

Clinico-Histological study of Basosquamous Carcinoma of the Skin

دراسة سريرية نسيجية لسرطان الجلد الحرشفى القاعدي

Rafal Abdulrazak Al-Rawi

College of Pharmacy|Hawler Medical University

رفل عبدالرزاق الراوي

كلية الصيدلة / جامعة هولير الطبية

Abstract

Basosquamous carcinoma is one of skin malignant tumor with features of both basal cell carcinoma and squamous cell carcinoma. It may behave more aggressively with an increased risk of recurrence and metastases. Investigations on the incidence, clinical, histological and immunohistochemical findings of basosquamous cell carcinoma in comparison with basal and squamous cell carcinoma were carried out. The clinical records of 3000 patients were reviewed from Razgary teaching hospital in Erbil from the period of 1-1-2008 to 1-1-2009 for the diagnosis of basosquamous carcinoma, basal and squamous cell carcinoma and an immunohistochemistry study was done to the basosquamous cell carcinoma. The incidence of basosquamous carcinoma is 8.82% among basal 63.24% and squamous cell carcinoma 27.94%. The commonest site is the nose and mostly occurs in patient over 50 years. Regarding immunohistochemical study of both epithelial membrane antigen (EMA) and low molecular weight keratin (LMWK) showed 5 positive cases out of 6 Basosquamous carcinoma cases. It was concluded that Basosquamous carcinoma incidence is less than that of basal and squamous cell carcinoma. The histological diagnosis of basosquamous carcinoma is confirmed by the use of LMWK and EMA immunohistochemical staining of the areas of both basal cell carcinoma area and squamous cell carcinoma area, respectively.

المستخلص

يعتبر الورم المحرشف القاعدي الخبيث من الاورام الخبيثه وله خصائص الورم القاعدي الخبيث والورم المحرشف الخبيث وله نهج عدوانى وامكانيه العوده والانتشار اكثرب من غيره . هدف البحث الى دراسة معدل حدوث الورم المحرشف القاعدي الخبيث وخصائصه الطبيه والنسيجيه المناعيه الكيميائيه بالمقارنة مع اورام القاعدية الخبيثه والاورام المحرشفه الخبيثه . تم اختيار اورام الجلد الخبيثه واستخلصت المعلومات الطبيه من خلال مراجعه 3000 مريض في مستشفى رزكاري التعليمي فى مدينة اربيل من الفتره من 1-1-2008 الى 1-1-2009 . كما تم اجراء الفحص النسيجي المناعي الكيميائي للاورام المحرشفه القاعدية الخبيثه . أشارت النتائج بان معدل حدوث الاورام المحرشفه القاعدية هو 8.82 % من اورام الجلد الخبيثه وهي نسبة اقل من اورام الجلد المحرشفه 63.24 % والقاعدية الخبيثه 27.94 % وان جميع الحالات وجدت في منطقة الانف ولمجموعه الاعمار التي تجاوزت 50 سنه . وكذلك وجد بأن تعبير LMWK ، EMA ، كان موجباً في 5 من 6 حالات بالنسبة للاورام الم حرشفه القاعدية . استنتج بان معدل حدوث الاورام المحرشفه القاعدية الخبيثه اقل من اورام الجلد المحرشفه والقاعدية الخبيثه ويمكن تعزيز التشخيص النسيجي لاورام المحرشفه القاعدية الخبيثه باجراء الفحص النسيجي المناعي الكيميائي باستخدام عامل EMA ، LMWK لمناطق اورام الجلد المحرشفه والقاعدية الخبيثه .

Introduction

Basosquamous carcinoma is a rare malignancy, with features of both basal cell carcinoma and squamous cell carcinoma. Basosquamous carcinoma may behave more

aggressive [1, 2] with an increased risk of recurrence and metastases than basal and squamous cell carcinoma ranges from (1.2-2.7) % [3, 4, 5].

Histopathologists debate whether these lesions arise de novo or differentiate from pre-existing basal cell carcinomas [6]. Basosquamous cell carcinoma also called metatypical carcinoma has the general configuration of a basal cell carcinoma but it also contains atypical squamous cell which should be distinguished from the keratotic type form of basal cell carcinoma. Its histopathological features shows mixed nodular appearance of atypical basal cells with peripheral palisading and atypical squamous cells with intercellular bridges formation [7, 8]. The keratotic pattern of basal cell carcinoma probably represent an expression of differentiation toward the infundibular portion of hair follicles which has no clinical significance, and should be distinguished from basosquamous carcinoma [9]. Basal cell and squamous cell carcinomas are the most common skin cancers, occurring mainly on sun-exposed skin of old persons [10]. Basal cell carcinomas arise from basally located cells of the epidermis and pilosebaceous unit, which may infiltrate and destroy adjacent tissues, but rarely metastasizes [11]. In Iraq skin cancer constituted 3.41% of all other malignancies in both gender and basosquamous carcinomas appears in 14 cases and constitute 2.7% of the total skin cancers in 2005 [12]. Immunohistochemistry study shows that the cells of basal cell carcinoma are positive for low molecular weight keratin (LMWK) but usually negative for epithelial membrane antigen (EMA). Squamous cell carcinoma of the skin exhibited immunoreactivity for high molecular weight keratin (HMWK) and EMA, while basosquamous carcinoma showed a positive stain for (LMWK) and (EMA) [9].

Materials and Methods

The clinical records of 3000 patients were investigated for the diagnosis of basosquamous carcinoma, basal and squamous cell carcinoma from Razgary teaching hospital in Erbil during the period of 1-1-2008 to 1-1-2009. Clinical information about gender, age, site and area of lesion were obtained. For each case of basosquamous carcinoma a representative sections were stained with haematoxylin (H) and eosin (E) and others were stained immunohistochemically for LMWK and EMA from the available formalin fixed paraffin embedded tissues. Primary monoclonal antibody used in this study is of purified liquid form. For the avidin-biotin complex (ABC) detection system (secondary detection system), alkaline phosphatase method were used in this study. The immunorecipient visualized as brown color in the cytoplasm for both EMA and LMWK were purchased from Chemicon International. Chromogen reagents used in this study were fast chromogen A and fast chromogen B. Positive results were classified as "Occasional", "Focal" or "Diffuse" [13, 14].

Statistical analysis of the categorical data sets obtained were performed using Chi-square test (contingency table) due to discrete variables arises from a counting collection process of data. The categorical data were grouped according gender (male vs. female), age, site and sun exposed (head) vs. sun protected area (abdomen and extremities). The chi-square was considered statistically significant when the alpha (α) level of significance (P) was equal or less than 0.05.

Results

A total of 6 cases of basosquamous carcinoma, 43 cases of basal cell carcinoma and 19 cases of squamous cell carcinoma were identified from 68 cases of skin cancer among the total of 3000 cases. Chi-square revealed a significant difference ($P<0.05$) between the incidence of basosquamous, squamous and basal carcinoma Table (1).

Table (1): Incidence of skin cancer

	Basosquamous carcinoma	Basal cell carcinoma	Squamous carcinoma	Total
Incidence	6 (8.82%)	43 (63.24%)	19 (27.94%)	68 (100%)

Chi Square = 31.08 (P<0.05) (Significant difference)

Four out of six cases of basosquamous carcinoma were male gender. Chi-square indicated no significant difference in the distribution of skin cancer according to the gender Table (2).

Table (2): Distribution of skin cancer according to the gender

Gender	Basosquamous carcinoma	Basal cell carcinoma	Squamous cell carcinoma
Male	4 (66.7%)	23(53.5%)	12 (63.1%)
Female	2 (33.3%)	20 (46.5%)	7 (36.9%)
Total	6	43	19

Chi Square = 0.74 (No significant difference)

All of the basosquamous carcinoma cases, 17 of the basal cell carcinoma and three of the squamous cell carcinoma were located in the nose. Chi-square revealed a significant difference ($P<0.05$) in the distribution of skin cancer according to the site Table (3).

Table (3): Distribution of skin cancer according to the site

Site	Basosquamous carcinoma	Basal cell carcinoma	Squamous cell carcinoma
Nose	6(100%)	17(39.5%)	3(15.8%)
Orbital	0	9(20.9%)	1(5.3%)
Cheek	0	7(16.3%)	3(15.8)
Scalp	0	11.6)(5	1(5.3%)
Lip	0	2.3%)(1	6(31.6%)
Others	0	4(9.3%)	5(26.3)
Total	6	43	19

Chi Square = 26.37 (P<0.05) (Significant difference)

Five out of six basosquamous cell carcinoma cases, 32 out of 43 cases of basal cell carcinoma and 15 out of 19 cases of squamous cell carcinoma occur in patients older than 50 years of age. Statistical analysis revealed a significant difference ($P<0.05$) in the distribution of skin cancer according to the age Table (4).

Table (4): Distribution of skin cancer according to the age

Age (years)	Basosquamous carcinoma	Basal cell carcinoma	Squamous cell carcinoma
< 30	0	0	0
30 – 50	(16.7%)1	11(25.6%)	4(21.1%)
> 50	83.3%)(5	32(74.4%)	15(78.9%)
Total	6	43	19

Chi Square = 41.12 (P<0.05) (Significant difference)

All of the basosquamous carcinoma and basal cell carcinoma and 17 out of the 19 cases of the squamous cell carcinoma occur in sun exposed area. Chi-square revealed a significant difference ($P<0.05$) in the distribution of skin cancer according to the sun exposed area Table (5).

Table (5): Distribution of skin cancer according to the sun exposed area

	Basosquamous carcinoma	Basal cell carcinoma	Squamous cell carcinoma
Sun exposed area	6 (100%)	43 (100%)	17 (89.5%)
Sun protected area	0	0	10.5% (2)
Total	6	43	19

Chi Square = 60.84 ($P<0.05$) (Significant difference)

The expression of low molecular weight keratin (LMWK) was positive (all showed diffuse staining pattern) in five out of six basosquamous carcinoma cases in basal cell carcinoma area Figure (1).

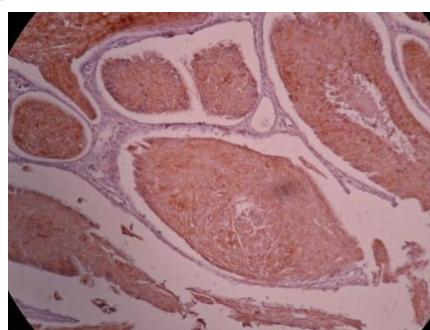


Fig (1): Basosquamous cell carcinoma shows positive reactivity for LMWK in basal cell area. The cytoplasm stains with brown color. (X 200) (Immunohistochemical staining)

Statistical analysis revealed a significant difference ($P<0.05$) (Table 6).

Table (6): Expression of epithelial membrane antigen (EMA) in basosquamous cell carcinoma

	EMA (+)	EMA (-)	Total
Basosquamous carcinoma	5 (83.3%)	1 (16.7%)	6

Chi Square = 4.00 ($P<0.05$) (Significant difference)

With the transition zone of squamous cell carcinoma area and basal cell carcinoma area showing diminished staining. The expression of epithelial membrane antigen (EMA) was positive (all showed diffuse staining pattern) in five out of six basosquamous carcinoma cases in squamous cell carcinoma area Figure (2). Statistical analysis revealed a significant difference ($P<0.05$) Table (7).

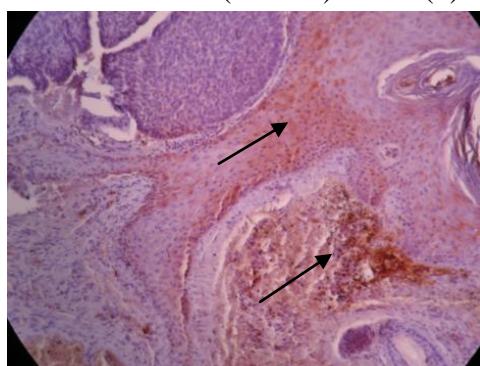


Fig (2): Basosquamous cell carcinoma shows positive reactivity for EMA in squamous cell area.

The cytoplasm stains with brown color. The upper basal cell area shows no staining (X 200) (Immunohistochemical staining).

Table (7): Expression of low molecular weight keratin (LMWK) in basosquamous cell carcinoma

Basosquamous carcinoma	LMWK (+) 5 (83.3%)	LMWK (-) 1 (16.7%)	Total 6
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Chi Square = 4.00 (P<0.05) (Significant difference)

Discussion

The terminology surrounding basosquamous carcinoma is confusing and there is a need for more uniform language. Data regarding the incidence, recurrence, and metastasis rates of basosquamous carcinoma were based mostly on retrospective series with a limited number of cases [3]. The reported incidence of basosquamous carcinoma ranged from (1.2- 2.7)% [3]. While in this study the incidence was 8.8%. It is more common that in patient older than 50 years the incidence of basosquamous carcinomas was high. Similar result was also found in other studies [15, 16]. Basosquamous carcinoma occurs more common on the sun exposed area on the face mainly on the nose [1, 10, 16]. This finding is similar to the result found in this result. Immunohistochemically, in this study, the tumor cells in the basosquamous cell carcinoma showed low molecular weight keratin (LMWK) expression in the basal cell carcinoma area with the transition zone of squamous cell carcinoma and basal cell carcinoma showing diminished staining. Epithelial membrane antigen was focally positive in the conventional squamous cell carcinoma area, so this means Basosquamous cell carcinoma has dual differentiations to basal cell carcinoma and squamous cell carcinoma areas [15]. The histological diagnosis of basosquamous cell carcinoma is confirmed by the use of EMA and LMWK immunohistological staining, this result is similar to that of other studies [1, 15]. Basosquamous carcinoma is aggressive tumor [17, 18] further investigation is recommended.

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