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Prevalence and Risk Factors for Recurrence of Basal Cell Carcinoma Following Surgical Excision in a 5-Year Follow-Up Period

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ABSTRACT

Material And Methods: Observational, descriptive, retrospective study in patients with clinical and histopathological diagnosis of basal cell carcinoma, attended at CMN La Raza in a period of 5 years, to determine the postoperative recurrence of CBC. Clinical and histological variables were included, which were analyzed with descriptive statistics and for the comparison of variables was used chi-square or exact test of Fisher and U of Mann Whitney, subsequently, multiple logistic regression was performed to determine the independent risk factors, with the use of the statistical package SPSS v25. The study was approved by the ethics and research committee of CMN La Raza.

Results: We included 280 patients with CBC, with a median age of 72 years. The majority were 211 women (75.4%). CBC recurrence was observed in 115 (41.1%) patients. In the univariate analysis, age, sex, smoking, history of sunburn, facial area, CBC subtype, perineural and vascular involvement were found to be statistically significant ($p<0.05$). In the regression model, the independent risk factors associated with postoperative recurrence of CBC were age, male sex, and smoking.

Conclusions: The clinical-pathological characteristics were similar to those reported in the literature. In our population, it was observed as independent risk factors for recurrence, adjusted to those already mentioned in the literature, were male sex, age and smoking, so it is important to closely monitor these patients to take measures regarding surgical treatment.

KEY WORDS: Basal cell carcinoma, recurrence, risk factors.

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BACKGROUND

Basal cell carcinoma (BCC) is the most common skin cancer worldwide, accounting for 75% of all non-melanoma cancers. An estimated annual incidence of 75,000 new cases of CBC is estimated, with an increase of 4-8% per year.

It is a malignant tumor of the germ follicular cells. It most often affects individuals from the sixth decade of life, who have a history of chronic exposure to the sun (ultraviolet radiation), which is the most important risk factor, especially when exposure occurs in childhood and adolescence, in addition to its intermittent and intense exposure. Other risk factors include male gender, Fitzpatrick I and II (with a risk of acquiring 2 to 4 times more than the general population), personal history of CBC, red or blond hair, light eyes, chronic arsenic exposure, exposure to ionizing radiation, chronic immunosuppression status, genetic syndromes, and family history; Tanning beds have also been reported as dose-dependent risk factors. In some populations the risk is higher, as in the case of patients with HIV it is double and in post-transplanted solid organ patients it can occur 5-10 times more than in the general population. Chronic scars and ulcers are important for the development of CBC in non-photoexposed areas (2,3). The lifetime risk of developing BCC in the US is estimated to be 20%, rising to 30% in Caucasian patients (4).

The diagnosis is clinical, dermoscopic and histopathological. In the clinic you can see a pearly lesion, with telangiectasias, of slow growth. It is most often located on the head and neck, followed by trunk, limbs and genitals. Dermoscopy shows arborizing telangiectasias, thin and short telangiectasias, cartwheel and maple leaf structures, as well as blue-gray blood cells and ovoid nests, with a sensitivity of 89-91% and specificity of 95%. Histopathological examination is essential to confirm the diagnosis and estimate the risk of recurrence.

The types of CBC can be classified into high and low risk, according to clinical behavior, risk of recurrence and invasion into dermis. Those of low risk include: nodular, which corresponds to 50-80% of all cases, superficial and sclerodermiform. Those at high risk are: micronodular, infiltrating, sclerodermiform and basosquamous. Morpheiform CBC has the highest rate of recurrence and

perineural invasion; This presents as a depressed, serous, scar-plate-like lesion, with or without ulceration. Infiltrating CBC is associated with a high rate of perineural invasion and recurrence. The micronodular type, which is composed of diffuse micronodules and the basosquamous type, behaves similarly to squamous cell carcinoma, with several transitional areas to be distinguished from transitional tumors (1).

Area H corresponds to the central area of the face, eyelids, eyebrows, periorbital region, nose, lips, chin, jaw, pre- and retroauricular areas, genitals, hands and feet. The L area corresponds to cheeks, forehead, scalp and neck. And area M corresponds to the trunk and limbs (2,6).

It can lead to destruction of the affected tissue; In addition, it has a low metastasis potential of 0.0028-0.55%. Despite their low mortality, their morbidity is high (2,4).

Treatment options include conventional excisional surgery, Mohs micrographic surgery, curettage with or without electrodesiccation, cryosurgery, photodynamic therapy, radiation therapy, topical or oral treatment or intralesional injections. The type of treatment depends on tumor size, location, histologic subtype, adherence to treatment, medical comorbidities, and cosmetic outcomes (2,4).

Conventional surgical excision is the treatment of choice for most BCCs, with a peri-tumour margin of 4 mm in most cases; this method presents a recurrence rate of less than 5%, even for high-risk CBCs, such as those located in zone H, with a recurrence rate of 12.2% at 10 years. However, a surgical margin of 10 mm is recommended in these cases, since the 4 mm margin is used for low-risk tumors. In some cases, patients show incomplete excision of the CBC margins, so there is a greater risk of recurrence, in addition to the type of risk inherent to CBC (2). The recurrence rate also (4) depends on the type of treatment employed. In the case of using curettage and electrocautery, the CBC recurrence rate is estimated at 3-20% (7). The lowest recurrence rate is achieved with Mohs micrographic surgery with up to 1% recurrence at 5 years (8). This was corroborated by the study by Fukumoto T et al., who conducted a systematic review to report the CBC recurrence rates of multiple treatments for this disease. A lower failure rate was found to treatment with conventional surgery and Mohs micrographic surgery compared to cryosurgery, photodynamic therapy, radiotherapy or topical treatment (9).

MATERIAL AND METHODS

An observational, descriptive, comparative, retrospective study was conducted in basal cell carcinoma patients with 1 year of having been surgically operated by the dermatology and plastic and reconstructive surgery service with complete excision, of the Hospital de Especialidades "Dr. Antonio Fraga Mouret" CMN La Raza, with a follow-up of 5 years. We included patients older than 18 years, men and women, with , with 5 years of follow-up in consultation at the CMN La Raza. With complete clinical record with the study variables, treated with complete excision of the lesion with a margin of 4 mm, with or without compromised surgical edges and bed, without surgical reintervention, only follow-up, in the dermatology service of CMN La Raza. With more than or equal to one year of the surgical intervention. The following clinical-pathological variables were included: Age, sex, comorbidities, time of evolution with CBC, time of onset of CBC recurrence, histological subtype of CBC, history of sunburn, affected facial region, use of tanning booths, smoking, tumor size, number of tumors, exposure to pesticides, recurrence of CBC, perinerual involvement, vascular involvement. Descriptive statistics were performed. For the comparison of the clinical pathological variables, Chi square test or Fisher's exact test and Mann Whitney's U test was performed. Multiple logistic regression was subsequently performed to determine independent risk factors for postoperative recurrence of CBC; For this purpose, variables known as independent risk factors such as facial region or histological subtype were excluded, variables with $p<0.05$ were added to the statistical model.

This study was approved by the ethics and research committee of the National Medical Center La Raza, adhered to the provisions of the Declaration of Helsinki (1964), Belmont Report (1979) and the provisions of the General Health Law on health research including information regarding ethics committees

Interns in Health Institutions (Articles 100, 103 and 105), Official Mexican Standard NOM012-SSA3-201219 22-26 (16,20)

RESULTS

We included 280 patients with CBC, with a median age of 72 years. The majority were 211 women (75.4%). The most frequent comorbidity was arterial hypertension 137 (48.9%). 64 (22.9%) had a history of sunburn, 8 (2.9%) a history of tanning booth use, 109 (38.9%) a history of pesticide exposure. A median evolution of CBC of 38 months was observed. The most affected facial area was M 110 (39.3%). The median tumor size was 2.45 cm and the number of tumors was 1. The most frequent histological subtype was nodular 157 (56.1%). CBC recurrence was observed in 115 (41.1%) patients, with a median recurrence time of 30.5 months after surgery (Table 1).

When comparing the clinical and histological characteristics of patients with and without recurrence, age, sex, smoking, history of sunburn, facial area, CBC subtype, perineural and vascular involvement, were found to be statistically significant ($p<0.05$).

A multiple logistic regression was performed to determine the risk factors associated with CBC recurrence, did not exclude the variables already known as risk factors, facial area, cbc subtype, and included that with $p <0.05$ (Table 2).

The risk factors associated with postoperative recurrence of CBC were age, male sex and smoking (Table 3).

DISCUSSION

In our study we found as independent postoperative risk factors for recurrence of basal cell carcinoma the following: age, male sex and smoking. This can be compared with studies such as that of Fidelis et al., who compared the number of CBC recurrences after incomplete conventional surgical treatment. We included 120 patients who presented involvement of the surgical margins, with the presence of tumor cells at the surgical edges, with a mean age of 69.6 years. 50% of patients were women. The most frequent histological type was nodular, with a mean tumor size of 1.1 cm. The tumor location with the highest incidence was the nose. Regarding surgical margins, the lateral margin was the most compromised, with positive edges. During clinical follow-up, only 40 patients had to be reoperated. The total number of patients who had recurrence was 34 (28.4%). It was observed that with respect to location, only the malar area had a significant risk of recurrence of the lesion (p=0.02). The mean follow-up was 29.54 months. It was concluded that the presence of positive margins does not necessarily imply a risk of recurrence (2). Płaszczyńska, A et al., conducted a study to identify and analyze the clinical, epidemiological and histopathological factors that influenced the recurrence of CBC. We included 1097 CBCs, with a recurrence rate of 3.3% per year, of which the majority were men (52.8%), with a mean maximum size of 18.4 mm. The most common location of tumor recurrence was the nose in up to 25% of cases. The histological subtype most frequently in these patients was infiltrating (52.8%), followed by superficial CBC in 22.2%. The area with the highest CBC recurrence rate was H at 47.2%, followed by M at 41.7% and L at 11.1%. Regarding surgical treatment, incomplete excision was performed in 30.6% in 30.6%; 22.2% received cryosurgery, 2.8% CO2 laser, 2.8% cryosurgery + CO2 laser. The treatment with the highest risk of recurrence was complete surgical excision (9). Girardi F et al. conducted a retrospective study to evaluate the pathological and clinical factors associated with the recurrence rate due to inadequate surgical margins in head and neck CBCs. A total of 389 patients were included. The following factors were statistically significant for the presence of inadequate surgical margins and tumor recurrence: presence of scleroderma (p=0.005), high Clark level (p<0.001), aggressive variants (p<0.001), tumor invasion beyond adipose tissue (<0.001), high stage T (p<0.001), perineural invasion (p=0.002), primary site (p=0.04), multifocality (p=0.01) and tumor diameter (p=0.02). Subsequently, in the mutivariate analysis, only Clark's level and depth of invasion were independent risk factors (10).

Kavoussi R et al. conducted a retrospective study to evaluate the results of surgical excision of high-risk CBCs in the head and neck. We included 122 patients, 47 women and 75 men, with a mean age of 57.6 years. The most frequent histological subtype was the nodular, most frequently located in the nasal region. 89.3% were considered to have complete healing after excision of the lesion, with a clinical follow-up of 4 years. A direct relationship was found between treatment outcomes and lesion recurrence, multiplicity of risk factors, time of disease evolution and histological subtype. A significant association was also observed between the number of surgical excisions and the multiplicity of risk factors, as well as the rate of recurrence, location and size of the tumor. It was concluded that patients with failure to surgical treatment have more risk factors, longer time of evolution of the lesion and high-risk histological subtypes (11).

Ceder H et al. conducted a retrospective study that included patients with high-risk BCC treated with surgical excision, to determine the complete excision rate, associated risk factors and recurrence rate. 987 cases were included, of which 20.6% presented incomplete excision of the tumor, of these, most were located in face and scalp skin (22.4%), especially in nose, ears, scalp skin and periorbital area. Circular excision was the procedure with the highest rate of incomplete excision and therefore recurrence of CBC (28.5%). No significant association was found between complete excision rate and tumor size, margin excision, use of presurgical biopsy, or surgeon experience (12).

Kondo R et al. conducted a study to evaluate the recurrence rate of CBCs undergoing conventional surgery, with pre-established margins, with subsequent flap reconstruction and graft placement. Of 116 procedures, only 3 cases (2.6%) were found, which were located in the nasal region and whose histological subtypes were of the sclerodermiform or micronodular type (13). Pons S et al. studied the risk of CBC recurrence and the most affected site of onset. We included 803 CBCs, of which 4.6% were confirmed as recurrent. 92% were in the lead. The site with the highest recurrence of CBC was the temporal and temporal/frontal region in 32.4% of cases, followed by the medial canthus and lower eyelid in 18.9%, wing and tip of the nose in 16.2% and the ears 8.1% (14). Morgan F et al. conducted a study to identify independent risk factors associated with local recurrence of CBC greater than or equal to 2 cm in diameter. We included 248 cbcs larger than 2 cm and 248 cbcs smaller than 2 cm. An increased risk of recurrence was found in CBCs larger than 2 cm. The risk factors for recurrence in these tumors were location in the head and neck (OR 9.7, 95% CI: 3-31.3) and depth of the lesion beyond fat tissue (OR 3.1, 95% CI: 1-9.6%) (15).

As can be seen, in most of the studies cited, the location of the tumor, the extension beyond the dermis, the elevated clark level, the histopathological variant, the poor surgical technique with positive margins were found as independent risk factors. However, all these factors are already known as risk factors for cbc recurrence, so our goal was to compare

two populations with and without cbc recurrence with similar characteristics and adjust the logistic regression model based on the variables already described as risk factors, obtaining other factors little mentioned in the literature.

CONCLUSIONS

In our population, it was observed that the risk factors for the recurrence of independent basal cell carcinoma, adjusted to those already mentioned in the literature, were male sex, age and smoking, so it is important to closely monitor these patients in order to assess the early treatment of cbc recurrence, In addition to taking measures regarding the surgical treatment offered, either with therapeutic adjuvants or with a greater surgical margin.

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Tablas and grapas

Tabal 1. Clinical and histological characteristics of patients with basal cell carcinoma	
Population (n)	280
Age (years)	72 (66.25-79)
Sex	
Man	69 (24.6%)
Woman	211 (75.4%)
Comorbidities	
Type 2 diabetes mellitus	131 (46.8%)
High blood pressure	137 (48.9%)
Smoking	102 (36.4%)
History of sunburn	64 (22.9%)
History of tanning booth use	8 (2.9%)
History of pesticide exposure	109 (38.9%)
Evolution time (months)	38 (19-92)
Facial area	
H	77 (27.5%)
L	93 (33.2%)
M	110 (39.3%)
Tumor size (cm)	2.45 (1.2-5.6)
Number of tumors	1 (1-2)
Histopathological features	
CBC Subtype	
Nodular	157 (56.1%)
Superficial	38 (13.6%)
Infundibuloquístico	3 (1.1%)
Morfeiforme	27 (9.6%)
Infiltrative	15 (5.4%)
Micronodular	17 (6.1%)
Basoescamoso	23 (8.2%)
Perineural condition	125 (44.6%)
Afección perivascular	115 (41.1%)
Recurrence	115 (41.1%)
Postoperative recurrence time (months)	30.5 (16-48)
Results are presented with frequencies (%) and median (q1-q3). CBC: carcinoma bascocelular.	

Table 2. Comparison of clinical and histopathological features of patients with and without recurrence of basal cell carcinoma.			
	With recurrence N=115	No recurrence N=165	*p*
Age (years)^	148.96	128.36	0.036**
Sex*			
Man	44 (38.3%)	25 (15.2%)	0.000**
Woman	71 (61.7%)	140 (84.8%)	
Comorbidities*			
Type 2 diabetes mellitus	57 (49.6%)	74 (44.8%)	0.436
High blood pressure	51 (44.3%)	86 (52.1%)	0.201
Smoking	68 (59.1%)	34 (20.6%)	0.000**
History of sunburn*	35 (30.4%)	29 (17.6%)	0.012**
History of tanning booth use*	6 (5.2%)	2 (1.2%)	0.068
History of pesticide exposure*			
Evolution time (months)^	47 (40.9%)	62 (37.6%)	0.403

Facial area *	146.13	132.42	0.163
H			
L	53 (46.1%)	24 (14.5%)	0.000**
M	47 (40.9%)	46 (27.9%)	
Tumor size (cm)^	15 (13%)	95 (57.6%)	
Number of tumors^	147.44	130.54	0.086
Histopathological features*	142.24	138	0.639
BCC subtype			
Nodular			
Superficial	61 (53%)	96 (58.2%)	0.000**
Infundibuloquístico	0	38(23%)	
Morfeiforme	2 (1.7%)	1 (0.6%)	
Infiltrative	20 (17.4%)	7 (4.2%)	
Micronodular	2 (1.7%)	13 (7.9%)	
Basoescamoso	13 (11.3%)	4 (2.4%)	
Perineural condition	17 (14.8%)	6 (3.6%)	
Afección perivascular	38 (33%)	87 (52.7%)	0.001**
	35 (30.4%)	80 (48.5%)	0.003**

The results are presented in frequency (%), middle ranges.
*Chi-square or Fisher's exact test. ^U by Mann Whitney. ***p<0.05*

Table 3. Risk factors associated with postoperative recurrence of basal cell carcinoma

	OR	IC95%	*p*
Age	1.029	1.009-1.049	0.005
Man	3.802	3.802-2.020	0.000
Smoking	5.651	3.227-9.896	0.000