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Poorly differentiated plasmacytoid squamous cell carcinoma: Case report of a rare malignancy

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ABSTRACT

Plasmacytoid squamous cell carcinoma is an especially aggressive variant of squamous cell carcinoma that has previously been described in the literature as a variant of oral cancers and most extensively, in vulvular [3], transitional cell, and urothelial carcinomas [2,13,15–20]. In this case report, we present a 36-year-old man with 6 to 8 weeks of a progressively enlarging mass over the lateral third of his clavicle, acromion process, and deltoid. The mass was resected, and the supraclavicular defect was reconstructed using an anterolateral thigh free flap. Final pathology determined the specimen was an invasive poorly differentiated squamous cell carcinoma with spindle cell and plasmacytoid features of cutaneous origin. Plasmacytoid squamous cell carcinomas have previously been described in the oral cavity, but in no other subsite of the head and neck. This article describes the patient's case and provides a literature review of the available reports related to plasmacytoid variant of squamous cell carcinoma.

1. Introduction

The patient is a 36-year-old man who was referred to our clinic after presenting to the MetroHealth Medical Center Emergency Department with a 6- to 8-week history of a progressively enlarging left supraclavicular mass. On initial presentation to the ED, the lesion was approximately 4 cm in diameter and indurated, without purulent discharge or fluctuance (Fig. 1). The patient reported a period of rapid, unchecked growth in the short interval between the appearance of the lesion and his presentation to the ED. On presentation he was also experiencing significant pain, particularly with arm motion. An x-ray of the left clavicular region showed the presence of a mass-like ovoid opacity projecting cranial to the mid-distal aspect of the left clavicle with preservation of the acromioclavicular joint. The final report suggested that the lesion was likely an enchondroma or bone infarct. An ultrasound completed at that time showed the lesion was 3.6 × 2.7 × 4.0 cm, with internal vascular flow. The patient was discharged home on a course of antibiotics for treatment of cellulitis overlying the area and instructed to follow-up in General Surgery Clinic.

On examination in General Surgery Clinic two weeks after presentation at the ED, the lesion had significantly grown in size and was noted to be a 5-cm fungating mass with necrosis. An FNA was obtained demonstrating highly atypical cells suspicious for squamous cell carcinoma (SCC). A CT neck demonstrated a heterogeneously-enhancing solid mass lesion with ulceration measuring approximately 5.1 × 4.3 × 3.5 cm. The patient was subsequently referred to Medical Oncology.

On evaluation by Medical Oncology approximately two weeks after the FNA, the patient was referred to the Otolaryngology Clinic for definitive management due to available expertise. At the time of his initial presentation in Otolaryngology Clinic two days following Medical Oncology evaluation, the patient denied unexplained weight loss, cervical lymphadenopathy, night sweats, dysphonia, odynophagia, or dysphagia. His past medical history was notable for a remote history of non-Hodgkin's lymphoma, diagnosed at age 13 years old and successfully treated with chemotherapy and mantle radiation to 4000 cGy. The specifics of this treatment are unconfirmed, as the patient's records have been archived; however it is known that treatment for his original malignancy ended by age 18. Furthermore, the patient reported an 18-

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Fig. 1. A. Image taken from initial presentation to MetroHealth Medical Center Emergency Department, seven weeks prior to surgery. B. Immediate preoperative image of the left supraclavicular mass. There has been significant growth of the lesion in the 3 to 4 week period since initial presentation. C. Planned surgical incision for excision of the mass measuring approximately 8 cm in diameter.

year smoking history, decreased to one pack per day from three packs per day several years prior to this examination.

An open biopsy was taken of the supraclavicular mass and sent to the pathology department for analysis (Fig. 2). Immunostains for antibodies to CK 5/6, p40, CD 138, and pan-keratin were all positive. CK 8/18 was also weakly positive. Additional immunostains for CK 7, CK 20, CD 20, Melan A, and S100 were all negative within the tumor. This combination of positive and negative immunostaining supported the diagnosis of poorly differentiated plasmacytoid SCC.

Approximately 7 weeks following initial presentation to the ED, the patient was taken for surgical resection of the lesion with reconstruction (Fig. 3). The defect at that time was 8 × 20 cm. Exploration of the neck revealed no metastatic lesions to the cervical lymph node chains. Resection included portions of trapezius muscle, pectoralis muscle, fibro fatty lymph node packets from both levels 4 and 5, with total resection of the mass allowing for 2-cm clear margins around the tumor. Orthopedic Surgery performed claviculectomy of the lateral one-third of the clavicle and the defect was then reconstructed with a dual pedicled anterolateral thigh free flap. The decision was made intraoperatively to complete a modified radical left neck dissection of levels 4 and 5 (Fig. 3). The spinal accessory nerve was resected during removal of the lesion due to direct tumor involvement and subsequently mobilized and repaired primarily with synthetic conduit. Frozen pathology demonstrated highly atypical cells consistent with SCC (Fig. 2).

The final pathology report described the tumor as grade G3, invasive poorly differentiated SCC (10.5 × 10.0 × 3.2 cm) with spindle cell and plasmacytoid features showing ulceration, lymphovascular invasion, and perineural invasion. Tumor was present at the deep soft tissue margin, but the portion of clavicle resected was free from tumor. One lymph node included with the main specimen was negative for malignancy. There were no positive nodes in the neck dissection specimens. The patient was presented at our multidisciplinary tumor board. The tumor was staged as T3N0M0 and the board recommended adjuvant chemoradiation with close monitoring of the ipsilateral axillary lymph node.

At a follow-up visit 7 weeks after surgery, the patient was noted to have increased fullness at the primary site. Biopsy taken of the area confirmed persistence of disease. A CT neck completed 8 weeks postoperatively showed a 10.5 × 6.6 × 6.3 cm mass encapsulating the residual aspect of the clavicle with accompanying mass effect on the left subclavian vein resulting in mild venous compression. There was no invasion or encasement of the neurovasculature but the mass itself abutted the spine of the scapula and brachial plexus with small nodes present in the adjacent axillary region. A CT chest completed at the same time showed significant erosion of the remnant portions of the left clavicle, as well as enlarged left level 2 cervical and level 2 axillary lymph nodes approximately 1.1 and 1.5 cm in size, respectively. There was no evidence of metastatic disease to the lungs or mediastinum.

Nearly 10 weeks after the initial resection and reconstruction, the patient presented to begin chemotherapy and radiation treatment having missed a few appointments (Fig. 4). The patient was treated with cisplatin and received 60 cGrays in 30 fractions. At a follow-up visit with Medical Oncology one week following initiation of therapy, the left clavicular mass had continued to increase in size. Regardless, the patient continued on his previously agreed upon chemotherapy and radiation regimen, with interval follow-up visits noting progressively improving range of motion of the left shoulder.

Repeat CT chest completed 23 weeks post-op noted interval decrease in the size of the left clavicular mass with no evidence of new lesions and complete resolution of the previously present left axillary lymphadenopathy. CT neck done concurrently showed a 5.4 × 2.9 cm lytic soft tissue mass involving the mid- and distal portion of the left

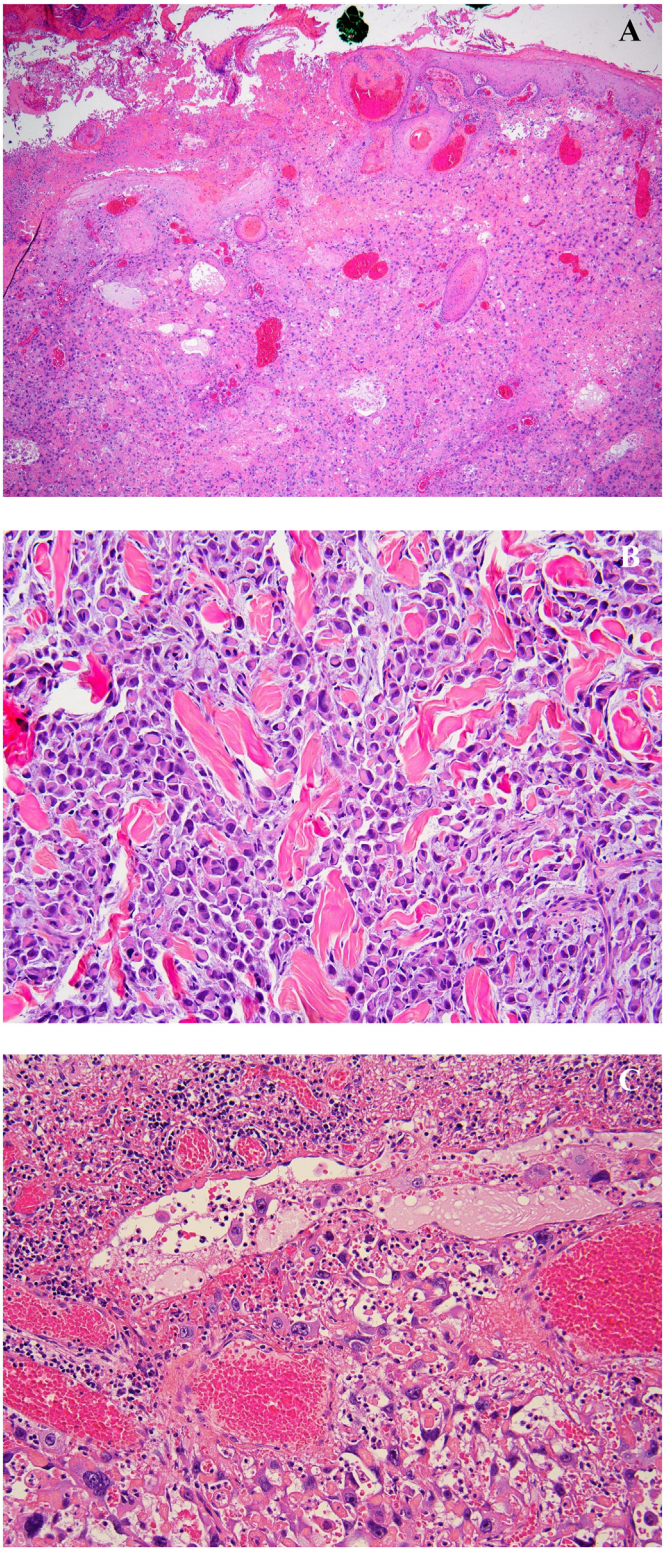

Fig. 2. A. Section from the resection specimen showing moderately differentiated highly pleomorphic squamous cell carcinoma, H&E, 4×.
B. Specimen showing tumor with plasmacytoid morphology, with abundant glassy eosinophilic cytoplasm, eccentric nuclei, and inconspicuous nucleoli. H&E. 20×.
C. Histology showing poorly differentiated and highly pleomorphic squamous cell carcinoma with intravascular invasion, H&E. 20×.

clavicle. A PET scan completed 29 weeks post-op showed no definitive evidence of recurrent or metastatic disease.

Repeat imaging 8 months after surgery showed postsurgical changes in the left supraclavicular region with post-surgical remodeling of the clavicle. In addition, there was note of irregular densities along the pleural surface of the lateral left lung. A soft tissue density in the area of the absent segment of the clavicle represented fibrous tissue. Imaging completed on one year follow up demonstrated disease recurrence in the left clavicular region with a 3 cm centrally necrotic mass and clavicular sclerosis, accompanied by further progression of post-radiation changes within the left lung.

2. Discussion

Plasmacytoid SCC is a rare variant of squamous cell malignancies. It is most frequently reported in urological (transitional cell carcinoma of the urinary bladder, urothelial carcinoma of the renal pelvis) [2,13,15–20] and gynecological (plasmacytoid SCC of the vulva) [3] literature. Plasmacytoid variants of both urologic and gynecologic SCC are extremely rare and high-grade variants of carcinoma. Both are typically diagnosed at an advanced pathologic stage [2], as the clinical course is insidious without accompanying pain [3] and progresses unchecked until symptoms become severe.

To the best of our knowledge, this is the first reported case of aggressive plasmacytoid SCC described in the head and neck arising from skin. Current review of the literature shows limited cases of the plasmacytoid variant, most commonly involving the salivary glands [4,7,12,14] and oropharynx [1,5,6,8,9]. Several other publications describe basal cell carcinoma with myoepithelial differentiation demonstrating the plasmacytoid variant with hyaline inclusions [10], plasmacytoid dendritic cells in cutaneous malignancy, and one instance of an amelanotic melanoma presenting with the plasmacytoid morphology and BRAF mutation [14].

Plasmacytoid variant of SCC is known to be an aggressive variant, particularly among gynecological and urological surgeons: One case report presented a 92-year-old female diagnosed with plasmacytoid SCC of the vulva. Treatment included a complete excision of the primary lesion. Unfortunately, the patient died six months after surgery, with a single regional inguinal lymph node accompanied by multiple lung metastases. Other reports describe urothelial carcinoma with poor prognosis, with resulting pelvic peritoneal tumor spreading along fascial planes that may represent a key characteristic finding of locally advanced urothelial carcinoma [2]. Our patient's case exemplified this aggressive tendency: on initial presentation, the mass was 4 to 5 cm in diameter, but the specimen sent to pathology following complete excision and reconstruction was 10.5 × 10.0 × 3.2 cm. Surgery took place no more than 8 weeks after initial presentation. Three months post-operatively, the patient re-presented with evidence of persistent disease. Given the exceedingly fast growth and the robust response to radiation treatment, our team believes that this could be radiation-induced malignancy related to his remote history of Hodgkin's Lymphoma and subsequent treatment [21,22,23,1].

Radiation-induced tumors following childhood radiation are most commonly appreciated 3 to 30 years following initial treatment. The most common forms of RIT include squamous cell carcinomas and sarcomas, with rarer RITs including neuroendocrine tumors, mucoepidermoid tumors, and meningiomas. These are typically found in the maxillary region, oro/hypopharynx, oral cavity, external auditory canal, nasopharynx and sphenoid sinus, and brain. A prospective study of the head and neck cancers following childhood radiation for Hodgkin's Lymphoma reported the median interval time to second head and neck cancer was 17.0 years. Absolute excess risk following childhood radiation was 13.3. This study reported an increased incidence of thyroid tumors, salivary tumors, neural tumors, and parathyroid tumors.

Another study analyzed the clinical-pathologic profiles of a series of

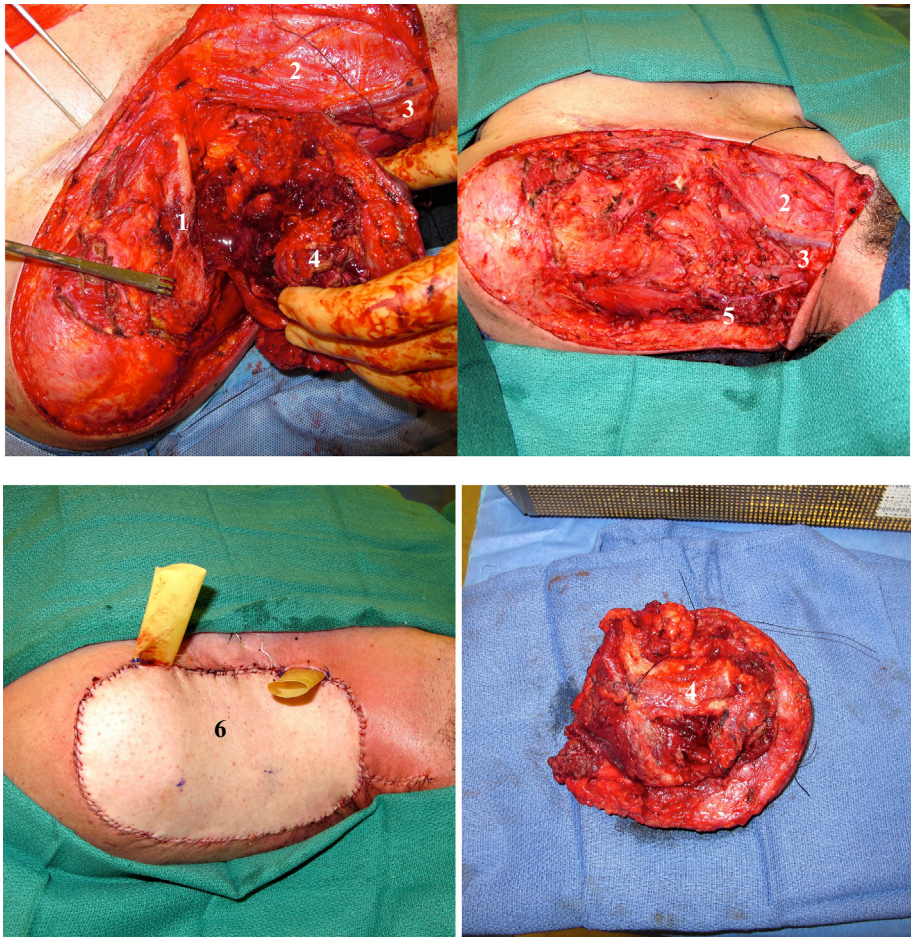

Fig. 3. Intraoperative series demonstrating progression of resection, complete removal of tumor, excised mass, and completion of anterolateral thigh flap. Key: 1 – Left clavicle, 2 – Left sternocleidomastoid muscle, 3 – Left external jugular vein, 4 – Tumor, 5 – Left Accessory nerve, 6 – Anterolateral thigh flap in place.

39 patients with SMARCB1-(INI1) deficient sinonasal carcinomas with all patients presenting with locally advanced disease (T3, n = 5, T4, n = 27). Histologically most tumors displayed predominantly basaloid (61%) or plasmacytoid/rhabdoid morphology (36%). By immunohistochemistry, the tumors were positive for pancytokeratin (97%), CK5 (64%), p63 (55%), and CK7 (48%); and they were negative for NUT (0%). Epstein-Barr virus and high-risk human papillomavirus was not detected by in situ hybridization. Immunohistochemical loss of SMARCB1-(INI1) has been associated with poorly differentiated/undifferentiated features that can be considered as a specific tumor type or difficult-to-classify sinonasal carcinoma type with varies proportions of plasmacytoid/rhabdoid cells, which demonstrates exceedingly aggressive clinical course. This will aid to optimize therapy and prevent under-diagnosis of this clinical entity [11].

Pathology determined that our patient's tumor stained positively for CK 5/6 (squamous cells), p40 (squamous cells), CD 138 (plasma cells),

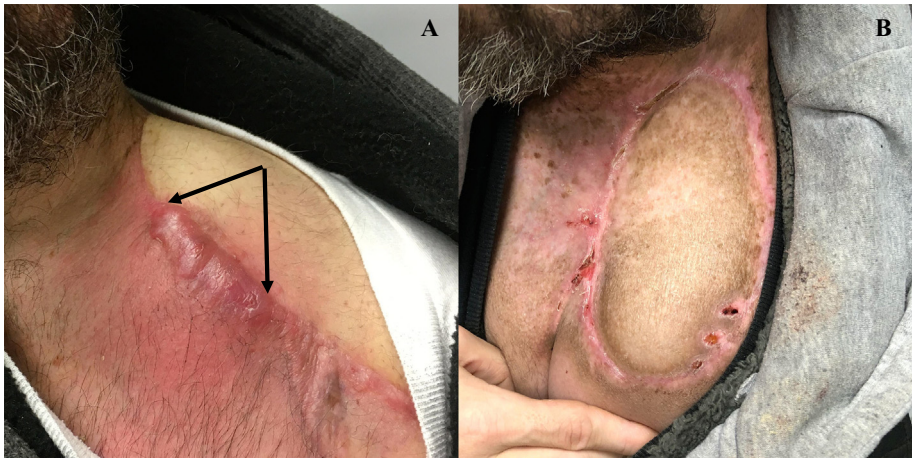

Fig. 4. A. Post-surgical site, image taken eight weeks after surgery in Otolaryngology Clinic demonstrating gross regrowth of tumor (arrows). B. Tumor site following completion of radiation therapy, image taken ten months post-op in Otolaryngology Clinic.

pan-keratin (epithelial nature of cells, therefore squamous cells), CK 8/18 (epithelial nature of cells, therefore squamous cells). Other stains for CK 7 and CK 20 (both associated with epithelial cells), CD 20 (plasma cell marker), Melan A (found in melanocytes), and S100 (present in neuroendocrine cells) were all negative. This differential staining, in conjunction with the morphological assessment of the cells, confirmed the diagnosis of plasmacytoid SCC.

3. Conclusion

We present a rare variant of squamous cell carcinoma with analysis of the morphological and immunophenotypic features. Like other plasmacytoid malignancies, plasmacytoid SCC of head and neck is a rare and in this case aggressive variant of SCC, which can be a significant diagnostic challenge. Rapid growth, aggressive clinical behavior and advanced clinical stage upon its diagnosis should be regarded as ominous clinical parameters. Therapy should be directed toward complete surgical resection with an emphasis on wide surgical margins.

Our patient's case emphasizes the necessity of accurate and expedient diagnosis and treatment. In this case our patient did not seek medical attention until he was functionally impaired, and the mass grew unimpeded until surgical resection 8 weeks later. He missed a few follow up appointments and therefore did not receive adjuvant therapy until after 10 weeks post operatively. Moreover, after initial resection and reconstruction the mass rapidly recurred, suggesting that haste when scheduling surgery and subsequent chemoradiation therapy is paramount in the approach to these patients.

Conflict of interest

There are no conflicts of interest or financial disclosures to report.

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