Carcinosarcoma of the hand

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Abstract

Carcinosarcomas are rare malignant tumors derived of both epithelial and mesenchymal elements. Herein, we report an elderly man originally diagnosed with a squamous cell carcinoma of the hand. Upon excision, the tumor was found to be a more aggressive carcinosarcoma. Immunohistochemical stains revealed that the sarcoma component of the lesion was vimentin positive, whereas the primary carcinoma tumor cells were positive for p63 and CK903. Both components were negative for CD34 and D2-40. This tumor was found to have angiolymphatic invasion and eventually metastasized to the axillary lymph nodes and lungs.

Keywords: carcinosarcoma, sarcomatoid carcinoma, spindle cell carcinoma, metaplastic carcinoma

Introduction

Carcinosarcoma, also known as sarcomatoid carcinoma, spindle cell carcinoma, or metaplastic carcinoma, is a malignancy composed of intimately admixed malignant cells of epithelial and mesenchymal differentiation [1]. These aggressive, biphasic cancers are most common in the liver, lungs, bladder, breast, and uterus, but are rarely found in the skin [2]. Histologically, these tumors vary from case to case, but the presence of malignant epithelial and mesenchymal derived components is necessary for diagnosis. The most common epithelial elements of primary cutaneous carcinosarcomas include basal or squamous cell carcinomas and more rarely adnexal carcinomas, such as malignant spiradenoma or porocarcinoma (arising from sweat glands) and pilomatrical or trichoblastic carcinoma (arising from hair follicles). The mesenchymal components may include undifferentiated spindle cell sarcoma, osteosarcoma, fibrosarcoma, or chondrosarcoma. [1, 3].

Case Synopsis

A 66-year-old man presented with an itchy, painful left-hand lesion (**Figure 1**) a year after Mohs surgery resection of a superficially invasive, well-differentiated squamous cell carcinoma at another institution. At presentation to our clinic the lesion was felt to be too large for dermatologic intervention and the patient was referred to a hand surgeon. Preoperative magnetic resonance imaging (MRI) demonstrated an irregular-appearing 3.3×3.1×1.7cm mass located within the subcutaneous soft tissue

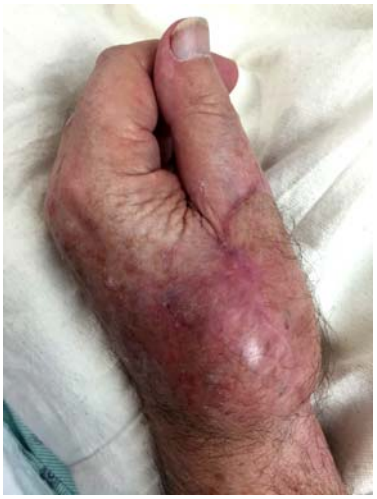

Figure 1. *Left hand with a predominantly subcutaneous mass and overlying erythema.*

along the radial aspect of the first metacarpal bone. The mass demonstrated a small tail extending from the subcutaneous fat distally to the level of the metacarpophalangeal joint.

The patient underwent wide excision of the mass. Histopathology examination revealed a biphasic tumor composed of invasive poorly differentiated keratinizing squamous cell carcinoma and a malignant mesenchymal component of undifferentiated-appearing spindle cells, morphologically diagnostic of carcinosarcoma (**Figure 2A-C**). The tumor extended to the deep margin and angiolymphatic invasion was present. Immunohistochemically, the carcinoma component was strongly positive for the high molecular weight cytokeratin stain CK903 (**Figure 2D)** and p63. The spindle cell mesenchymal component was negative for these markers but stained positively for vimentin. Additionally, immunohistochemical stains revealed that the primary tumor cells were positive for p53, with greater affinity in the sarcomatous component.

A subsequent excisional biopsy of the left axillary lymph nodes revealed metastatic carcinosarcoma, comprised predominantly of the carcinoma component (**Figure 2E)**, which stained positively for CK903. Following local recurrence of the tumor, the patient was taken back to the operating room for amputation in order to achieve adequate local control. Follow up chest radiograph showed multiple lung nodules and lung biopsy showed metastatic carcinosarcoma, composed of the sarcomatoid spindle cell component (**Figure 2F)** with no element of conventional squamous cell carcinoma present. Immunohistochemistry showed the tumor cells were strongly vimentin positive but negative for CK903 and p63. The patient was subsequently started on a chemotherapy regimen of doxorubicin and olaratumab and continues to be followed.

Case Discussion

Although rare, most cases of primary cutaneous carcinosarcoma occur on sun-exposed areas of the

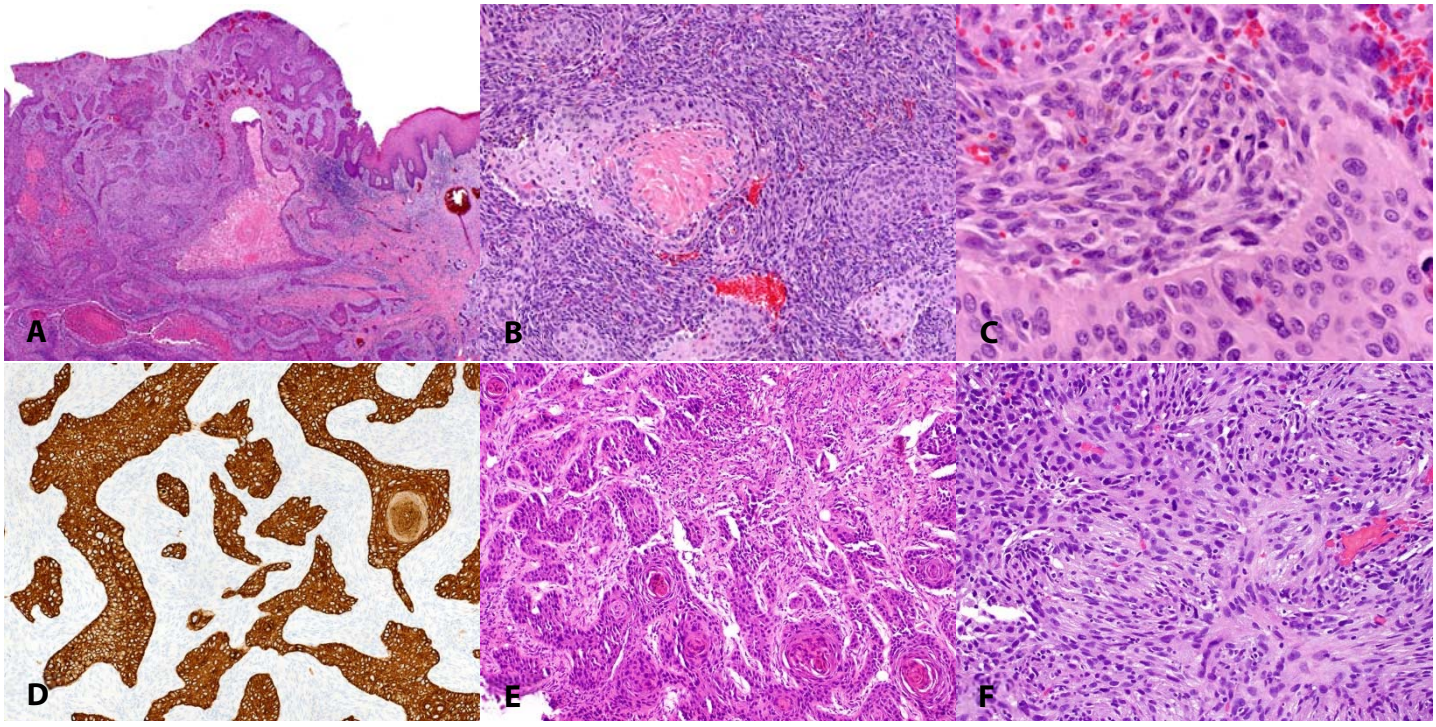

Figure 2. ***A)*** *Low-power image of primary carcinosarcoma involving the hand, with involvement of the overlying squamous epithelium. H&E, 40×.* ***B)*** *The tumor is composed of keratinizing squamous cell carcinoma with an adjacent undifferentiated spindle cell component. H&E, 200×.* ***C)*** *A high-power image shows a sharp demarcation between the epithelial and spindle-shaped tumor cells. H&E, 400×.* ***D)*** *The carcinomatous component is diffusely, strongly positive for cytokeratin 903, whereas the spindle cell component is negative. Immunohistochemical stain, 100×.* ***E)*** *An axillary lymph node metastasis is composed nearly entirely of the carcinomatous component. H&E, 100×.* ***F)*** *In contrast, the lung metastasis is composed entirely of the sarcomatous component. H&E, 200×.*

head, neck, or extremities of older adults, and there is a 1.7:1 male to female ratio [3]. The exact histogenesis of carcinosarcomas is unclear and debated in the literature; however, there are two predominant theories. The first and most favored, the monoclonal theory, proposes that undifferentiated, totipotent cells differentiate into the epithelial and mesenchymal components of the neoplasm from a single origin [4]. Specifically, carcinoma develops first, followed by an epithelial to mesenchymal transition (EMT). This EMT is a de-differentiation of the carcinomatous components and is characterized by loss of E-cadherin expression and alterations of the WNT1 signalling pathway [5]. This means that mesenchymal divergence occurs later, and may explain the period of rapid growth experienced by many of these patients compared to the slower initial carcinoma growth from which the tumor originated [6]. In support of this theory are overlapping molecular changes common to both tumor components and whose signatures favor a carcinomatous origin [5]. On the other hand, the multiclonal hypothesis proposes that the mesenchymal and epithelial elements arise separately from two different under-differentiated cell lines. In other words, the lesion is a result of two simultaneous but distinct tumors colliding [5]. This theory is based on immunohistochemical findings that the neoplastic components share no common features [1]. Although this mechanism is possible in some cases, it does not fit with the histological patterns of most of the reported carcinosarcomas [5].

In patients with these neoplasms, sun damage seems to have led to mutations in *p53*, *p63*, *p13*, and *PTCH1* genes for those with basal cell carcinoma, whereas deletions or point mutations of *TP53* genes are associated with squamous cell carcinoma [3]. The usefulness of p53 and p63 staining is of note. Immunohistochemistry (IHC) for p53 frequently shows staining in both the epithelial and mesenchymal elements, with variable staining patterns. In contrast, IHC for p63 generally demonstrates staining in the epithelial elements alone, making p63 labelling of particular use in determining the presence of an epithelial component [4]. Vimentin staining is also useful to differentiate mesenchymal and epithelial components as typically only the sarcomatous component will stain positive [5].

The prognosis for patients with carcinosarcomas varies depending on the subtype. The risk of distant metastatic disease is around 2% in patients with basal cell carcinosarcoma, whereas the risk of metastasis in patients with squamous cell carcinosarcoma or adenexal carcinosarcoma is between 12 and 50% [3]. Treatment of carcinosarcoma is typically a carcinoma-based chemotherapy with agents that show cross coverage for sarcoma.

Conclusion

Cutaneous carcinosarcomas are rare malignancies, occurring most often in older men and women on sun-exposed areas. Comprised of both epithelial and mesenchymal components, these tumors are aggressive and require prompt diagnosis and management to prevent metastasis and mortality. The patient we report presented with a dorsal hand squamous cell carcinoma that was locally resected and recurred as a biphasic tumor composed of invasive poorly differentiated squamous cell carcinoma and a malignant mesenchymal component of undifferentiated-appearing spindle cells. This aggressive carcinosarcoma was treated operatively but the patient had local recurrence and ultimately metastasis to the axillary lymph nodes and the lungs. The patient required amputation and chemotherapy is ongoing.

Potential conflicts of interest

The authors declare no conflicts of interests.

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