Cutaneous Angiosarcoma Masquerading as Herpes Zoster

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Angiosarcoma is a rare malignant neoplasm of vascular or lymphatic endothelial origin that has a poor prognosis. The insidious symptoms, aggressive nature, and rare occurrence of this neoplasm leave a paucity of optimal treatment information. We describe the atypical presentation of an 88-year-old man who was diagnosed and treated for herpes zoster (HZ) in a local emergency department; consultation and biopsy obtained through our dermatology clinic later revealed a diagnosis of cutaneous angiosarcoma (CA).

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Case Report

An 88-year-old white man presented to his local emergency department with a rash on his left cheek of 4 days' duration that he noticed after spreading straw for his chickens. The patient described the lesion as a red area with some scabbing or crusting that was minimally tender. The lesion initially was diagnosed and treated as herpes zoster (HZ). The rash continued to develop rather than abate with treatment, and subsequent follow-up with his primary care physician resulted in a referral to our dermatology clinic.

On presentation approximately 3 months following his initial diagnosis, his medical history, family history, and social history were noncontributory, while physical examination revealed an inconsistent lesion that encompassed much of the left medial side of the face and measured 11×5 cm (Figure 1). The lesion was a combination of a principal violaceous plaque with violaceous to erythematous satellite nodules that included some superficial crusting extending from the left medial superior cheek down to the submental upper neck. There was no purulent drainage noted and no palpable lymphadenopathy on his head or neck. Punch biopsy specimens were obtained and revealed pathologic findings consistent with cutaneous angiosarcoma (CA)(Figure 2).

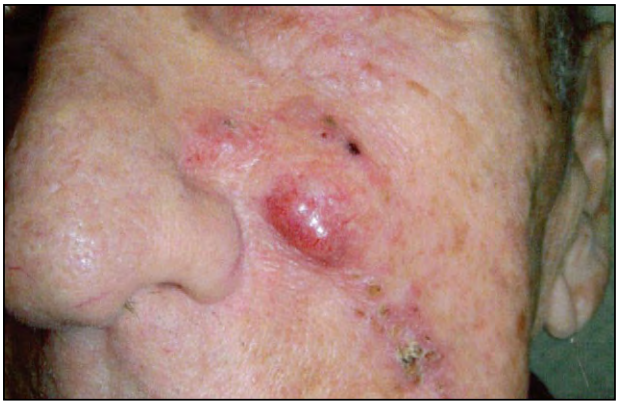

Figure 1. Cutaneous angiosarcoma on presentation to the dermatology clinic approximately 3 months after initial diagnosis and treatment in the emergency department for herpes zoster.

On microscopic examination a punch biopsy revealed effacement of rete ridges with an atypical spindle cell infiltrate in the dermis. There were irregular anastomosing vascular channels lined by a single layer of enlarged endothelial cells, associated isolation, and an enclosure of collagen bundles. Nuclear atypia was moderate and there were areas of necrosis, perineural invasion, and elevated mitotic activity. The cells stained positive for CD31 and CD34 and negative for factor VIII and S-100. These histologic findings also were consistent with CA. The patient was referred for wide local excision and split-thickness skin graft reconstruction. Additional preoperative skin biopsies were obtained to establish and

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The authors report no conflict of interest.

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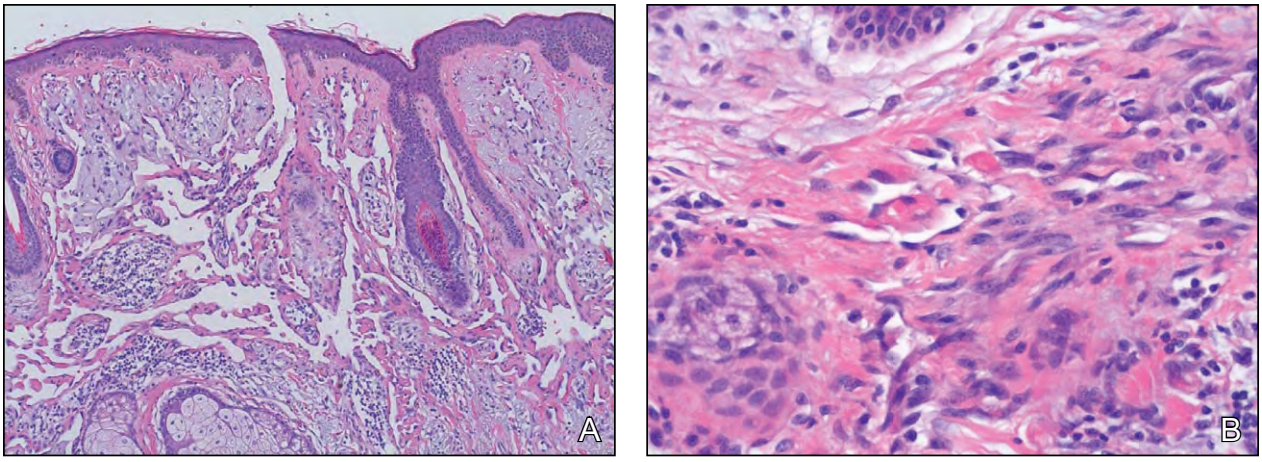

Figure 2. Punch biopsy on microscopic examination revealed an atypical spindle cell infiltrate, irregular anastomosing vascular channels lined by a single layer of enlarged endothelial cells, associated isolation, and an enclosure of collagen bundles (A)(H&E, original magnification ×10). A closer view revealed moderate nuclear atypia with elevated mitotic activity; the cells stained positive for CD31 and CD34 and negative for factor VIII and S-100 (B)(H&E, original magnification ×30).

demarcate the tumor margins, but the final excision showed several positive margins. The patient declined further treatment.

Comment

Our report presents a unique case of CA with a zosteriform pattern. In 1984, Hudson et al[1] described a case of a patient with CA in a site of prior HZ infection. Cases of acquired zosteriform cavernous hemangiomas and acquired tufted angioma on a healed site of HZ also have been observed.[2,3] Although cutaneous metastases that mimic HZ are rare, several types such as melanoma, lymphoma, breast cancer, and other histotypes have been reviewed in a literature meta-analysis by Savoia et al.[4]

Angiosarcoma is a rare, malignant, mesodermal neoplasm of vascular or lymphatic endothelial origin that comprises approximately 2% of all soft tissue sarcomas.[5-8] Although angiosarcomas can present on several regions of the body, Morgan et al[5] observed that 60% (28/47) occurred in the skin and adjacent soft tissues.[5] Cutaneous angiosarcoma is most common on the head and neck and 40% to 50% of cases involve these anatomic locations.[5,8,9] The majority of cases of CA tend to be elderly patients, most notably white men with the average age of presentation being 75 years, with a male to female ratio of 2 to 1.[5,10] Although cases of CA in the pediatric population are rare, there are a few cases described in the literature.[11]

Pioneered by Jones[12] in 1964 as malignant angioendothelioma, CA has been identified more recently in 4 distinct settings: idiopathic angiosarcoma of the face, head, and neck; chronic lymphedema of the upper extremity (postmastectomy angiosarcoma or Stewart-Treves syndrome); postirradiation angiosarcoma; and primary angiosarcoma of the breast.[13] Synonymous nomenclature used for angiosarcoma include hemangioendothelioma, angioendothelioma, hemangioblastoma, hemangiosarcoma, lymphangiosarcoma, and metastasizing angioma.[12,14] Clinical presentation often is varied with physical characteristics and symptoms rapidly evolving over weeks to months. Prompt diagnosis is essential for the most resolute prognosis, but diagnosis frequently is delayed, as CA often presents as a localized area of trauma, cellulitis, an allergic reaction, an arteriovenous malformation, pyogenic granuloma, or a rosacealike lesion.[6,15,16] The differential diagnosis is both lengthy and diverse, including the aforementioned conditions as well as Kaposi sarcoma, malignant melanoma, cutaneous lymphoma, and sarcoidosis.[6,7] In typical cases, CA tends to present as indistinct, dusky, erythematous to violaceous nodules or plaques that rapidly expand and are otherwise asymptomatic.[7,10] The lesion often will have satellite nodules or plaques, and sometimes edema and ulcerations are present.[7] On diagnosis most CA lesions are large, often greater than 5 cm in diameter, and close to 3 mm at depth of invasion with ill-defined clinical margins, which makes complete surgical resection difficult to achieve.[5,10]

Diagnosis confirmed through histologic examination of skin biopsy is paramount, as the physical characteristics of CA are ambiguous. The histology of CA commonly reveals atypical endothelial cells lining well-formed anastomosing vascular sinusoids that dissect through the dermal collagen bundles.[5,10]

These tumors can be categorized as high or low grade with respect to their cellular differentiation, pleomorphism, and mitotic activity, which often varies even within the same neoplasm.[10,16] Three classifications of tumor proliferation are accepted: angiomatous (most differentiated), spindle (intermediate differentiation), and undifferentiated.[13] Immunohistochemical cell markers that are specific for endothelial differentiation (ie, factor VIII–related antigen, ulex europaeus lectin type 1, CD31, CD34) may be useful in confirming the diagnosis.[17]

A novel observation in the identification of CA has been termed the *head-tilt maneuver*; pioneered by Asgari et al,[18] it has been reported to be "quick, easy, and noninvasive clinical aid that emphasizes the vascular etiology of these tumors." To perform this maneuver, the patient places his/her head below the level of the heart for 5 to 10 seconds while the physician observes the noted area of suspicion. If the area becomes markedly more violaceous and engorged, a vascular neoplasm should be suspected and a prompt skin biopsy should follow.[18]

The etiology of CA remains speculative. Implications of UV-induced transformation have received attention, as many patients with CA also have a notable history of long-term sun damage; however, no conclusive evidence is available due to the rarity of CA.[5] Clearly a link exists between chronic lymphedema of the upper extremity, irradiation exposure, and an increased risk for CA.[8,9] Exposure to chemical risk factors such as vinyl chloride, arsenic, and thorium oxide (a contrast agent) increase the risk for angiosarcoma of the liver and other anatomic sites. These chemicals remain inconclusive as potential risk factors for CA.[16,19]

Because there is a lack of evidence for potential treatments of CA, no gold standard or standby treatment protocol exists. Treatment generally includes wide local excision with margins of 3 to 6 cm of clinically normal-appearing tissue, though positive surgical margins still are a frequent obstacle.[5,20] Punch biopsies prior to excision or Mohs micrographic surgery have been employed to try and delineate the tumor margins; however, positive margins still tend to be a concern. The combination of invasive nature, indistinguishable borders, and a typically large CA at presentation make primary closure of an excision site highly unlikely.[20] Radiation therapy often is employed as postoperative adjunctive therapy, as monotherapy in cases that are not amenable to excision, or as a palliative measure.[5,10,20] There is some evidence that surgery with postoperative radiation therapy confers the most resolute prognosis for survival.[20] Considerations for lymph node dissection should be reviewed based on initial tumor size.[21] Chemotherapy and gene therapy also have been employed but with less-consistent results.[20,22] Local reoccurrences of CA on the head and neck are common with metastasis that occurs through hematologic spread predominantly to the lungs and liver, as well as the spleen, regional lymph nodes, heart, and the brain.[5,8,9] The average survival period after metastasis is 4 months.[5] Overall the prognosis is poor with a median survival period of 28.4 months and a 5-year survival rate of 10% to 34%.[5,10,20,23] Poor prognostic factors include a presenting diameter greater than 5 cm, depth of invasion greater than 3 mm, high-grade lesions, positive surgical margins, and metastases.[5,16,20]

Cutaneous angiosarcoma that presents as HZ is unique, and we illustrate its deceiving presentation. Other more common metastatic diseases with scarcely reported zosteriform cutaneous metastases also have been described.[4] The ideology of zosteriform morphology for cutaneous metastases varies including a Köbner-like phenomenon, neural alteration, invasion of the perineural lymphatic vessels, or invasion of the vasculature of dorsal root ganglia. It is unclear whether 1 or more of these channels is responsible for this morphology, which may or may not have been affected or influenced by an earlier episode of HZ.[24] In our case, histology revealed perineural invasion, which could potentiate this presentation of CA as HZ morphology. No other sound evidence has been found to support that this association was more than coincidence of appearance. Our report contributes to the limited number of cases of CA and shows that CA can present with zosteriform characteristics.

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