern (presence or absence %) in different histopathological grades of primary OSSC

the remaining 12 sections (60%) exhibited complete absence of laminin around the tumor epithelial cells and strands (Table 4, Graph 1, Figs 1 to 5).

Comparison was made between each group of the well, moderate and poorly-differentiated SCCs for both the presence and the absence of laminin using Gaussian test(z) (Tables 5 to 7). While comparing well *vs* moderately-differentiated SCCs, for both laminin presence and absence, it was found to be statistically significant (Table 5). Whereas, on comparing well *vs* poorly-differentiated SCCs it was statistically very highly significant ($p < 0.001$) for the presence and significant ($p < 0.05$) for the absence of laminin (Table 6). And on comparing moderate *vs* poorly-differentiated SCCs statistical analysis revealed no significance ($p > 0.05$) for both the presence and the absence of laminin (Table 7).

The extent of laminin staining (presence/absence) in the different histopathologic grades of OSCC is found to be statistically highly significant ($p < 0.01$) using the Chi-square test (χ-square = 8.696) (Table 4 and Graph 1).

DISCUSSION

Epithelial structure are separated from surrounding stroma by basement membrane that normally behaves like a barrier to the passage of both epithelial and mesenchymal cells also it appears to be crucial particularly during tumor invasion and metastasis.

Laminin major basement membrane glycoprotein synthesized by epithelial and endothelial cells has been shown to be a multifunctional component of many eukaryotic tissues. It is presently thought to regulate the adhesion, spreading, migration, growth and phenotypic expression of various normal and transformed cell types[10-12]

Table 5: Comparison in the pattern of laminin staining in well- and moderately-differentiated primary OSCC

Laminin	*Histopathologic grading*		*Test of significance*	*p-value*
	Well	*Moderate*		
Presence	16	10	Z = 2.098	p < 0.05 significant
Absence	04	10	Z = 2.098	p < 0.05 significant

Table 6: Comparison in the pattern of laminin staining in well- and poorly-differentiated primary OSCC

Laminin	*Histopathologic grading*		*Test of significance*	*p-value*
	Well	*Poor*		
Presence	16	08	Z = 3.539	p < 0.001 very highly significant
Absence	04	12	Z = 3.39	p < 0.001 very highly significant

Table 7: Comparison in the pattern of laminin staining in moderately and poorly-differentiated primary OSCC

Laminin	*Histopathologic grading*		*Test of significance*	*p-value*
	Moderate	*Poor*		
Presence	10	08	Z = 1.12	p > 0.05 not significant
Absence	10	12	Z = 1.12	p > 0.05 not significant

because alterations in expression of this protein can occur during carcinogenesis, this has been used as marker to study basement membrane in cancer.

In the present study, using peroxidase-antiperoxidase-technique, immunostaining for laminin was carried out on 60 formalin-fixed paraffin-embedded tissue section comprising of proportionate samples of histopathologically diagnosed well, moderate and poorly-differentiated OSSCs.

On evaluating the laminin immunostaining pattern it was observed that 80% of well, 50% of moderate and only 40% of poorly-differentiated OSCCs demonstrated laminin presence (Table 6 and Graph 1) and only 20% of well, 50% of moderate and 60% of poorly-differentiated SCCs demonstrated an absence of laminin staining at tumor stromal interface, a gradual decrease of laminin staining, with decreasing cellular differentiation indicating a relationship between differentiation of the lesion and expression of laminin, differentiated lesion showed more conspicuous staining of basement membrane glycoprotein laminin than less differentiated lesion in the present study. This is in agreement with observation of Sakr et al[13] wherein well-differentiated SCC maintained their ability to produce basement membrane components in contrast to less differentiated SCC, probably an attempt at normal epithelial organization.

However, it was observed that few of the poorly-differentiated primary OSCC showed some amount of laminin immunoreactivity which is inline with the view of some authors, who suggested that even high grade tumors can exhibit some degree of laminin immunostaining and are thus, capable of basement membrane production,[14] however, these poorly-differentiated cells do so at a much slower rate than the more well-differentiated tumor cells.[15] Campbell JH and Terranova VP suggested that altered laminin may still be secreted by tumor cells, but at an abnormal slow rate and that quantity and form of basement membrane are grossly altered in high grade tumors.[2]

Furthermore, immunohistochemical study of Hagedorn et al showed a correlation between presences of basement membrane components with biological course of the tumor, indicating less aggressive tumor growth with relatively high amount of retained basement membrane material.[16]

Invasion is a multifactorial process in which the balance between basal lamina production and degradation may be important. In the present study, the laminin staining is in the form of continuous linear deposition—probably these tumor cells irrespective of the grades have retained their ability to produce basement membrane components. Barsky et al in their study on basement membrane component in invasive tumors supported the view that when the tumors are derived from the cells that are normally associated with basal lamina production, the basement membrane component like laminin and type IV collagen are detected around the tumor cells relating to the differentiated phenotype of the tumor cells.[17]

In the present study, a complete loss of basement membrane components were also observed irrespective of the grades at tumor stromal interface. This could be due to lack of synthesis, decreased assembly and the increase turnover or degradation/dissolution of basement membrane components during invasion supporting the concept of Bernstein et al[18] a cyclic behavior of tumor cells adhesion, synthesis and secretion of hydrolytic enzymes in degradation of basement membrane components and the extracellular matrix for cellular invasion.

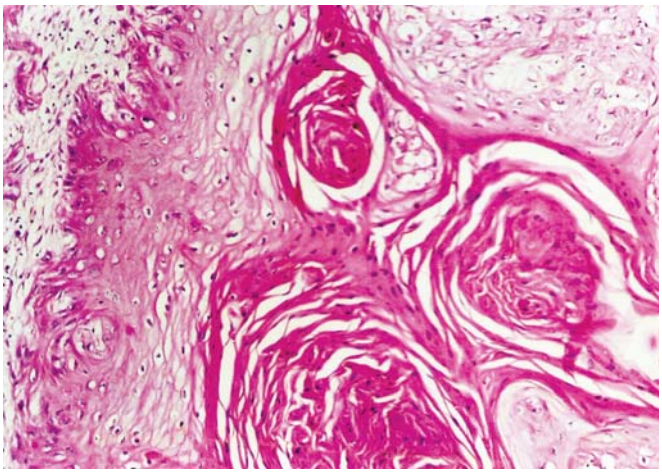


Fig. 1: Photomicrograph showing well-differentiated squamous cell carcinoma (H&E staining 10×)

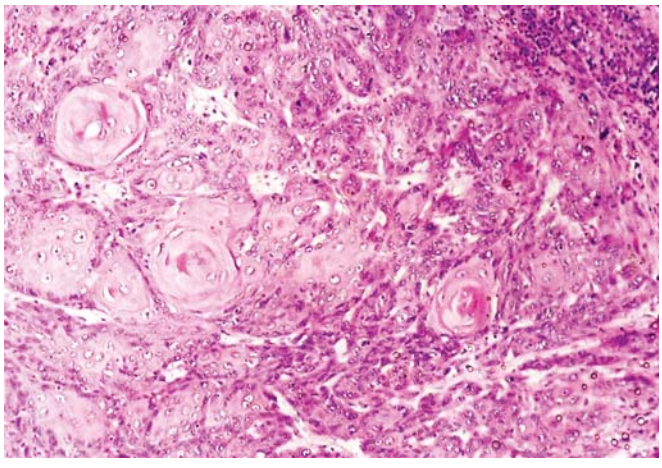


Fig. 2: Photomicrograph showing moderately-differentiated squamous cell carcinoma (H&E staining 10×)

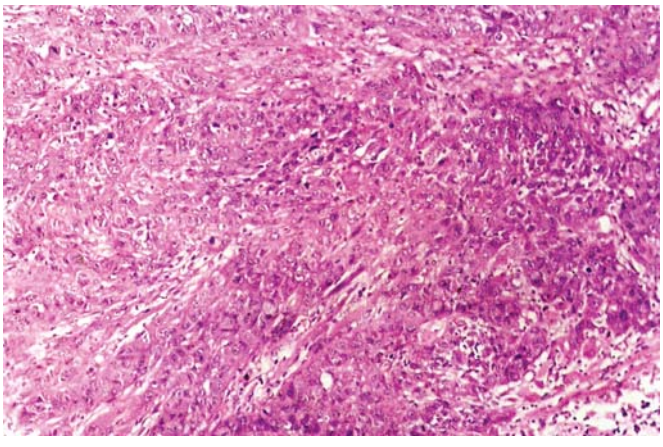


Fig. 3: Photomicrograph showing poorly-differentiated squamous cell carcinoma (H&E staining 10×)

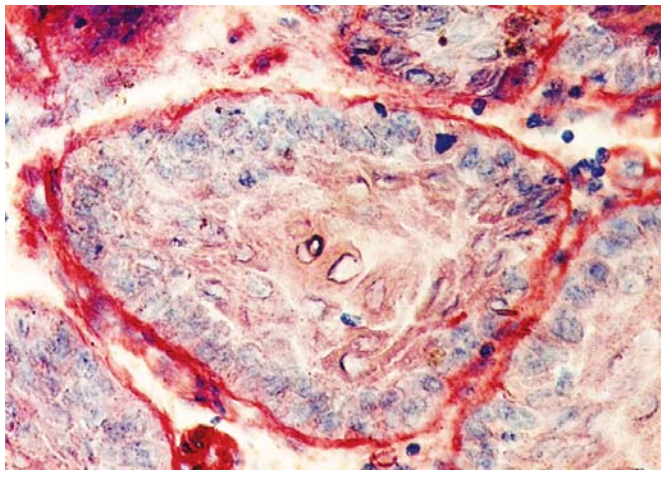


Fig. 4: Photomicrograph exhibiting presence of laminin staining around tumor islands (40×)

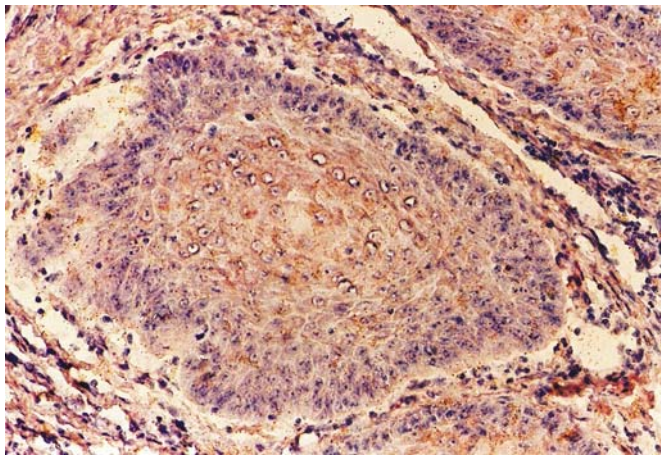


Fig. 5: Photomicrograph exhibiting absence of laminin staining around tumor islands (20×)

Furthermore Visser et al,[19] Sakr et al[13] also observed similar defects in the basement membrane component exclusively in areas adjacent to inflammatory cells. As these cells were capable of releasing enzymes which digest the basement membrane components. However, in the present study no correlation was observed between the intensity of inflammation and degree of loss of laminin staining in different grades of OSCC.

Moreover, the statistical analysis of the present study provides a clear evidence of increased laminin loss with decreasing differentiation, also by using Chi-square test the extent of laminin staining in different grades of OSCC is found to be highly significant ($\chi^2 = 8.696$, $p < 0.01$).

However, further studies on different types of laminin and other components of basement membrane may provide an insight into the pathophysiology of the invasive process in OSCC.

CONCLUSION

It was observed that there was a gradual decrease of laminin staining with decreasing cellular differentiation, with differentiated lesions showing a more conspicuous staining of basement membrane glycoprotein than less differentiated lesions. Moreover, statistical analysis provided a clean evidence of increased laminin loss with decreasing differentiation.

Thus, the presence or absence of laminin staining in different histopathological grades of OSCC indicates an unquestionable interacts of tumor and host tissue, an important factor which reflects the biological parameter of tumor aggressiveness. Further studies on different types of laminin and other components of basement membrane could provide prognostically useful information.

CLINICAL SIGNIFICANCE

Currently, the prognosis for patients with oral squamous cell carcinoma depends upon both histologic subtype (grade) and clinical extent (stage) of the tumor. However, histopathologic grading system remains subjective, and has little meaning of accurately predicting the prognosis of the individual patient. More recently, several studies have provided encouraging evidence for differences in matrix components to be correlated with clinical prognosis. An understanding of how the extracellular matrix influences tumor development and invasion is fundamental in the development of new prognostic indicators and treatment strategies for oral squamous cell carcinoma. In this review, we summarize how changes in the extracellular matrix contribute to oral cancer development.

REFERENCES

1. Barsky SH, Siegal GP, Jonnotta F, Liotta LA. Loss of basement membrane components in invasive tumors but not by their benign counterparts. Lab Invest 1983:49(2):140-47.
2. Cambell JH, Terranova VP. Laminin: Molecular organization and biological function. J Oral Pathol 1988:17:309-23.
3. Kefalides NA. Int Rev Connective Tissue Res 1973:6:63-104. Cited in Risteli L, Timpl R. Isolation and characterization of laminin from human placental and renal basement membranes. Biochem J 1981;193:749-55.
4. Vracko R. Basal lamina scaffold-anatomy and significance for maintenance of orderly tissue structure. A review. Am J Pathol 1974;77:314-38.
5. Chung AE, Freeman IL, Braginski JE. Biochem Biophys Res. Commun 1977:79:859. Cited in: Wewer UM, Engvall E. laminins. Methods in Enzymology 1994;245:85.
6. Timpl R, Rohde H. Laminin—a glycoprotein from the basement membrane. J Biol Chem 1979:254:9933-37.
7. Murray JC, Stingl G, Kleinmann HK, Martin GR, Katz SI. Epidermal cells adhere preferentially to type IV (basement membrane) collagen. J Cell Biol 1979;80:197-202.
8. Terranova VP, Rohrbrach D, Martin GR. Role of laminin in the attachment of PAM 212 (epithelial) cells to basement membrane collagen. Cell 1980;22:719.
9. Albrechtsen R, Nielsen M, Wewer, Engvall E, Ruoslahti E. Cancer Res 1981:41:5076-5081. Cited in: Wewer U, Albrechtsen R, Manthorpe, Varon S, Engvall, Ruoslahti. Human laminin isolated in nearly intact, biologically active form from the placenta by limited proteolysis. J Biol Chem 1983;258: 12654-60.
10. Kleinman HK, Cannon FB, Laurie GW, Hassell JR, et al. Biolgical activities of laminin. J Cell Biochem 1985:27:317-25.
11. Von der Mark, Kuhl U. Laminin and its receptors. Biochem Biophys Acta 1985:823:147-60.
12. Martin GR, Timpl R. Laminin and other basement membrane components. Annu Rev Cell Biol 1987:3:57-85.
13. Sakr WA, Zarbo RJ, Jacobs JR, Crissman JD. Distribution of basement membrane in squamous cell carcinoma of the head and neck. Hum Pathol 1987;18(10):1043-50.
14. Vogel HP, Mendelsohn G. Laminin immunostaining in hyperplastic, dysplastic and neoplastic lesions of the endometrium and uterine cervix. Obstet Gynecol 1987:69:794.
15. Forster SJ, Talbot IC, Clayton DG, Critchley DR. Tumor basement membrane laminin in adenocarcinoma of rectum; an immunohistochemical study of biological and clinical significance. Int J Cancer 1986:37:813-17.
16. Hagedorn H, Schreiner M, Wiest I, Tubel J , Schleicher ED, Nerlich AG. Defective basement membrane in laryngeal carcinoma with heterogenous loss of distinct components. Hum Pathol 1998;29(5):447-54.
17. Barsky SH, Siegal GP, Jannotta F, Liotta LA. Loss of basement membrane components by invasive tumors but not by their benign counterparts. Lab Invest 1983:49(2):140-47.
18. Bernstein LR, Liotta LA. Molecular mediators of interactions with extracellular matrix components in metastasis and angiogenesis.Curr Opin Oncol 1994;6:106-13.
19. Visser R, Van Der Beek JMH, Havenith MG, Cleutjens JPM, Bosman FT. Immunocytochemical detection of basement membrane antigens in the histopathological evaluation of laryngeal dysplasia and neoplasias. Histopathology 1986: 10(2):171-80.

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