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Negative surgical margin before reconstruction in the treatment of advanced nasal basal cell carcinoma: An oncologic point of view

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Abstract---25% of basal cell carcinoma (BCC) occurs in nose. The recently accepted treatment includes wide excision with safety margin of 4 mm of clinically normal skin. 3 major points in the treatments are clearance, cosmetic and functional value. Often, due to its central location and delicacy of the surrounding tissue makes it hard to achieve standard surgical margin for lesions located in nose. The size and the depth of the lesion may complicate therapy. These 3 cases reporting large lesion BCC treated with multiple wide excisions before underwent reconstruction. Case 1 and 2 had 3 and 4 time excisions due to failure of gaining negative margin in the previous surgeries. Multiple surgeries were preferred for although it delayed reconstruction, from oncologic point of view it is principle to accomplish perfect clearance of the tumor. Recurrences do not happen on big percentage of cases with positive margin, but may lead to even more complicated reconstruction that compromises patient health. The 2 cases gave satisfactory results with no recurrence within 3 years after surgery. Even, in case 3 where early reconstruction needed and more complex surgeries were not possible (due to old age, covid era, and socio-economic limitations) we can still achieve maximum result by not rushing the perfect reconstruction. Case 3 showed closure of the defect using skin graft also gave proper result. Conclusion in this case is Without sacrificing cosmetic and functional value, oncologic fundamental rule in BCC treatment which is clearance, is possible to achieve and need to always be prioritized.

Keywords---basal cell carcinoma, nasal BCC, surgical margin.

Introduction

Basal cell carcinoma (BCC) accounts for more than 75% of non-melanoma skin cancer. It is a neoplasm that comes from non-keratinizing cells originate for the basal layer of epidermis. BCC is slow growing, rarely metastasizes yet tends to be very invasive to local structures. Relapse are not uncommon after treatment. BCC is more common in men and it happens a lot more often with aging. The main predilections of BCC are areas which are highly exposed to sunlight. 80% affect head and neck area and around 30% located in nose (Bertozzi N, Simonacci F, Grieco MP, Grignaffini E, 2019). Other factors such as genodermatotic, immunosuppression and carcinogenic exposure are known to be related to increased incidence of BCC. Mortality is low in this type of cancer (less than 0.1% of all cancer deaths) but functional and cosmetic value may severely damaged (Ciażyńska *et al.*, 2018).

There are some morphological classification of BCC; 1)nodular (with micronodular), 2)infiltrative (with morphoeic), 3)superficial and 4)mixed subtype, with nodular subtype accounts for majority of BCC. At early stages, BCC manifests as a small plaque or a papule layered with telangiectasias. Some crust over a delicate wound that bleeds during shaving and hardly heal can be found. The aggressive form of nodular type is the micronodular form which usually grayish in color and more rarely seen as ulcer compared to the nodular BCC. The infiltrative and morphoeic type may cause extensive destruction of surrounding structures and may take place in nasolabial folds, angle of an eye or around the ears. This lesion usually has no clear border. Morpheaform subtype often looks like scar tissue with depressed structure. Superficial subtype seen as erythematous macule with clear border and central clearing. Pain is not a common complain among the patients unless it is an infiltrating tumor. Recurrence is high particularly for those with large lesions over 20 mm with central location in the face (periocular, perioral, nasal), history of recurrence, and morphoeic and micronodular histological subtype. Previously, it had been shown that more aggressive histological growth was associated with increased subclinical extension, indicating that more aggressive tumors require larger surgical margins to be eradicated. Recurrences between 5% and 14% are evident when tumors are completely excised (Mackiewicz-Wysocka *et al.*, 2013).

There are three main things that need to be put in concern in the treatment of BCC which includes: (1) clearance which means to excise the lesion completely in order to prevent recurrence in the future, (2) to prevent any functional disturbances as a result of tumor excision, and (3) to provide the best possible cosmetic outcome, especially for large lesions on the central facial. Complete surgical excision of the tumor can be achieved either with safety margins or with micrographic control. The purpose is to avoid progression or recurrence which may lead to further tissue destruction and complicated treatment. The management of basal cell carcinomas with positive margins remains controversial, with an important dilemma: to surgically enlarge the lesion immediately or to opt for the observation and follow-up of these patients reserving

the treatment in the event of subsequent clinical recurrence of the neoplasia (Drucker *et al.*, 2020).

The currently accepted treatment of basal cell carcinoma is an elliptical excision with a 4-mm surgical margin of clinically normal skin. But a 4-mm surgical margin is often not possible because of cosmetic and functional constraints on the face. Therefore, for small, well-defined, pigmented lesions, and lesions located in more cosmetic and sensitive areas, a narrow safety margin is recommended. But often, due to its central location and delicacy of the surrounding tissue makes it not so easy to achieve standard surgical safety margin in those lesions located in nose. The size as well as the depth of the lesion may complicate its therapy (Quazi *et al.*, 2020). The choice of the best treatment should be individualized, considering factors that may influence the prognosis of basal cell carcinoma, such as tumor size, location, histological type, definition of compromised margin and clinical conditions of the patient (Lara, Eduardo and Melo, 2017).

Case

This study reporting 3 cases of BCC with large lesions which were treated with multiple wide excisions to finally achieve adequate negative margin before underwent reconstruction. Case 1 and 2 reporting female patients age 55 and 49 with BCC, both work as farmers.

Case 1



Figure 1 Case 1. Patient complaint of extensive ulcer on the nasal bridge. In the beginning it was a nodular growth which was black in color. The lesion was getting larger over time, easily bleed and sometimes itchy. There was no pain, difficulty of breathing, swallowing or abnormal discharge going out of the lesion. No history of trauma, weight loss, similar lesion on the other part of the body and no significant family history. On physical examination, vital signs were stable.

Local examination found ulceration 6x4 cm in size extended from inferior 2/3 of dorsum nasi to the upper labia oris. No active bleeding or palpable lymph nodes were observed

Case 2



Figure 2. Case 2. Patient complaints of ulceration which grown from nodular lesion that kept growing over lateral edge of right ala of nose, brown and black in colour, a little bit tender and bleed on touch. Patient with history of hypertension since the last 15 years with regular medication and no history of similar lesion before or in the family. On local examination, there was 8x6cm lesion extending from right side of the nose to the right medial canthus. Neither active bleeding nor palpable lymph nodes found on clinical examination

Patients were educated about the disease and the possible treatment they might receive. Informed consent were gained and patients were planned for wide local excision followed by rotational flap and skin graft. Excision were done with reassurance that it covered 5 mm of clinically healthy area that was free of telangiectasia, ulcer or sclerotic plaques which were common macroscopic form of BCC. However, when pathologically analyzed, the margins were still positive for BCC. Each of the cases had 3 to 4 times excisions due to the failure of gaining negative margin in the previous surgeries. Besides, microscopically oriented histographic surgery, also known as MOHS surgery that can achieve clear margin and clear depth in one time surgery possible was not available in our hospital. That was why this multiple surgeries were preferred for although it postponed the reconstruction surgery, from oncologic point of view it is principle to accomplish perfect clearance of the tumor. Recurrences of BCC even though do not happen on big percentage of total cases with positive margin, are still very possible and will lead to even more complicated reconstruction that will compromise patient health physically and mentally.

In these 2 cases, full thickness defect were found, led to complexity of reconstruction. For these defects, it was best to re-create anatomy of the nose by reconstructing in three layers; lining, nasal architecture and skin coverage. Lining was needed to accommodate multiple grafts necessary to rebuild the nose. In most circumstances including in these cases, forehead skin was enough to manage the total nasal defect since it's thin, supple and well vascularized. Costal cartilage and calvarial bone grafts were used for adequate restoration of contour

and support. These stages can be seen clearly in case 3. Finally, closure using skin graft from thigh were performed.

In case 1, since the defect reached more than 2/3 of the upper lip with an intact oral commissure, full-thickness flap now known as Abbe flaps was performed. Following closure, a period of wound contracture was allowed to minimize the size of the defect. The Abbe flap pedicle is the superior or inferior labial artery, originating from the facial artery just lateral to the oral commissure. After went through all these steps of treatment, all cases gave satisfactory results and there were no recurrence happen within 3 years after surgery.

Case 3 shows another form of nodulo-ulcerative type of BCC occurred in women age 69 working as a fisherman with comorbid of hypertension and type 2 diabetes. The difference to the previous 3 cases was that this case uniquely proved that despite the temptation for simpler reconstruction for complicated large lesion located in the H region of the face, surgeon should never put the oncologic point of clearance aside. In this case 3 proved that even in cases in which early reconstruction is needed where more complex surgeries are not possible (due to old age, comorbid factors, covid era, and socio-economic limitations) we can still achieve maximum result by not rushing for perfect reconstruction.



Figure 3. Case 3. Shows closure of the defect using skin graft also gave proper functional and cosmetic result

Results and Discussions

The exact cause of BCC is unknown until now. Basal cell carcinoma usually occur in men, and the ratio of male to female was 1.6 : 1. This higher incidence can be caused by occupational exposure to the sun (Bertozzi N, Simonacci F, Grieco MP, Grignaffini E, 2019). In our study, not as commonly described on literature, we found that all of the four patients were female. However each of them had intense history of sun exposure; 2 were farmers, 1 was fisherman while other one was a gardener.

Once the definite diagnosis of BCC is confirmed, the next thing to be planned is tumor eradication by correlating tumor characteristics with patient's age, medical history, social history, and cosmetic expectations. Treatments involving standard surgical excision, Mohs micrographic surgery, nonsurgical ablation, and topical chemotherapy. All these modalities also related to different recurrence rate. Based on one study, surgical excision have the highest recurrence rate (10.1%) compared to radiation therapy (8.7%), curettage and electrodesiccation (7.7%) and cryotherapy (7.5%). Mohs micrographic surgery have the lowest incidence of recurrence which is 1%. In our study we used the standard recommended treatment of BCC which is wide excision (Jadotte *et al.*, 2013).

BCCs can be divided into several subtypes: superficial, nodular, pigmented, morphea like, and basosquamous. To determine the extent of lesion macroscopically is quite a tricky process. However, there are early and late signs to know on each type of lesion that will guide surgeons on making adequate clearance or excision for the treatment. The early form of nodular type BCC which is the most common type of BCC, cystic, pigmented, keratotic and flesh colored with telangiectasis are the gross features we may observed grossly which on later stage can cause ulcerations. In the superficial type, lesion is erythematous and well-circumscribed, often seen as elevated plaque or discrete scaly macule. In micronodular type, usually it is non ulcerative with well-defined margin. In morpheaform or infiltrative type, classic features include plaques that firm in consistency and rarely ulcerates. Margins are not clearly defined as tumor infiltrates the dermis in between the fibrous collagen. The extent of the tumor is usually not apparent on clinical examination and may result in positive caving saving. This may explain what makes excision is not always simple for BCC, especially for the aggressive type. From all these distinct biologic behaviours, it is concluded that safety margin should included clinically normal skin that was free from these distinctive features. 4 mm surgical margin eradicates well-defined primary BCCs of less than 2 cm in 95% of cases. It has been demonstrated that a in facial nodular BCCs of less than 1 cm in diameter removed via standard excision with 1-, 2-, and 3 mm margins lead to positive margins in 16%, 24%, and 13% of tumors, respectively (Mackiewicz-Wysocka *et al.*, 2013). In our cases, we have already performed the standard safety margin in the first wide excision. However, positive margin was still detected led to multiple surgeries to finally achieve the edge that was free of tumor. High risk lesions that depends on the size of the lesion, subtypes, site, history of recurrence which counts as high-risk lesions should be considered in the surgical planning of patients with BCC because it related directly to the cure rate (Mackiewicz-Wysocka *et al.*, 2013).

In cases where pathologic examination shows involved resected margins, ones study recommend re-excision. This is due to the reported recurrence rates for incompletely excised BCC is known to be more than 80%. Studies proved that curettage prior to excision to delineate tumor margins as it has been shown to decrease surgical failure rate by 24% in BCC and is routinely performed by most dermatologic surgeons. In advanced disease, especially those in complicated area as explained in these cases, the temptation to conserve tissue on the face while removing BCCs may lead surgeons to employ inadequate margins, resulting in margin positivity during standard excision (Chiller *et al.*, 2000).

It has been stated in a study that with standard excision the pathologically reported incomplete excision rate was higher than 10% and was significantly associated with the location on the face, particularly on the nose and inner canthus, and with infiltrative and multifocal histologic types. When it is incompletely excised, the chance for it to recur is between 12% to 41% of the time. Studies found greater outcome in Mohs micrographic surgery compared to standard re-excision. Some authors agreed that the only way to make sure that there is no tumor persistence in the event of positive margins is to re-excite and prepare serial sections of the specimen to identify residual tumor.⁹ We applied this principle in our 4 cases for the best treatment result and prevent more complicated reconstruction in the future.

A study conducted by Sarma et al described 3 cases of residual tumor among 43 patients with positive caving saving. Similar studies found incidences of residual tumor ranging from 7% to 45%. This study comes to the conclusion that conventional histological approaches in non-aggressive BCC resected with 2 mm lateral margin have a sensitivity of 44% for detecting residual tumor. It indirectly said that negative margin found in 56% of the tumors that actually have involvement of the abnormal margins (Robinson and Fisher, 2000). Another study by Wolf and Zitelli and Breuninger showed 30% positive margins in total cases underwent excision with 2 mm safety margin. However, only 44% of this 30% will be detected by the normal histological study. In other words, 17% of the tumors resected according to these criteria can be falsely identified as having tumor-free margins while it is actually not (Beiraghi Toosi, Mohamadian Roshan and Ghoncheh, 2017). Looking at this possibility, in our cases we chose to keep the margin as safe as possible before then optimizing the functionality with the provided structures.

The goals of nasal reconstruction are to gain satisfactory aesthetic outcomes while preserving its function. Nasal structure is reconstructed in layers: lining, nasal architecture, and skin coverage. In most of the conditions, the ala and sidewall need to be supported with cartilage to avoid nasal valve collapse. In full-thickness defects, it is necessary to re-create the anatomy of the nose by reconstructing in three layers: lining, nasal architecture, and skin coverage (Austin and Shockley, 2016). In the reconstruction of total or subtotal nasal defects, lining is a critical matter. If it not under special and rare circumstances, there is usually enough forehead skin to manage a total nasal defect, as well as sufficient bone and cartilage grafts, even if nasal septum and ear cartilage have been depleted. The source of lining must be thin, supple, and well vascularized.

The lining tissue also needs to accommodate multiple grafts necessary to rebuild the nose (Chiller *et al.*, 2000).

Another important point in nasal reconstruction is to achieve and maintain support of the soft tissues to prevent functional damage such as nasal obstruction and also to lower the risk of contraction and migration of the reconstructed nasal segments. For example the non-anatomic placement of cartilage grafts in the alar and supra-alar region in order to repair the shape of the ala subunit while at the same time avoiding alar collapse as well as retraction. In reconstruction of total or subtotal nasal defects, there might be necessities to take costal cartilage or calvarial bone grafts for giving back proper contour and support although mostly in nasal defects septal and/or conchal cartilage are enough for reconstruction (Weathers *et al.*, 2013).

For superficial defects, a skin graft may be the best choice and prevent additional incisions in the therapy. But for more advanced defects, a two or three- staged interpolated flap gives better result. The subunit principle is applied when using interpolated flaps in locations with inherent convexity such as the nasal tip and ala. Many surgeons feel that local flaps provide a superior result to full-thickness skin grafts. However, it is known that skin grafts provided aesthetic outcomes comparable to those of local flap procedures in properly selected nasal defects. In our case we found that closure of the defect using skin graft did meet adequate functional and cosmetic value even for patients with advanced BCC lesion (Weathers *et al.*, 2013).

Conclusion

The anatomic site, size of the tumor, and histologic features determine management of BCCs. Advanced disease even though does not commonly related to risks or mortality, when present, is associated with significant morbidity. That is why selecting an effective and appropriate initial treatment modality for BCCs to ensure eradication of the tumor is mandatory. Without sacrificing the cosmetic and functional value, oncologic fundamental rule in BCC treatment which is clearance, is possible to achieve and need to always be put in concern.

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