Rapid and unusual spread of basaloid squamous cell carcinoma of the maxillary sinus

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Abstract. Rapid and unusual spread of basaloid squamous cell carcinoma of the maxillary sinus. Basaloid squamous cell carcinoma is a variant of epidermoid carcinoma with a morphology consisting of both basaloid and squamous cell components. It is a high-grade tumour with a propensity for nodal and systemic metastases. In this report, we present the aggressive course of a basaloid squamous cell carcinoma of the maxillary sinus in a 28-year-old patient who died only four months after the initial diagnosis. We describe the unusual spread of the disease to the scalp, pancreas, kidney, adrenal gland, ovaries, lungs and bone marrow.

Introduction

Basaloid squamous cell carcinoma (BSCC) is a variant of epidermoid carcinoma and a high-grade tumour with a propensity for nodal and systemic metastases.¹ This variant usually arises in the upper aerodigestive tract and has a predilection for the hypopharynx, larynx and tongue.¹² However, it may arise elsewhere, such as the anus, thymus, and uterine cervix.³⁵

Early stage maxillary sinus carcinomas within the antrum, which have a good prognosis, are rarely diagnosed, because the symptoms generally resemble those of chronic sinusitis.⁶⁴ Thus, maxillary sinus carcinomas often present with locally advanced disease invading the surrounding structures, such as nasal cavity, orbita, ethmoid and sphenoid sinuses, nasopharynx, pterygoid fossa and the skull base.⁵⁷ Although the disease tends to be locally advanced at the time of initial diagnosis, patients with maxillary sinus carcinoma seldom have regional and/or distant metastases at that time and thereafter.⁷

BSCC may have aggressive biologic behaviour and may respond to therapies other than those that are effective in similar carcinomas. Hence, this neoplasm should be distinguished from small cell undifferentiated carcinoma, as well as early stage squamous cell carcinoma, and adenoid cystic carcinoma.⁷¹⁰¹²

The main purpose of this report was to present the aggressive course of a BSCC of the maxillary sinus, with four months from the initial diagnosis to the patient’s death, and to describe the rapid and unusual spread of the disease to the scalp, bone marrow, pancreas, kidney, adrenal gland, ovaries, and lungs.

Case report and histopathological findings

A 28-year-old woman presented with a four-week history of severe left sided toothache, periorbital headache, local soreness and swelling on the left maxillary region, and nasal obstruction. She also suffered from chronic sinusitis. On the endoscopic examination, the medial wall of the maxillary sinus was found to bulge into the inferior meatus. Both a CT scan of paranasal sinuses and an orbital MRI revealed a 5 x 5 cm mass that filled the left maxillary sinus, eroded the medial-inferior aspect of the bony orbital floor, pushed the orbital contents superiorly without evidence of orbital fat invasion, and extended into the nasal cavity and ethmoid sinuses. Histopathological examination of an endoscopic incisional biopsy obtained from the inferior meatus
revealed an undifferentiated carcinoma that did not directly connect to overlying mucosa (Hematoxylin and eosin (HE) staining was performed).

Regional and distant metastases were searched for with CT scans of the head, neck, thorax, abdomen and pelvis, and with bone scintigraphy. After the radiological and histological examinations, the lesion was staged as T3N0M0 squamous cell carcinoma of the maxillary sinus, according to the Cancer Staging Manual of the American Joint Committee on Cancer.13 Following the recommendation of the tumour council, the patient underwent preoperative chemoradiotherapy to reduce the tumour for better control of surgical margins. This treatment reduced the tumour volume to 70% with a regression of the intraorbital extension. The patient then underwent left total maxillectomy. During the surgery, it was observed that the orbital periosteum was not invaded by the tumour.

Sectioning of the total maxillectomy specimen showed strands of neoplastic cells appearing to “drop off” from the mucosal basal cell layer, which did not appear in the sections from the endoscopic biopsy. The overlying squamous epithelium was hyperplastic and focally dysplastic. Submucosal lymphatics with tumour cells were easily seen (Figure 1A).

Histological evaluation of the surgical specimen followed by immunohistochemical (IHC) analysis confirmed the diagnosis of BSCC. IHC analysis was performed on paraffin-embedded tissue sections using the streptavidin-peroxidase procedure. Expression of the following markers was evaluated: HMWCK (34bE12; Dako 1:50), panCK (Novacastra, 1:50), vimentin (Novacastra, 1:50), neuron-specific enolase (NSE; Zymed, 1:50), S100 (Ylem, 1:50), SMA (Novacastra, 1:50), synaptophysin (Zymed, prediluted), chromograninA (Novacastra, 1:50), polyclonal carcinoembryonic antigen (CEA; Novacastra, 1:50), EMA (Novacastra, 1:300), was evaluated. A counterstain was performed with Mayer’s hematoxylin; negative and positive controls were stained in parallel with the study material.

Light microscopic images of the maxillary resection are shown in Figure 2. The tumour consisted of closely packed, moderately pleomorphic, basaloid cells that formed variably sized nests and cords with obscure peripheral nuclear palisading. These nests and cords were separated by thin fibrous tissue. Also, primitive cells were observed at the base of the pseudostratified columnar epithelium or appeared to “drop off” from the basal cell layer of the squamous mucosa. Many of the larger cell nests had central, comedo-type necrosis. In the smaller nests, necrosis of individual cells was prominent and a cribriform-like growth pattern, similar to that seen in adenoid cystic carcinoma, was present but not prominent. Cells had high nuclear to cytoplasmic ratios and dense, hyperchromatic nuclei. Only some cells had particularly vesicular nuclei with scattered nucleoli. Mitotic figures, including atypical forms were observed. In some of the metastatic foci, round large nests similar to mucoepidermoid carcinoma were observed. Squamous cells with larger eosinophilic cytoplasm were noted within the center of the basaloid cell nests. Intercellular bridging and pavement-like arrangement of these cells were the criteria used to identify squamous differentiation. With careful searching, it could be seen that the BSCC was in direct continuity with the surface epithelium. No intracellular or extracellular mucin was observed in the tumour.

Immunohistochemical images are shown in Figures 3 and 4. The tumour was stained strongly and diffusely by the antikeratin antibodies tested, HMWCK and panCK, but was not reactive to neuroendocrine antibodies; synaptophysin, chromogranin A, nor to vimentin, S100, SMA. There was variable immunoreactivity to NSE and no immunoreactivity to CEA and EMA.

Eleven weeks after surgery, examination revealed a mucosal mass on the alveolar process of the right (contralateral) maxilla, and multiple subcutaneous nodules on the scalp. On the histologic examination, the mucosal lesion was found to be a recurrence of the primary disease.

There were 21 scalp nodules varying in size from 0.5 to 2.5 cm (Figure 5). One of them was excised for histologic examination (Figure 1B). The evaluation of the immunohistochemistry slides of the skin nodule revealed only undifferentiated basaloid cells without the CK (panCK) immunoreactivity that was seen in the primary tumour. A wide range of IHC panels that were established for the tumour had included vimentin, desmin, S100, SMA, CD68, CD45, CD3, CD20, CD56, CD99, CD34, EMA, Melan A. All of these markers were negative, while the tumour was questionably positive for NSE.

A meticulous diagnostic work-up was performed to find out
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whether there were other metastases. CT scans revealed numerous, probably metastatic, soft tissue lesions in the parenchyma of the lungs, pancreas, kidney, adrenal gland (Figure 6), and ovaries (Figure 7). No metastatic lymph nodes were encountered in the neck, whereas multiple lymph nodes over 1 cm were found in the mesenteric, retroperitoneal, and paraaortic regions. Although bone scintigraphy depicted increased focal osteoblastic activity only at the maxillo-orbital region, there were a few osteolytic lesions on the CT scans of the lumbar spine and the iliac bones. Subsequently, bone marrow infiltration was proven by a bone marrow biopsy of the ileum. The patient had no immunological or systemic disorders. Based on all the findings, the patient underwent palliative chemotherapy after oncological consultation. At the beginning of this therapy, severe pulmonary insufficiency and electrolyte imbalance developed. Consequently, a sudden cardiopulmonary arrest occurred and the patient died within a few days, one month after the diagnosis of local

Figure 1
Initial biopsies of the maxillary sinus mucosa (A) and metastatic scalp nodule (B). A. Invasive cancer arising from the squamous epithelium (SE) is covered by an ulcerated surface (U). B. The entire depth of the dermal tissue is occupied by a tumour with no squamous differentiation (Hematoxylin and eosin (HE), A,B. × 100, × 100).

Figure 2
A,B. In the maxillectomy specimen an invasive tumour, composed of basaloid cells underlying the ulcerated surface (U), demonstrates squamous differentiation and connection with intact squamous epithelium (SE) (HE, A,B. × 100, × 100).

Figure 3
Atypical basaloid epithelial cells are arranged in anastomosing cords and closely packed nests with central comedo-type necrosis in a scanty stroma, demonstrating diffuse and strong HMWCK expression (inset) (peroxidase). (HE, × 100, inset. Peroxidase, × 100).

Figure 4
Foci of cells with large eosinophilic cytoplasm and pavement-like arrangement show individual cell necrosis and direct contact with atypical basaloid cells with scant cytoplasm, significant pleomorphism, and high mitotic activity (inset) (HE, × 200, inset. × 400).
recurrence and distant metastases, approximately four months after the initial diagnosis. An autopsy could not be performed because the family did not provide consent.

**Discussion**

Malignant diseases in the nasal cavity and paranasal sinuses comprise 0.2-0.8% of all malignant neoplasms and about half of these neoplasms arise in the maxillary sinuses.\(^6,9,14\) Maxillary sinus carcinomas usually present as locally advanced disease invading the nearby structures.\(^6,7\) However, patients with maxillary sinus carcinomas rarely have regional or distant metastases.\(^8,9\) As a consequence, local recurrence of the disease is the most common cause of treatment failure. Therefore, local control is the principal factor determining the length of survival.\(^6,9\)

In their retrospective study on 73 patients with maxillary sinus carcinoma, Jiang et al.\(^9\) stated that the histological type of maxillary cancer was a strong determinant of the nodal recurrence rate. Furthermore, without elective lymphatic treatment, they found a 5% incidence of nodal recurrence in the patients with adenoid cystic and mucoepidermoid carcinomas, while the incidence was 38% in patients with squamous cell and undifferentiated carcinomas. Distant metastases occurred in 17 patients (23%) and were located in the lungs in 15 of these patients. Additionally, squamous cell and undifferentiated carcinomas developed lung metastasis within a year (median, 9 months) after the completion of treatment, and the patients with lung metastases died 1-19 months (median, 5 months) after the diagnosis of the metastases.

BSCC was first described by Wain et al.\(^1\) and characterized as a variant of epidermoid carcinoma with a morphology consisting of both basaloid and squamous cell components. They proposed that a totipotent primitive cell was a precursor of the tumour, and that
primitive cells occupied the base of the pseudostratified columnar epithelium or the proximal salivary gland ducts of the larynx, hypopharynx, and tongue. BSCC presents at advanced stages and is considered to be a poorly differentiated variant of SCC. Thus it is more aggressive and has a lower survival rate than conventional SCC and requires different management.1,2,15

The differential diagnosis of BSCC requires meticulous histopathologic examination, complemented with IHC analysis, as reported by Tulunay et al.2 Histopathologic characteristics of BSCC are the presence of foci of conventional SCC, dysplasia or carcinoma in situ of the overlying mucosa, or focal squamous differentiation within the basaloid component. The junction between the squamous cells and the adjacent basaloid cells is often abrupt with little or no transition.1 In our patient, focal squamous differentiation within the basaloid component and malignant changes of the overlying mucosa were observed by meticulous sectioning of the tumour. Demonstration of the malignant mucosal changes and the connection of the tumour with the surface epithelium in the resected specimen is generally difficult because the preceding biopsy leaves an ulcerated surface that obscures the mucosal tumour and the connection of the tumour with the surface epithelium.2 Metastases may manifest both components or only one of the components, as in the present case, regardless of the predominant component of the primary tumour.15

A specific immunomarker has yet to be discovered for BSCC. However, immunoreactivity with CKs and NSE, and failure to react with the antibodies VIM, desmin, SMA, and neuroendocrine markers help to differentiate BSCC from adenoid cystic carcinoma and undifferentiated neuroendocrine carcinoma.2 NSE may be seen in both BSCC and small cell undifferentiated carcinoma. Strong and diffuse NSE positivity and neuroendocrine-marker negativity of the tumour are characteristic of BSCC.16

Mimicry of a mucoepidermoid growth pattern in some areas allowed the identification of BSCC, even in the absence of triple tumour cell types and negative staining for mucin, CEA, and EMA. Tumours that appear analogous to mucoepidermoid carcinomas of the salivary gland occur in the sinonasal tract, but they are rare.17 In published reports, these tumours have been diagnosed as probable multiple inclusion cysts that occurred as complications of cosmetic procedures. They have also been interpreted as neoplasms that resembled mucoepidermoid carcinoma of the types seen in the salivary glands.17

Cutaneous metastasis from internal cancer is infrequent and usually associated with advanced disease. Thus, survival after skin metastasis is generally short.18,19 The mechanism of cutaneous metastasis is thought to be through local dermal lymphatic channels or hematogenous dissemination.18 The scalp is highly vascular, immobile and warm, which may enhance its vulnerability to metastases.18 Scalp metastases have been reported in primary cancers of the breast, lung, kidney, prostate, testis, ovary, uterine cervix, urinary bladder, as well as in melanoma, leukemia and lymphoma.18,19 However, to our knowledge, scalp metastases from maxillary sinus carcinoma has not been reported. We discovered 21 metastatic subcutaneous nodules on the scalp of our patient, and she died one month after the diagnosis of these cutaneous metastases. The lack of CK immunoreactivity in the analysis of the scalp lesions suggested the dedifferentiation of BSCC in these metastases.

In the present study, we reported a case of BSCC of the maxillary sinus, a rare entity, and the course of the disease, with multiple metastases. Our patient was 28 years old at the time of initial diagnosis. Local relapse and numerous distant metastases were encountered 11 weeks after the completion of treatment. Consequently, the patient died of the disease one month after the relapse and distant metastases, which was four months after the initial diagnosis. It seemed likely that palliative chemotherapy might have adverse effects leading to sudden death, as it did for this patient. Nonetheless, we believe that the disease had a particularly aggressive and dramatic course for such a young patient with maxillary sinus carcinoma.

**Conclusion**

We have presented a 28-year-old patient who developed BSCC of the maxillary sinus, with rapid metastases to multiple sites, including the scalp. Such a location and aggressive course of BSCC is rare, particularly in a patient younger than 30 years of age. We believe that this study will supply additional information to head and neck surgeons, in the scope of maxillary sinus cancer.
References


