

Giant Metatypical Carcinoma: An Unusual Tumor

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SUMMARY Metatypical carcinoma (MTC) or basosquamous carcinoma is a remarkable malignancy with features of both basal and squamous cell carcinoma. It is typically located on the back and face, often with clinical features of basal cell carcinoma but tending to be more aggressive with enhanced prospects of lymph node or distant metastases. Our report describes a huge neglected MTC of the back of ten-year duration, a giant ulcero-vegetative tumor measuring 20x25 cm. Histologic examination of specimens from the margins and periphery revealed aspects of both basal and squamous cell carcinoma, while the ulcerated center showed sclerotic tissue without tumor. Radical excision and reconstruction by grafts were performed. No metastases were observed after two years. There are many controversies surrounding the histologic definition and biologic behavior of MTC, including its metastasizing potential. The MTC we describe exhibited benign biologic behavior. This may have been related to an intense inflammatory host response with elimination of neoplastic tissue and consequent local sclerosis evident in the central tumor-free portion. This central tumor regression is to our knowledge a unique finding in MTC.

KEY WORDS: basal cell carcinoma, basal cell epithelioma, basosquamous carcinoma, metatypical carcinoma, basal squamous cell carcinoma, tumor regression

INTRODUCTION

Metatypical carcinoma (MTC), also known as basal squamous cell carcinoma and basal squamous cell epithelioma, has been recognized for many decades, characterized as an aggressive variant of basal cell carcinoma with histologic features of squamous cell carcinoma (1-10). The World Health Organization histologic classification of skin tumors distinguishes it as a nosologic variety of skin carcinoma (11). This neoplasm is clini-

cally similar or identical to basal cell carcinoma (BCC), and is histologically characterized by the lack of peripheral nuclear palisading in some cellular lobules and presence of different types of cells either with larger nuclei and abundant eosinophilic cytoplasm, or occasionally with a spindle cell appearance and prominent intercellular bridges.

Separating MTC from a typical BCC is important from the a prognostic standpoint because this



Figure 1. A huge neglected ulcer on the right upper buttock.

tumor is more likely to be aggressive locally and to metastasize (4,8,9,12-16). The patient we describe had a giant form of MTC that did not metastasize even after 12 years from its appearance, perhaps related to an intense tissue reaction and central neoplastic regression, the latter to our knowledge not noted previously with MTC.

CASE REPORT

A 70-year-old woman of low socioeconomic status was first seen with a huge ulcer on the right upper buttock. It had slowly grown for 10 years, painlessly but with occasional pruritus, and began to ulcerate three years before. She had neglected the tumor, not seeking medical assistance.

On physical examination the ulcer measured 20x25 cm in diameter and involved the whole lower part of the right back with extension to the right buttock (Fig. 1). It did not appear homogeneous, with undermined rolled margins and an exophytic lateral portion (Fig. 2). Clinically, it resembled a giant ulcerated BCC. There was no hepatosplenomegaly or lymphadenopathy. Altered laboratory test values showed moderate microcytic anemia with hemoglobin of 7.70 g/dL (12-16 g/dL) and hematocrit 24.60% (42%-52%); platelets 488,000 (nl, 130,000-400,000); serum creatinine 2.28 mg/dL (0.70-1.50); urea nitrogen 25.6, calcium 8.23 mg/dL (8.50-10.20), and sodium 130 mmol (135-145 mmol). Serum electrophoresis revealed hypoproteinemia of 5.60 g/dL (6.0-8.5 g/dL) and hypoalbuminemia of 2.89 g/dL (3-5 g/dL). Microbiologic culture from the ulcer showed the presence of both beta-hemolytic *Streptococcus* and *Pseudomonas aeruginosa*. Radiologic examinations including magnetic resonance imaging (MRI) did

not reveal any metastatic disease. The patient was initially treated with liquids, blood and plasma transfusions, diuretics and antibiotics.

Surgical treatment consisted of radical excision with 2-cm margins. The deep muscular layer was apparently healthy, so the whole area was covered by split thickness skin grafts. The neoplasm was divided into four quadrants. Nine full thickness biopsies were taken: two from each quadrant and one from the center. Histologic examination revealed a metatypical carcinoma. The patient was monitored every two months for a period of two years with no evidence of local recurrence or distant metastasis.

HISTOLOGY

Microscopic evaluations revealed different findings in the nine histologic blocks obtained from multiple areas of the lesion. The histologic features diagnostic of MTC were characterized by three main aspects: basal, squamous and intermediate. The basal aspect showed large islands of epithelial cells with the characteristic palisading at the periphery, without evidence of cell maturation or differentiation (Fig. 3). The evidence of epithelial cells arranged in a whirly appearance with numerous apoptotic cells and a high mitotic index was observed (Fig. 4).

Histologic findings in other areas showed aspects of squamous cell carcinoma with islands of epithelial cells, differing in size and shape,



Figure 2. Focal exophytic aspect of the neoplasm.

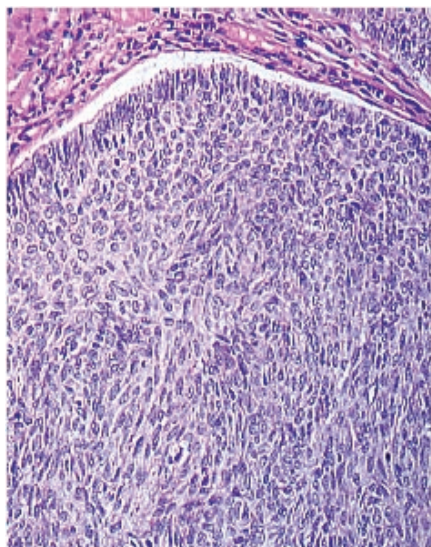


Figure 3. Basal aspect of the tumor demonstrating large islands of epithelial cells with characteristic palisading at the periphery, without evidence of cell maturation or differentiation. (hematoxylin-eosin, magnification x25).

infiltrating the underlying dermis, and foci of keratinization with horny pearls (Fig. 5). The intermediate aspect had areas of epithelial undifferentiated spindle cells where characteristics of both basal and squamous cell carcinoma were unrecognizable (Fig. 6). Moreover, there were areas where the two basal and squamous features coexisted within the same islands of neoplastic cells. A peripheral basaloid area with palisading and foci of squamous differentiation in the central zone were evident in these fields. In the central portion of this neoplasm the skin appeared ulcerated, with granulation and inflammatory tissue, and the lack of tumor (Fig. 7).

DISCUSSION

Metatypical carcinoma was first described in 1910 (1). In 1937, MacKee and Cipollaro (4) observed that basal squamous cell carcinoma was known by the French as *épithéliome metatypique*, *épithéliome mixte*, or *épithéliome pavimenteux et intermédiaire*, and had been described previously by a number of authors (2,3). MacKee and Cipollaro (4) commented: "It has been known for many years that about 10 or 15 per cent of clinical basal-cell epitheliomas contain prickle or squamous epithelial cells". Montgomery (2) found characteristics of MTC in 12.6% of a series of 119 cases of clinical basal cell epithelioma. This type of neoplasm had been noted then and has been observed since to

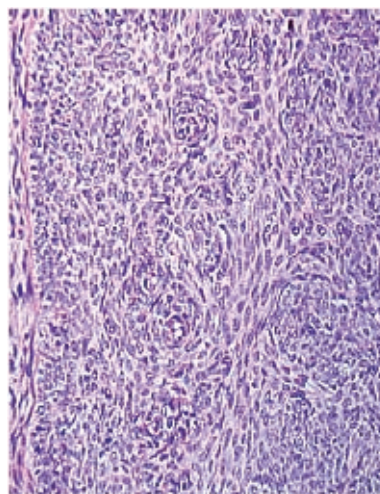


Figure 4. Epithelial cells arranged in a whirly appearance with numerous apoptotic cells and a high mitotic index (hematoxylin-eosin, magnification x25).

be clinically indistinguishable from the BCC, but with a course more likely to be rapid with metastases and death, the findings consistent with recent studies (7-13). MTC has thus been widely recognized for a long time as a specific entity, defined as a neoplasm with the features of BCC with foci of squamous differentiation and spindle cell areas. The tumor lobules are more irregular and peripheral palisading is less pronounced but focally present. Stromal proliferation is more prominent. Often, areas of typical BCC may be seen to merge

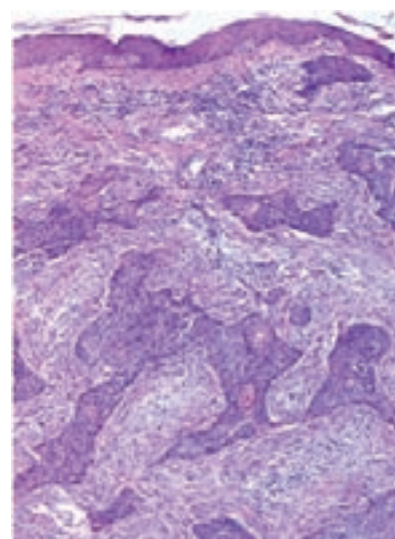


Figure 5. Histologic aspects of the squamous cell carcinoma with islands of epithelial cells differing in size and shape, infiltrating the underlying dermis. Note foci of keratinization with horny pearls. (hematoxylin-eosin, magnification x10)

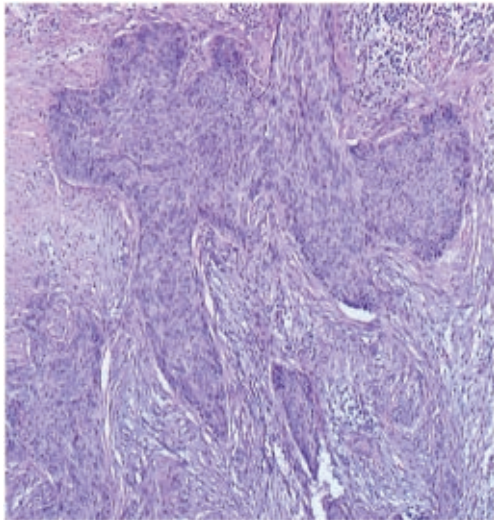


Figure 6. Intermediate aspect with areas of epithelial undifferentiated spindle cells where characteristics of both basal and squamous cell carcinoma are unrecognizable. (hematoxylin-eosin, magnification x25)

into a metatypical region. The most important histologic finding that confirms the MTC diagnosis is the absence of a transition zone between the basal cell and squamous cell types. Thus, MTC is not a collision between BCC and SCC. MTC is generally considered more aggressive than the common BCC or the sun-induced cutaneous SCC (4,7,12-16). Metastases occur mainly to the lung, bone, lymph node, liver, spleen and adrenal gland (9). In our case, despite a relatively long history (12 years) and protracted clinical course producing a giant-sized tumor, its biologic behavior was relatively benign since there was no evidence of local recurrence and no distant metastases. To our knowledge, this is one of the largest if not the biggest metatypical carcinoma described. Another was noted to involve the anterior scalp, left orbit and left side of the face (12).

Metatypical carcinoma is a well-recognized entity within the group of skin epitheliomas. In a retrospective study of 2075 skin cancers from pathology records, 31 MTCs were identified in 28 patients, with a median age at diagnosis being 68 (range, 10-94) years (16). Thus, MTCs constituted 1.5% of the total number of skin cancers. Most were located on the head and neck. It may be seen in many settings, including in association with nevus sebaceous and with xeroderma pigmentosum (17,18). The clinical diagnosis is difficult and must be confirmed by histologic findings. The course of the tumor may be aggressive with the potential of

recurrence and distant metastases. The aggressive course may be attributed to the immune response of the patient, size of the lesion, and degree of anaplasia of the squamous cell carcinoma component which is responsible for the potential of metastasis, since the basal cell carcinoma rarely metastasizes (13-16). Therefore, although the tumor dimension can play an important role in the prognosis, the emphasis should be on histologic findings, especially the squamous cell carcinoma component. We wonder if the benign biologic behavior in our patient may have been related to her strong inflammatory host response with the elimination of neoplastic tissue and the consequent local sclerotic tissue reaction that was evident in the central tumor-free portion. This is to our knowledge a unique finding.

A number of histologic and immunohistochemical techniques have been utilized to compare the MTC, BCC, and SCC (10,19-21). In a study of markers, all stained to varying degrees the malignant aspects of the specimens, with similar patterns between tumors, the MTC showing a transition zone between typical BCC and SCC. This was most striking for Ber-EP4, where over two-thirds of the BCCs stained, none of the SCCs, and half of the MTCs demonstrated reactivity (10). Another study found the values of the mitotic regimen in MTC to differ from similar values in BCC: the mitotic activity, the specific content of dividing cells at the stage of metaphase, and the rate of pathologic mitoses were considerably increased. Multipolar and monocentric mitoses as well as

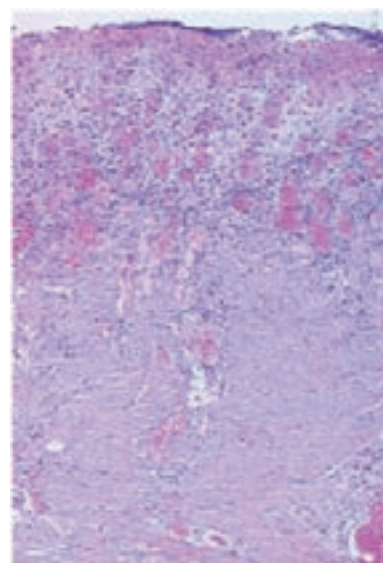


Figure 7. Central portion with granulation tissue, inflammation and absence of tumor. (hematoxylin-eosin, magnification x10)

intercellular bridges were present in MTC (21). Some have questioned the existence of MTC, believing it may represent either a keratotic BCC or a BCC with differentiation into two cell types (7, 22-25). However, since BCC is derived from embryonal pluripotential cells and SCC is a neoplasm of anaplastic ones, we favor the postulation that a cell population within BCC differentiates towards an SCC to produce a MTC (7,26).

The best therapeutic approach is complete resection with negative surgical margins and long-term follow-up for early detection of the possible local recurrence and distant metastatic spread (16,22). In a retrospective study, 745 BCCs, 228 SCCs, and 27 MTCs (1,000 tumors in total) were treated in 580 patients (9). The average number of stages required for clear margins in cases of BCC, SCC, and MTC was found to be 1.62, 1.51, and 2.00, respectively. The prevalence of metastasis was 0.87% for SCC and 7.4% for MTC, which was statistically significant ($p < 0.001$). MTCs displayed tissue invasion similar to that of BCC or SCC but had a higher frequency of pulmonary metastasis than SCC. The prognosis depends on many factors, including the morphology and histology of the tumor as well as the immune status of the patient.

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