New Typology of the Basal Cell Carcinoma: a clinical review

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Abstract:

Background

Metatypical cell carcinoma (MTC) is a new entity of skin cancer. It represents an intermediate type between basal cell carcinoma (BCA) and squamous cell carcinomas (SCC). The behavior of the metatypical cell carcinoma lies between these two varieties of skin cancer. The differential diagnosis can not be made depending on morphological and clinical features, so histological examination is mandatory.

Methods

It is a retrospective study carried out on of 120 patients with metatypical skin cancer who were treated by surgery, radiotherapy and chemotherapy.

Results

It was found, that more males (62.5%) are affected with MTC than females (37.5%) with predilection for cervicofacial areas (71.7%), then the trunk (10%), the limb (9-6%), the scalp (3.7%) and other regions (5%) **(Table 1).** The disease recurred in 12 cases (10%) mainly in head and neck areas.

Conclusion

In this study, I have focused on the importance of differential diagnosis and specific treatment of MTC, even though more clinical studies and long-term follow up are needed before establishing specific guide lines.

Introduction

Non-melanoma skin cancers "BCC and SCC" are the most common types of cancer. Each year 1.3 million new cases are diagnosed and treated worldwide **[1]**. Non-melanoma skin cancers comprise different tumors, 95% of which consist of BCC or SCC **[1, 3].** The cause of non-melanoma skin cancers is still multifactorial even with the advances in molecular genetics which localized many causative mutations. Environmental factors including ultraviolet radiation (UVR) and lifestyle factors together with the aging, certainly play an important role in the onset of a tumor **[3].** Although skin cancers are more common in Caucasians, they are also prevalent those people with a dark complexion (e.g. African-Americans) **[1, 3].** Basal cell carcinoma occur more on the head and neck, and other sun exposed areas, whereas SCC has a strong relation with age (i.e. > 40 years), and UVR exposure **[9].** They commonly develop on non-facial sites with tendency to occur in sun-exposed areas **[5].** Both BCC and SCC may also develop on non-sun exposed areas **[4].**

Basosquamous carcinoma, which is also known as MTC, is a non- melanoma skin cancer that has the features of both BCC and SCC **(Figure 1 & 2)**. It should be considered as another skin cancer, with its own characteristics including behavior and histological characteristics **[4].** As it is an intermediate typology between BCC and SCC, the MTC simulate the BCC clinically and morphologically. But as compared with BCC, it is more aggressive and tend to metastasize. Therefore, the separation of MTC from the group of basalioma is of very important, as this tumor has the ability to metastasize **[9, 10].** Metatypical cell carcinoma diagnosis is difficult because it is similar to basalioma clinically and histologically **[11].** The difference in cell proliferation between primary BCC, recurrent

BCC and MTC may be valuable criterion for detecting the degree of tumor malignancy **[13, 14, 15].** However, there are some studies about the mitotic rate in cases of MTC and BCC cases of basalioma that have shown this finding to be an adequate for differential diagnosis of these tumors **[18, 21].** The values of the mitotic regimen in MTC differs from the similar types of values in the basolioma; the specific content of dividing cells at the stages of metaphase, and the rate of pathologic mitoses increased considerably. In relation to the surgical intervention, it has been found that a significant proportion of excised BCC demonstrates positive surgical margins histologically **[32, 33].**

Figure 1: patient with basosquamous cell carcinoma

This high incidence of positive surgical margins of excised BCC may be caused by the irregular infiltration of these tumors, so surgeons cannot detect the subclinical spread clinically. The inadequate excision of BCC and of the MTC that are clinically similar is possible. Furthermore, the more appropriate margin is still controversial for both BCC and MTC **[54].** We retrospectively reviewed the cases of MTC-operated patients during an eight year period (1998 to 2005) at the department of plastic surgery of "Diwaniyia Teaching Hospital", to find the rates of recurrence and metastasis of these lesions within this group, and to see whether or not the histological presentations.

Figure 2: patient with basosquamous cell carcinoma

Materials and methods

The study is a retrospective study carried on 120 patients with MTC affecting different regions (the trunk, upper and lower limbs, scalp, neck, and face). The patients are 90 males and 30 females with age between 45-95 years. They are retrospectively analyzed from 1998 to 2005 at the Department of Plastic Surgery of the Diwaniyia Teaching Hospital. Tumors were measured and the excision margins were marked depending on visual or palpable alterations on surface contours, consistent with a non-melanotic skin carcinoma. The minimum surgical margin was that of the short axis of the ellipse. Appropriate surgical margins for each tumor were determined depending on tumor size, location, and if loose donor skin at the surgical margins is present which help to provide an ideal surgical closure while removing the tumor in a single excision. Ellipses were designed as an accentric parallelogram before infiltration with local anesthesia and without stretching the skin. A specified margin of apparently healthy skin was taken around the outer border of the ink marking the tumor: peripheral clearance margins of 3 mm around tumors in facial areas and 5 mm margins around lesions in other sites. Although, in cases with a clinical history of rapid growth, in which a standard 5mm surgical margin have been adopted for head and neck lesions and 10 mm for other regions. Full-depth dermal incisions,

vertical to the skin surface were made along the outer inked edge of each marked ellipse. These ellipses were removed beneath the dermis. A histological examination was made to determine whether there was a tumor present at the surgical margins. If a tumor was present, more skin was removed and histologically verified until ensuring clear margins were obtained. Diagnosis was obtained by histology. Management foresaw surgical excision, radiotherapy and chemotherapy. The cases were followed up for five years after surgery.

Results

In this study, MTC affected more males than females (31.25% versus 17.25%) the most affected site was the cervicofacial area, 71.7% , 86 cases); then the trunk, 10% (12 cases); limbs 6.9% (11 cases) , scalp 3.7% , (5 cases) and other regions (5%) (6 cases) **(Table 1).** In all cases, diagnosis of MTC was confirmed.

Table 1: Correlation between number of cases and Percentage of the affected areas by MCT.

Areas	Percentage of the affected areas	No. of cases
CF	71,7%	86 cases
Trunk	10 %	12 cases
Limb	9.6%	11 cases
Scalp	3.7%	5 cases
Other region	5%	6 cases

The average diameter of the lesions was 1.3 cm, the largest measured 5 × 3 cm, and the smallest 0.6 ×0.4 cm. The margins varied depending on the anatomical location and the growth pattern depending on clinical history. The mean surgical margin was 3 to 5 mm on the face and 5 to 10 mm on the other areas. The wider excision in cases of incomplete eradication of a MTC was 5 mm around the entire scar of the previous surgery **(Table 2)**.

Table 2: Surgical margins adopted for MTC excision

	Standard	Rapid- growth history
Primary excision (Head and neck)	3 mm	5 mm
Primary excision (body)	5 mm	10 mm
Wider excision	5 mm	5 mm

Histological examination showed different subtypes such as mixed (32%), intermediate (686%). Ulceration occurred occasionally in 10 % of cases and an infiltration have been detected in 2.5% of cases **(Table 3).** 62% of patients with MTC were males with an average age of 68.6 years, and 38% females with an average age of 71.8 years. Tumor recurrence occurred in 12 cases (10 %) mainly on head and neck areas. These areas were re-operated again using a wider excision.

Table 3:.Histological types of MTC cases.

	Standard	Rapid- growth history
Intermediate	80	68%
Mixed	20	32%
Ulcerated	15	10%
Infiltrative	5	2.5%

Discussion:

The incidence of non-melanoma skin cancer varies based on geographic location, with the highest incidence of 1 to 2% per year in countries of high ultraviolet exposure, such as Australia **[3].** Among the more common BCC and SCC, the MTC differs in rates of local

recurrence, spread and mortality **[13.19].** Differential diagnosis between MTC and the group of basaliomas is difficult because they are similar clinically, but it is obligatory because of the risk of metastases associated with MTC as compared to BCC **[16, 18].** Then MTC should be considered as another entity of non-melanoma skin cancer, as intermediate typology between BCC and SCC **[34, 37, 40].** In this study we found more lesions on the head and neck region (71.7%) as compared to other regions such as the trunk (10%) or the limbs (9.6%), scalp (3.8%), and others (5%). Among these cases the intermediate MTC was found in 68% of cases, affecting mainly younger males whereas the mixed MTC was found in 32 % of cases 62% were males (average age of 68.6 years), and 38% females (average age of 71.8 years). As a result, we can confirm that MTC was more prevalent in old ages and facial/head-neck areas as SCC. There was no significant correlation between the histological types and sex as it was not a representative population. Another study showed that mixed MTC occurred in 24% of cases with an average age of 71 years, and prevalence on head (81%); while intermediate MTC occurred in 76% of cases affecting mainly the head (70%), then the trunk (19%) and limbs (9%). These findings are consistent with our results. Regarding the surgical excision margins of MTC lesions, we reviewed the literatures of the BCC and SCC standard surgical margin and recurrence rate risk. Histologically positive surgical margins of excised BCC are considerably high (>16%) in head and neck regions. Some studies showed very high recurrence rates reaching up to 52% of inadequately excised BCC **[6, 8, 20].** lesions in the temporal and forehead areas are specifically prone to recurrence or metchronous BCC may occur in these area, so clinically for BCC and SCC larger recurrence occur **[10, 13, 32].** Peripheral margins are marked on head and neck areas to avoid recurrence and then increase the risk of disease spread. Studies report wide ranges of surgical margins, ranging from 2 to 10 mm or more for BCC because it is difficult to determine the margins of basal cell carcinomas clinically. Different studies with a 3 to 5 mm margin for primary BCC excisions showed incomplete excisions of about 4% for either basal cell or squamous cell carcinoma, only in cases with clear clinical tumor margins as for the nodular basal cell carcinoma. Other studies found a higher percentage of lesions need a wide margin, while Goldberg recommended 2 to 5 mm surgical margins, and 10 mm for infiltrative tumors **[23, 29].** In relation to SCC, the anatomical locations affect the tumor aggressiveness, and the possibility of reconstructive surgery **[6, 8, 9, 19, 25].** The mucosal variant requires special attention because of its high tendency for recurrence and metastasis **[26, 27, 30, 34]**. SCC of the ear represents one of the most common origins for metastasis, and is the anatomical site with the highest rate of recurrence (18.7%). It has been shown that tumor thickness is correlated with metastasis rate **[35, 40].** Although reports published on SCC were not satisfied in regarding to the optimal margin to predict recurrence rates, subsets of SCC may still recur, despite having a complete excision **[3, 15].** For SCC the degree of cellular differentiation represented by keratinization has been correlated with tumor aggressiveness, as poorly differentiated SCC has a reported recurrence rate of 28% and metastatic rate of 32.8% whereas well-differentiated SCC is 13% and 9.2% respectively **[18, 19, 24].** The suggested standard surgical margin for primary non-melanoma skin cancers is 4 mm. This surgical margin of 4 mm would have achieved an optimal excision in 96% of basal cell and 97% of squamous cell carcinoma **[24, 34**]. Depending on these previous studies, and on clinical experience with SCC and BCC, we adopted a surgical margin of 3 to 5 mm for the head and neck lesions and of 5 to 10 mm in the other areas, using the wider margin in cases of rapid growth clinical history. When we have clear histological margins, this does not always mean that the tumor will not recur because the presence of discontinuous subclinical tumor extension may lead to tumor recurrence. In these cases, neither conventional surgery nor mohs' micrographic surgery can be expected to remove such discontinuous tumors, so in this case we should excise the tumor by conventional surgical operation with wide margins including such tumor discontinuities. A prospective randomized study of local recurrence after both techniques did not show that one method was statistically superior to the other during a 30- month follow-up period **[16]**. The recurrence rate of our study group for a 3-5 mm and a 5-10 mm surgical excision, occurred in 12 cases (10%), these were re-operated with a wide excision until obtaining free of disease surgical margins. This could lead us to confirm the tendency of MTC to have the aggressiveness of SCC. Although mortality rates are low for both, they are significantly higher for

SCC than for BCC. Mortality from SCC is frequently secondary to metastases of tumor originating from the ear **[7, 22].** In addition to the morbidity and mortality associated with SCC of the ear, SCC of the lip carries the highest rate of metastases (13.7%) **[5].** BCC rarely metastasize with incidence of 0.0028% to 0.55%. Although variable, the risk of metastasis of SCC is greater, it is about approximately 5%, and ranging from 0.5% to 6%, and some reports reaching 16%. The MTC is aggressive and metastatic with 7.4% rates of metastasis. It is in between the SCC and the BCC rate. In our five-year follow up, mortality did not occur, but four patients (2/120, 1,6%) needed positive regional lymph node dissection.

Conclusion

In this study, surgery reaffirms the value of conducting a differential diagnosis, and the importance of the specific treatment for MTC. Although more clinical studies and long term follow up are needed in order to establish specific guide lines. MTC requires a management that differs when compared with that of the BCC, especially if it has been excised incompletely. However, these differential diagnoses can occasionally pose difficult morphological problems. The excision should be wider than those used in managing BCC, especially as the lesion has a history of rapid growth. However, in medical literature, no guidelines regarding MTC excision margins have been established yet. Depending on our experience, we believe that we should adopt a wider excision when dealing with a MTC that has been proved histologically, and a follow up is needed. Because the clinical differential diagnosis cannot be achieved surely, we should avoid a wide excision and skin sacrifice, particularly in facial areas. Because MTC have a higher growth rate than BCC, an adequate surgical excision for early lesions is mandatory. Early diagnosis and treatment of MCC may lead to a satisfactory recovery.

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