Case Report

A Rare Case of Neglected Giant Basal Cell Carcinoma in a Nurse-Case Report and Literature Review

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ABSTRACT: Basal cell carcinoma (BCC) is the most common skin cancer in the fair-skinned adult population over 50 years of age and the incidence is rising. Generally, BCC has an indolent course, low mortality and a good prognosis due to low rates of metastasis. Giant basal cell carcinoma is a rare reported oncological entity which accounts for 0.5% to 1% of all cases of BCC and has a diameter larger than 5cm. Basosquamous carcinoma is a rare high-risk type of BCC with clinical and histopathological features of both BCC and squamous cell carcinoma. A 61-year-old female presented to our clinic for a giant bleeding tumor located under her left breast. She initially noted the tumor almost 15 years ago. Although the patient was a nurse, she was afraid to seek medical advice until an episode of significant bleeding. At presentation the tumor was a 15/7cm in size, was invading the underlying structures and had a central ulceration. The margins of the tumoral plaque had several nodules and pearly structures suggesting the possible clinical diagnosis of BCC.

KEYWORDS: *Basal cell carcinoma, giant basal cell carcinoma, basosquamous carcinoma.*

Introduction

Basal cell carcinoma (BCC) is the most common skin cancer in the fair-skinned adult population over 50 years of age and the incidence is rising.

Generally, BCC has an indolent course, low mortality and a good prognosis due to low rates of metastasis.

Although metastasis is rare, BCC tends to be locally invasive and, as a result of neglect, can progress to a locally advanced tumor.

Before lesions extend, bleed or invade the underlying tissue, they are usually asymptomatic [1-3].

Cumulative exposure to ultraviolet (UV) radiation is involved in the pathogenesis of BCC so it tends to appear on sun-exposed areas [4].

An independent risk factor is age, the incidence rate of basal cell carcinoma doubles from 40 to 70 years of age.

Men have higher BCC rates than women (1.5-2 to 1) [5].

Clinically and histopathologically, BCCs present various subtypes: nodular (the most common subtype with a predilection for the neck and head), superficial (second most common subtype), fibroepithelioma of Pinkus (an uncommon, indolent subtype with a predilection for the trunk), infundibulocystic (well-circumscribed pearly papules), morpheaform (lesions with aggressive biologic behavior), infiltrative (poorly defined, indurated plaque), micronodular (subclinical extension and higher recurrence rates due to their multifocal nature) and basosquamous (neoplasms that have histologic features of both BCC and squamous cell carcinoma) [6-8].

In a small number of cases, tumors are larger than 5cm and they are termed as giant basal cell carcinomas (GBCC).

This rare subgroup is associated with an impaired quality of life and a higher risk for local or distant metastasis [9].

A written informed consent was obtained from the patient for this publication.

10.12865/CHSJ.48.03.13

Case Report

A 61-year-old female presented to our Dermatology Department for a giant bleeding tumor located under her left breast.

She initially noted the tumor almost 15 years ago.

Although the patient was a nurse, she was afraid to seek medical advice until an episode of significant bleeding.

At presentation the tumor was a 15/7cm in size, was invading the underlying structures and had a central ulceration.

The margins of the tumoral plaque had several nodules and pearly structures suggesting the possible clinical diagnosis of BCC.

The infected, heavily bleeding tumor, was covered by a yellow, foul smelling discharge (Figure 1).

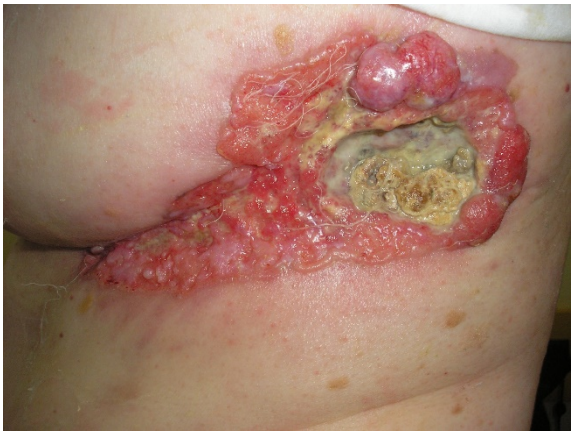

Figure 1. A giant bleeding tumor with central ulceration and several nodules and pearly structures in the periphery, covered by a yellow discharge, located under the breast.

Blood tests showed chronic anemia and inflammatory syndrome.

On the chest X-ray there was no involvement of the bony structures.

The patient was treated with systemic antibiotics (Cephalexin 2g IV daily and Metronidazole 1.5g PO daily).

We performed two biopsies, one fragment from the pearly margin and one from the nodular margin, and referred them to the Histology Department.

The histological exam of the first biopsy showed features of a nodular BCC: relatively circumscribed basaloid lobules with nuclear palisade at the periphery and small areas of adenoid differentiation, with a pseudo glandular pattern of the basaloid cells (Figure 2).

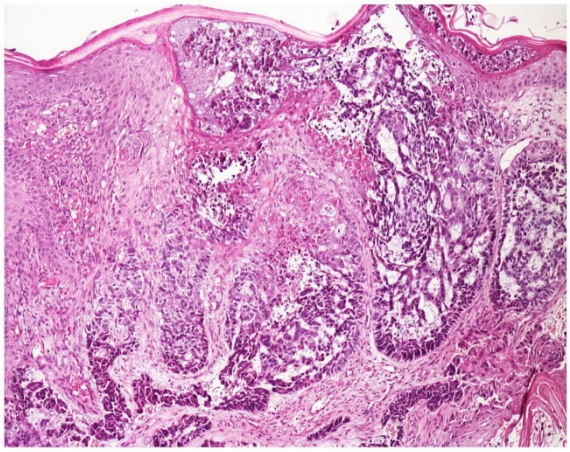

Figure 2. Nodular BCC and small areas of adenoid differentiation (HEx40).

The second sample showed a biphasic tumor with foci of squamous differentiation which are features of a basosquamous carcinoma (BSC) (Figure 3).

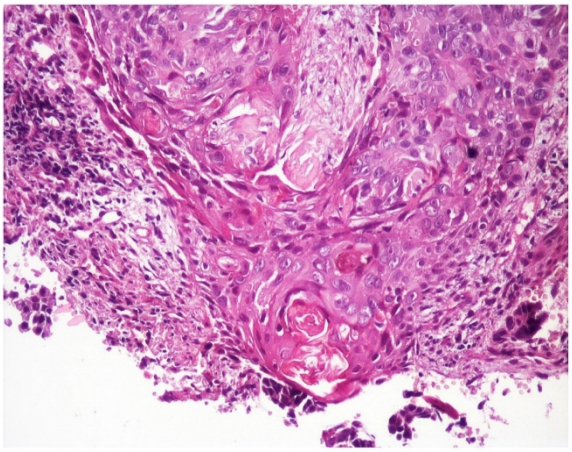

Figure 3. Basosquamous carcinoma- a biphasic tumor with foci of squamous cell differentiation (HEx100).

The patient was referred to the Plastic Surgery Department where a large surgical excision was performed with subsequent skin grafting.

The histological exam of the excised tumor confirmed the diagnosis noted on the initial biopsy.

The margins of the surgical piece were free of tumoral cells.

The patient was reexamined at one month (Figure 4) and at three months after the surgical excision.

Gradually, we observed the reduction of inflammation and the favorable course of wound healing.

To date, the patient has a good prognosis with no signs of local recurrences.

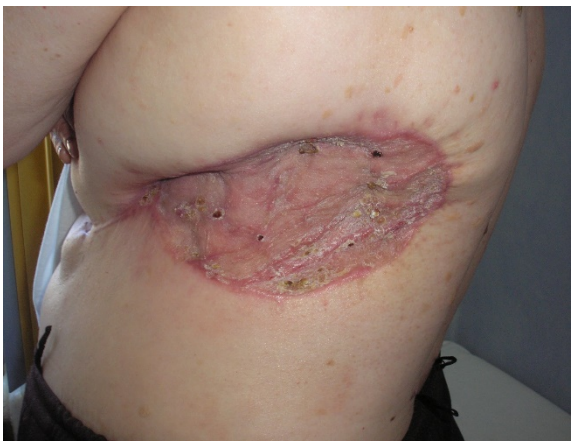

Figure 4. Appearance of the wound one month after the surgery with epidermal skin graft application.

Discussions

BCC is the most frequent malignancy worldwide and its hallmarks are the absence of distant metastasis and a less aggressive behavior.

Regarding the aggressive subtypes, although the perineural invasion is well documented, intravascular invasion has rarely been reported in literature [10].

On the contrary, GBCC is a type of BCC which is characterized by the development of metastasis and aggressive biological behavior with involvement of extra dermal structures such as muscle, cartilage or bone.

Therefore, it usually has a poor prognosis.

In the literature, GBCC is a rare reported oncological entity which accounts for 0.5% to 1% of all cases of BCC and has a diameter larger than 5cm.

These tumors are classified as T3 according to the TNM classification.

Considering the diameter, the rate of metastasis increases by 45% if the tumors are equal to or greater than 10cm, which is the case of our patient.

In a study conducted by Vaca-Aguilera et al., which included a number of 115 GBCC, the tumors had an average size of 6.6cm, with the largest measuring 15cm.

In other studies, the mean size was 14.77cm, including tumors of 40cm.

The subtypes of BCC which have a size greater than 20cm are reported in the literature as “super giant” [11].

Usually, this presentation is due to patient neglect, resulting in a continuous tumor growth over a time span of 10 to 20 years.

Other risk factors include inadequate treatment of smaller tumors and chronic alcoholism.

The average age of patients presenting with this type of BCC is 67 years.

Similar to our paper, Olde et al. reported a case of a GBCC in a 60-year-old man located on the left flank.

The tumor started to ulcerate 10 years before presentation and slowly progressed over time up to 30/15cm [12].

In general, BCCs are located on sun-exposed areas such as head and neck, with only 10% of cases located on the trunk.

These lesions cannot be easily ignored by the patient so they seek medical advice earlier in the course of the disease.

On the other hand, GBCCs are more frequently found on unexposed areas, where self-evaluation is difficult to perform and they are often neglected by the patient, such as the case of our patient.

Therefore, UV radiation is not the main cause in GBCC pathogenesis.

Archontaki et al. analyzed 51 cases of GBCC and found that the main predilection area was the trunk, followed by the face and upper extremity.

Other authors highlighted that the tumor was located on the trunk in all reported cases.

In contrast, other studies showed that the most common localization (63% of cases) was the region of the head and neck, followed by the trunk (28% of cases) and extremities (8% of cases) [11,13].

Previous studies showed that there is a link between GBCC and invasive histological subtypes such as BSC and morphea form.

However, the metastatic potential of GBCC is due to the size of the tumor rather than the histological subtype.

In this study, the histological diagnosis of BSC was obtained not only from biopsy but also from surgical excision.

Regarding histopathological variants of GBCC, a previous study showed that the high-grade variants were observed in 51% of cases and the low-grade variants in 49%.

Among the high-grade subtype, the infiltrating form was the most frequent (42%) followed by BSC (19%) [14-16].

BSC is a rare high-risk type of BCC with clinical and histopathological features of both BCC and squamous cell carcinoma (SCC).

In 1894, Beadles made the first description of this tumor as a type of rodent ulcer [17].

The most common clinical presentation of BSC is a long-standing nodule that progressively becomes ulcerated.

10.12865/CHSJ.48.03.13

Unlike our case, this tumor usually arises on sun-exposed areas [18].

Due to its potentially aggressive biologic behavior, the early diagnosis of this tumor is important and biopsy with histologic examination are the gold standard diagnostic method.

According to other authors, BSC is characterized by a more aggressive behavior than BCC, with a higher potential for recurrence, metastasis and tumor growth.

According to the literature, the frequency of metastasis in BCC ranges from 0.0028% to 0.55% of all histologically diagnosed BCCs.

Compared to other BCC subtypes, BSC has an increased risk of metastasis with a frequency of up to 5% of cases.

The metastatic capacity is more similar to SCC, therefore BSC is associated with a worse prognosis than BCC [19].

Regarding the metastatic capacity of BCC, squamous differentiation is known as a key component.

Farmer et al. reported important squamous differentiation in nearly all of their cases of metastatic BCC (15 out of 17) and, furthermore, they noticed a progressive increase in squamous differentiation in those cases which presented recurrences prior to metastasis [20].

On the contrary, Domarus et al. noticed that less than 15% of metastatic BCCs expressed squamous differentiation [21].

Another study, conducted by Laga et al. supported these conclusions and reported squamous differentiation in only two out of eleven cases of metastatic BCC [22].

The therapeutic strategy used for GBCCs is an important prognostic factor.

The main option is a wide surgical excision with free margins, frequently combined with flaps or grafts, which plays a role in obtaining a low local recurrence rate and longer survival.

Mohs micrographic surgery (MMS) allows, in the course of the surgical procedure, histological margin control with a cure rate up to 99%.

Therefore, this technique is more appropriate for high-recurrence risk cancers and is an alternative to conventional surgery in this case [23].

Radiation therapy and topical chemotherapy are reserved for elderly patients or those who are not eligible for surgery [24].

In cases of advanced BCCs where radiotherapy and surgery are inappropriate, Hedgehog pathway inhibitors (HhIs) gained EMA approval.

Vismodegib and Sonidegib has similar tolerability and efficacy profiles [25].

Oudit et al. conducted a study over a period of 20 years which included a number of 43 cases of GBCC and highlighted the association between local recurrence of these tumors and the therapeutic strategy.

Of the 43 patients, they related 2 deaths: one treated by Vismodegib after unsuccessful surgery and one before treatment.

Regarding the other 41 patients, 19 were treated by surgery, 15 were treated by photodynamic therapy (PDT) and 7 by radiotherapy.

There were no recurrences reported in the group treated by surgery, although none of the cases had a surgical margin larger than 1cm.

Therefore, in contrast to other studies, they concluded that 1cm is an eligible margin for the excision of GBCCs, 10 of the 23 patients treated with PDT had recurrent GBCC.

Radiotherapy was reserved for elderly patients and superficial histological subtypes.

Of the 7 patients treated by radiotherapy, only one patient had a recurrence [15].

Wruhs et al. reported a case of a GBCC which metastasized to the lung and was successfully treated with Vismodegib.

After 12 months of therapy, complete remission was achieved in both clinical and radiological terms [26].

Conclusions

GBCC is a rare and aggressive type of BCC.

Such giant lesions usually develop in patients that combine negligence with fear of medical procedures.

However, in our case, this type of behavior was unexpected for someone working in a hospital environment.

Since the tumor is usually non-painful, the patients postpone seeking medical advice for many years, in our case almost two decades, and they finally present for complications like infection or uncontrolled bleeding.

Our patient needs close follow-up due to the aggressiveness of the histological subtype.

Conflict of interests

None to declare.

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 10.12865/CHSJ.48.03.13