

Basal Cell carcinoma of unusual localization

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ABSTRACT

Background: 85 to 90% of basal cell carcinomas (BCC) are usually located on head and neck. The presence of BCC in non-exposed areas is rare, and suggests the existence of still unknown etiologic factors.

Objectives: To analyze BCC's anatomical distribution; to define usual/unusual sites for BCCs; to relate site and histopathological subtypes; to compare obtained data with national and international literature.

Material and Methods: A retrospective study was performed. Patient data included sex and age at diagnosis; tumor data included histological subtype and anatomical site.

Results: 611 patients, 319 females. Mean age: 68,39 years. Total number of BCCs was 873. Body-site distribution was as follows: cephalic area 65,4%; trunk 20,7%. Less frequent localizations included lower limbs 5% (leg 29, thigh 10, foot 3, knee 2); upper limbs 4,4% (arm 18, forearm 15, hand 15, palm 4); sacrolumbar area 2,7%; folds 0,8% (groin 3, popliteal area 1, axilla 2, interdigital feet fold 1); genitalia 0,6% (5); buttocks 0,3% (3). According to Lever's histopathologic classification, the distribution of the above was: nodular 58,2%; partly nodular/infiltrative 19,9%; superficial 17,5%; and infiltrative 4,5%.

Conclusions: Body site distribution in this series does not differ from others. More than 86% of the tumors arose in head, neck and trunk. Statistically defined unusual sites are those anatomical location below 95 percentile (frequency less than 2%): abdomen, forearm, thigh, hand, scrotum, inguinal folds, buttocks, feet, vulva, axilla, knee, palm, popliteal fossae, interdigital feet fold. Unusual site tumors summarize 36 lesions (4,12%). Nodular, partly nodular/infiltrative and infiltrative were predominant histological subtypes in head and neck, while superficial subtype was more frequent in trunk. Histological subtypes distribution did not show different patterns in less frequent anatomical sites. (Dermatol Argent 2010;16(1):25-33).

Keywords:

Basal cell carcinoma, anatomic site distribution, histological subtypes.

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Introduction

The Basal Cell Carcinoma (BCC) is the most common skin neoplasm. It usually originates in chronically solar exposed areas. Around 85-90% is localized in the head and neck, followed by back and limbs. The appearance on non-exposed areas to UV radiation is infrequent and would indicate the participation of other etiologic factors.

The definition of unusual localized BCC is yet controversial. The recognition of unusual localizations would not only imply the anecdotal but would also serve to establish monitoring and behavioral therapies.

The majority of authors assign an “unusual” localization in accordance with a presumption that comes as a result of visual observation. They do not provide a definition of an “unusual” localization, rather they describe several clinical observations, and show the incidence percentage. In this study, we expose our results on BCC’s distribution on different anatomic areas and analyze the histological types, with the aim to define “frequent/infrequent” localizations, identify the most common histological types on each localization, and compare our results with the most extended national and international publications to our knowledge.

Objectives

1. Determine BCC’s anatomical distribution on a series of BCC cases observed over the last 11 years.
2. Define usual and unusual sites for BCC.
3. Correlate BCC’s anatomic site with the histopathologic subtype.
4. To revise the available bibliography in order to compare obtained data with national and international literature.

Materials and Methods

Study Design

Descriptive, observational, single center, retrospective.

TABLE 1. Proportion of BCC per anatomic site.

Location	Frequency	%	% Accumulated
Head and neck	571	65,4	65,4
Trunk	181	20,7	86,1
Lower limb	44	5,0	91,2
Upper limb	38	4,4	95,5
Lumbosacral	24	2,7	98,3
Fold	7	0,8	99,1
Genital	5	0,6	99,7
Gluteus	3	0,3	100,0
Total	873	100,0	

Population under Study

We studied BCC cases detected on patients who attended the Dermatology Unit. We reviewed digital medical records, pathology protocols, and records of consultations of the Skin Cancer Campaign of the SAD, from March 1997 until March 2008, from Dermatology Unit of the General Acute Hospital “Dr. Cosme Argerich”.

Inclusion Criteria

- Count with the following complete information: histopathological and anatomic site confirmation at the time of diagnosis.

Exclusion Criteria

- BCC found through histological protocols of patients had not previously consulted the Dermatology Unit.
- Recurrent BCCs.
- BCC in patients with basal cell nevus syndrome, xeroderma pigmentosum, endemic regional chronic hydroarsenicism (ERCH).
- Variables under Study
- Total number of BCC.
- Number of tumors per patient.
- Proportion of BCC by anatomical site: cephalic extremity (scalp, face, neck), trunk (abdomen, back, chest), upper limbs (arm, forearm, hand, palm), lower limb (thigh, knee, leg, foot), lumbar area, buttocks, folds (groin, popliteal space, axilla, interdigital feet folds), and genitals (vulva, scrotum).
- BCC proportion per anatomic sites discriminating between the histological subtypes as: superficial, lobular, corded and lobular, and corded. The lobular BCC was identified when tumor masses of different sizes and shapes were found in the dermis, identifying a connection of more than 90% to the epidermis. The corded BCC was identified when basaloided cells formed cords or strands a few layers thick with little or no peripheral stockade, and the boundary between the tumor and the stroma was inaccurate. When tumors showed both lobular and corded or infiltrating areas they were ascribed as “lobular and corded” BCCs. The superficial BCC results in outbreaks and irregular proliferations of tumor tissue attached to the underside of the epidermis¹.

Processing and statistical analysis

The data was analyzed using database software (such as Excel), a 2.4 GHz Pentium 4 microprocessor, and the statistical package SPSS 11.5. For each variable, appropriate statistical descriptors were determined according to the measurement and distribution scale. When necessary, the following estimates were calculated: estimation of 95% confidence intervals, and chi-square and Student-t tests. The level of significance was set as $\alpha = 0.05$.

TABLE 2. Distribution by location.

Location	Frequency	%	% Accumulated
Face	516	59,1	59,1
Back	90	10,3	69,4
Trunk	75	8,6	78,0
Neck	31	3,6	81,6
Leg	29	3,3	84,9
Scalp	24	2,7	87,6
Lumbosacral	24	2,7	90,4
Spleen	18	2,1	92,4
Abdomen *	16	1,8	94,3
Forearm *	15	1,7	96,0
Thigh*	10	1,1	97,1
Hand *	4	0,5	97,6
Scrotum *	3	0,3	97,9
Groin *	3	0,3	98,3
Gluteus *	3	0,3	98,6
Foot *	3	0,3	99,0
Vulva *	2	0,2	99,2
Axilla *	2	0,2	99,4
Knee *	2	0,2	99,7
Palm *	1	0,1	99,8
Popliteal fossae *	1	0,1	99,9
Interdigital feet fold *	1	0,1	100,0
Total	873	100,0	

* Infrequent places from statistical point of view.

Results

611 patients were studied: 319 women (52.2%) and 292 men (47.8%), with an average age of 68.39 years old (range: 19-98 years). The total number of BCC was 873 tumors. The average number of tumors per patient was 1.43 (being 1 minimum, and 10 maximum).

The proportion of BCC per site or anatomic localization is shown in table 1, over a total of 873 tumors. The 65.4% was localized on cephalic extremity. The distribution is detailed in table 2, it can be observed that 59.1% of the tumors were localized on the face, and “unusual-site-tumors” are described, from a statistical point of view, as unusual those who stand below the 95 percentile of frequency, which is equivalent to a frequency lower than 2%, such as tumors in the abdomen, forearm, thigh, hand, scrotum, groin, buttocks, foot, vulva, axilla, knee, palm, popliteal area and interdigital feet folds. These give a total sum of 36 tumors, which represent 4.21% of the total. The histopathological subtype distribution is detailed in Table 3, for which 871 tumors were taken into consideration; 2 tumors with meta-type histology were not considered. The differences



PHOTO 1. BCC on thigh.

between percentages of histological types according to location were statistically significant.

In order to compare with international publications, we decided to reorganize our locations. Therefore we ended with 5 site groups:

1. Head and Neck.
2. Trunk (includes trunk and lumbosacral region).
3. Upper limb (arm + forearm + hand + wrist).
4. Lower limb (thigh + leg + foot + buttocks + popliteal area + feet folds + groin).
5. Genitals.

Statistical analysis was performed with reference to the study of Bastiaens et al.,² due that the histopathologic classification was comparable with that of the present study (lobular is equivalent to *nodular*; superficial remains the same; corded is equivalent to *infiltrative*, lobular and corded is equivalent to partly nodular/infiltrative).

Details are shown in Table 4. The differences were not significant by Bonferroni correction.



PHOTO 3. BCC on interdigital fold foot.



PHOTO 4. BCC on back of hand

Discussion

The BCC is the most common cutaneous neoplasia among Caucasians^{3,4}. In spite of the high prevalence of this tumor, there are no epidemiological studies with unified clinical

and histological criteria. BCC cancer registries come from, Finland⁵, Switzerland⁶ and The Netherlands⁷. It most commonly originates in areas of chronic sun exposure. The main features of BCC's types were first described in an American study of Kopf et al., work that included 3,531 cases, with a frequency of 85% for head and neck, with predominance of the nodular form⁸. Dahl et al.⁹ pointed lately the predominance of the superficial type on the trunk area. The presentation in other places such as palms and soles, genital and perianal areas, axilla and nipples do not register estimated percentages due to the low incidence.¹⁰⁻²⁰

Its pathogenesis is strongly associated with prolonged exposure to sunlight, however it has been related to other factors such as dermatitis, chronic trauma, exposure to carcinogenic substances such as arsenic, scars from burns, post-radiotherapy and vaccines²¹⁻²⁴.

This study shows that of 873 BCC in 611 patients, 65.4% were located in the head and neck, and was followed in order of frequency, trunk, lower limbs, upper limbs and the lumbosacral region. Thirty-six tumors (4.12%) were statistically rare since they were introduced at sites that do not exceed 2% in frequency. These tumors were located in the abdomen, forearm, thigh, scrotum, groin, buttocks, feet, vulva, axilla, knee, palm, popliteal area, interdigital feet fold. Series of case studies of BCCs infrequent or unusual localization are difficult to compare due to the lack of consistency in the definition of "infrequent" or "unusual." In the literature of Argentina, the most extensive work corresponds to that published by Di Fabio et al.²⁵, in 1986, who found 17.78% of BCC. These authors defined as unusual site tumors those located in head and neck. In a 6-year period revision, they found a total of 602 tumors, of which 82.22% had cephalic location. The 17.78% which were found in other sites showed the following distribution: 4.2% in the chest, 4.32% on the back, 0.83% in the abdomen, 3.32% in the lumbosacral area, 0.50% in genitals, 2.33% in upper limbs and 2.16% in lower limbs.

In other study, Dagatti et al.²⁶ considered as frequent localization head, neck, trunk and limbs, with 1.12% corresponding to BCC of unusual site (lower lip, axilla, breast, umbilical area, lower abdomen, groins, scrotum, vulva, inter-gluteus fold, and foot lateral edge). None of these studies presents a statistical analysis of data supporting an unusual localization definition for BCC.

In the international literature is worth mentioning the series of Bastiaens et al.². In these, 1711 patients with a total of 2990 tumors were analyzed. The study focuses not only on demographic differences, but also on the histopathologic type. Important differences were observed between the lobular variant (recorded in the literature as nodular), which was more frequent in head and neck, and the superficial variant, which was more frequently observed on women and

at younger ages, with a preferential localization on the trunk (males) and legs (women).

The authors suggest that these two most common types of tumors (lobular and superficial) would be different forms of neoplasia, induced by different causal factors; the lobular form could be the result of chronic exposure, and the superficial form of intermittent exposure to UV radiation. We have taken these cases in consideration to our comparison purposes, because the histological classification used was homologous to that of the present study (lobular is equivalent to nodular, superficial remains the same, corded is equivalent to *infiltrative*, lobular and corded is equivalent to partly nodular/*infiltrative*).

Raasch et al.²⁷ published a series of 5044 patients with 9532 tumors which were analyzed to obtain information about the incidence of BCC by histopathological type and anatomical site. Like the previous study, they found that the superficial forms occur at younger ages and more in women. For all histological types and for both genders the most frequent location was the face followed by the neck. As Bastiaens, they emphasize the occurrence of surface forms, preferably in the trunk in men and in lower limbs in women.

The third series to consider is that of Scrivener et al.²⁸, who recruited 10,245 patients with 13,457 tumors to study variations in gender, age, location and histological type. 78.7% of the tumors were nodular, at a mean age of 66.3 years old in males, while superficial BCCs were more frequent in women at a mean age of 63 years old.

The third series to consider is that of Scrivener et al.²⁸ who recruited 10,245 patients with 13,457 tumors to study variations in gender, age, location and histological type. 78.7% of the tumors were nodular, at a mean age of 66.3 years in males, while the BCC surface were more frequent in women at a mean age of 63 years. The morpheiform variant was also more common in females. The latter, together with the nodular type, was located preferably in cephalic extremity. The trunk was the most frequent area for the superficial variant (mostly men) while women with predominant superficial forms were located in the cephalic extremity. 0.2% of the cases were located in the genitals.

The most recent study published in Argentinean literature is from the German Hospital in Buenos Aires, where 125 patients with 222 lesions were analyzed. They found a male/female ratio of 1.4:1, a predominance of skin type II and III, and a distribution that differs slightly from that found in our study (head and neck 46%, of which 53.6% corresponded to infiltrative subtype, trunk 27%, of which 54.3% corresponded to superficial forms, and limbs 17%, in which the infiltrative variant was present in 39.4% of cases)²⁹. This study we observe that 65.4% of tumors were located in head and neck and which 68.2% were nodular. Followed in order of frequency by the trunk with 20.7%, of which 50.8% were superficial.



PHOTO 5. BCC on palm of hand



PHOTO 6. BCC on Vulva

Analyzing each anatomical area in particular, we see that the frequency of carcinomas on lower limbs ranges between 1.5 to 13.5% according to various authors³⁰. Pearson et al., in a study involving 4,336 patients with BCCs in various locations, found 89 women (4.9%) and 33 men (1.3%) with



PHOTO 7. BCC on inguinal fold.



PHOTO 8. BCC on inguinal fold.

BCCs in the lower limbs. Other authors also mention this statistically significant predominance in women. The causes are attributed to a higher sun exposure with cosmetic purposes and changes in their clothing habits^{30,31} (**Photo 1**). Other factors include chronic venous stasis and ulcers³²⁻³⁴. Most authors agree that the most common histological subtype is superficial. Deserves a special mention the presence of BCC in feet (**Photo 2**). The few related articles, mention BCC located adjacent to the nails, with often being clinical aspects resulting in being underdiagnosed. BCC is around 4 times more frequent in fingers than in feet, and has a slight predilection for males. Interdigital location is the least frequent^{35,36} (**Photo 3**). Ulceration variant of presentation would be most frequent³⁷⁻³⁹. In our study, the percentage of BCC in lower limbs was 44/873 (5%). Histopathological variants were similar for superficial (34.1%) and nodular (31.8%) and in less proportion for partly nodular/infiltrative (22.7%) and infiltrative (11.4%) (**Table 3**). We found 4.4% of tumors located in the upper limbs. Localization in hands is very rare (less than 1% of the BCC), considering chronic sunlight exposure as the main etiological factor in its development (**Photo 4**). Two works belonging to de Vandeweyer and van Zuuren, analyze cases of BCC on the dorsum of the hands on 7 and 11 patients respectively^{40,41}. There, BCC presented as ulcers of chronicle evolution and slow growth. In some patients, prior radiation stands as another triggering factor for BCC and other malignant lesions⁴¹. The localization in palms is extremely rare, and they are generally part of the nevus basocelular syndrome⁴² (**Photo 5**). Palms BCC have been often observed together with traumatic factors, considered as triggers, as in our study, where the patient reported a history involving repeated local trauma from the use of dental instruments. The literature also describes BCC located in the fingers with a predilection for the periungual area, presenting with ulceration in more than half of patients (MS 4.43). Our study shows that 4.4% involving the tumors were located in the upper limbs (arm 18, forearm 15, 4 hand, palm 1). The histopathological type was prevalent nodular (39.5%).

In the genital area BCC was found in the penis, scrotum, vulva, anal and perianal regions (**Photo 6**)⁴⁴. In a large survey of histopathology study by De Giorgi et al.⁴⁵, 63/3.604 vulva cases with an average age of 70.35 years old and an average size of 21cm were found. Similar results were found in a study on 51 patients conducted by Gibson et al.¹⁴, with 0.27% of genital location (perianal, pubic area, vulva, scrotum and penis), an average age of 73 years old and average size of 1,95 cm. This study emphasizes that the search for HPV (serotypes 6, 11, 16, 18, 31, 33, 51) was negative, and that advanced age and local trauma may contribute to the development of BCC. In our study, we present 5 cases, 3 in the scrotum and 2 located in the vulva (frequency: 0.6%).

TABLE 3. BCC Distribution by histopathologic subtype ($\chi^2=293,897$; $P<0,0001$).

	Superficial	Lobed	Corded	Lobed and corded	Total (by location)
Head	25 (4,4%)	388 (68,2%)	26 (4,6%)	130 (22,8%)	569 (65,4%)
Face	21	354	22	117	514
Neck	3	18	3	7	31
Scalp	1	16	1	6	24
Trunk	92 (50,8%)	70 (38,7%)	5 (2,8%)	14 (7,7%)	181 (20,7%)
Back	47	34	2	7	90
Torax	33	32	3	7	75
Abdomen	12	4	-	-	16
Lower limb	15 (34,1%)	14 (31,8%)	5 (11,4%)	10 (22,7%)	44 (5%)
Thigh	5	4	1	-	10
Knee	-	-	-	2	2
Leg	9	10	4	6	29
Foot	1	-	-	2	3
Upper limb	11 (28,9%)	15 (39,5%)	3 (7,9%)	9 (23,7%)	38 (4,4%)
Arm	5	5	3	5	18
Forearm	6	8	-	1	15
Hand	-	2	-	2	4
palm	-	-	-	1	1
Lumbosacral	8 (33,3%)	10 (41,7%)	-	6 (25%)	24 (2,7%)
Folds	-	6 (85,7%)	-	1 (14,3%)	7 (0,8%)
Groin	-	2	-	1	3
Popliteal fossae	-	1	-	-	1
Axilla	-	2	-	-	2
Interdigital feet fold	-	1	-	-	1
Genital	1 (20%)	2 (40%)	-	2 (40%)	5 (0,6%)
Vulva	-	1	-	1	2
Scrotum	1	1	-	1	3
Gluteus	-	2 (66,7%)	-	1 (33,3%)	3 (0,3%)
Total (by histologic subtype)	152 (17,5%)	507 (58,2%)	39 (4,5%)	173 (19,9%)	871

TABLE 4. Comparison with Bastiaens's series.2

	Author	Infiltrative (corded)	Nodular (lobed)	Partial N/I (lob and cord)*	Superficial	p**
Head and neck	Bastiaens et al.	163	1280	443	74	$\chi^2=9,28$
	Abeldaño y cols.	26	388	130	25	$p=0,0258$
Trunk	Bastiaens et al.	16	254	57	281	$\chi^2=0,5431$
	Abeldaño y cols.	5	80	20	100	$p=0,90$
Upper limb	Bastiaens et al.	3	42	12	28	$\chi^2=2,5666$
	Abeldaño y cols.	3	17	9	11	$p=0,46638$
Lower limb	Bastiaens et al.	11	58	26	61	$\chi^2=2,3504$
	Abeldaño y cols.	5	20	12	15	$p=0,5029$
Genitals	Bastiaens et al.	-	2	-	1	
	Abeldaño y cols.	-	2	2	1	

*Includes nodular and partly nodular/infiltrative others. ** Not significant by Bonferroni's correction

7 cases involving folds were found and distributed as follows: 3 on the groin, 2 on the armpit and 1 on the interdigital feet folds (**Photo 7-9**). There was a clear predominance of the lobular type (85.7%). The development of BCCs on

axilla has been described before^{16,46-47} on patients with a history of other skin tumors on photoexposed, basal cell nevus syndrome or radiotherapy. In our patients we have not detected triggering factors.



PHOTO 9. BCC on popliteal space.

Conclusions

The present series allows to defined as uncommon sites areas such as abdomen, forearm, thigh, hand, scrotum, groin, buttocks, feet, vulva, axilla, knee, palm, popliteal space and foot interdigital fold. Similar to what has been published national and internationally, BCC were predominant on head with predominance of nodular forms and on trunk with predominance of superficial forms. Statistically significant differences were found between the percentages of histological types according to their location. These results support the hypothesis that there is a relationship between histological type and localization of the lesions. However a larger number of cases would allow to draw conclusions with greater reliability. We may infer further that the presence of BCC in unusual anatomical areas and many of which are not subject to sun exposure involves other oncogenic factors related to the biological behavior of BCC.

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