Angiosarcoma: A Case Report and Review of the Literature

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GOAL

To understand angiosarcoma to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the clinical presentation of angiosarcoma.
2. Identify the differential diagnoses of angiosarcoma.
3. Discuss the treatment options for patients with angiosarcoma.

CME Test on page 309.

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Angiosarcoma is an aggressive neoplasm that predominantly affects elderly patients. Most cases appear on the scalp and face de novo; however, trauma, longstanding lymphedema, and irradiation are predisposing factors. Management includes a multidisciplinary team and may involve a combination of surgery, radiation, and chemotherapy tailored to the patient's age and associated comorbidities.

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Bruiselike patches on the face and scalp of elderly patients should raise the index of suspicion for angiosarcoma. A biopsy of the lesion and a workup for other organ involvement should be considered. We present the case of an elderly patient with an angiosarcoma and discuss the management and follow-up along with a brief review of the current literature.

Case Report

In February 2002, an 80-year-old white man presented with approximately a 3-month history of a growing raised area on the nose (Figure). The patient first noticed a sudden onset of redness on the right side of his nose in December 2001. The redness gradually darkened over the next 3 months.

Examination revealed a 30-×20-mm purplish red plaque on the right side of the patient's nose. Results of a 4-mm punch biopsy showed an angiosarcoma. The patient was referred to an ear, nose, and throat physician with a special interest in oncology. He also was evaluated by an oncologist. Results of the patient's physical examination were unremarkable except for the skin lesion on his nose. Results of a complete blood count, x-ray, and computed tomography of the chest, as well as an abdominal ultrasound and magnetic resonance imaging of the head and neck, were unremarkable for masses, lymphadenopathy, or other significant findings.

In March 2002, the patient underwent excision of the tumor followed by skin grafting. Six weeks after the operation, the patient was started on external beam radiation therapy. He was treated with 98 Gy over 49 days (2.0 Gy daily). Results of follow-up physical examinations by the multidisciplinary team did not reveal any signs or symptoms of tumor recurrence.

On the patient's last follow-up visit in April 2005, he showed no evidence of recurrence of the lesion or metastasis. No follow-up photographs were taken.

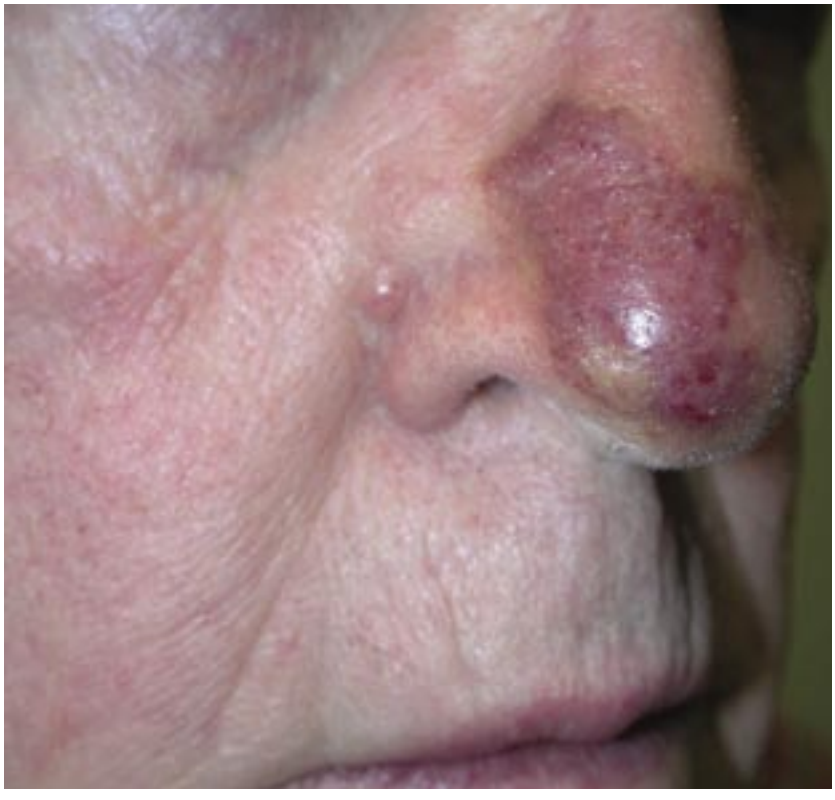
Comment

Cutaneous angiosarcoma of the face and scalp is a distinct entity among the angiosarcomas. It was first described in detail by Jones[1] in 1964 as malignant angioendothelioma of the skin.[2] This aggressive vascular neoplasm predominantly affects elderly patients (average age, 70 years).[3] Men are affected twice as frequently as women. Men also tend to develop the disease at an earlier age. The tumor is localized mostly to the upper half of the face and the scalp.[3] Predisposing factors in the onset of angiosarcoma include trauma, longstanding lymphedema, and irradiation of benign vascular lesions; however, most cases present with no obvious etiology.[4]

The clinical presentation of angiosarcoma is variable. Ill-defined bruiselike areas or facial edema with minimal erythema are the initial signs. Progressively more indurated plaques appear with nodular or ulcerated components. The neoplasm spreads quickly, centrifugally, and transdermally.[5,6] Multifocality also is possible. The original clinical size of the tumor rarely correlates to the degree of microscopic tissue invasion.[7]

Unusual presentations have included yellowish plaques over the upper eyelids that resemble xanthelasma and cause ptosis,[8] rosacealike lesions,[9] and lesions presenting with scarring alopecia.[10] Angiosarcoma presenting with intermittent angioedema of the face that comes and goes is another uncommon manifestation.[11] Rhinophymalike features also should be considered as an unusual clinical manifestation of cutaneous angiosarcoma.[12] Diagnosis often is delayed by the variable presentation and the benign appearance of the lesion, which simulates a bruise or a hemangioma. Retrospective studies show that clinical diagnosis of cutaneous angiosarcomas often is difficult.[13]

Other lesions that may need to be differentiated from angiosarcoma on the face include



A bruiselike patch on the right side of the nose.

hemangiomas, Kaposi sarcomas, malignant melanomas, metastases, and vascular venous malformations. A summary of the characteristic features is included in the Table.

Pathologically, 2 main patterns of angiomas are recognized: angiomatous and solid.[9] The angiomatous pattern is characterized by irregular, anastomosing vascular channels that dissect through the collagen. The vessels are lined by endothelial cells with features that range from normal-appearing endothelial cells to pleomorphic, hyperchromatic cells that exhibit multilayering. Papillary processes may be present within the lumen. Numerous normal or abnormal mitotic figures are present as well. A dense mononuclear cell infiltrate is present and correlates with a better prognosis. In the solid form of angiosarcoma, tumor cells may be spindle or polygonal shaped. Vascular architecture may not be identified in the poorly differentiated areas. Reticulin staining highlights the vascular channels.[9]

Possible immunohistochemical markers for angiosarcoma include ulex europaeus 1 lectin (sensitive marker; used in conjunction with epithelial membrane antigen and cytokeratin to exclude epithelial tumor); factor VIII antigen (highly specific; low detection sensitivity); CD34 cells (highly sensitive; stains dermal dendrocytes, sweat gland basement membrane, and hematopoietic progenitor cells); and CD31 cells (highly sensitive; good specificity).[7,19]

Differential Diagnosis of Angiosarcoma*[1,14-18]

Disease	Diagnostic Features
Hemangioma	Most common cutaneous tumor of infancy
	Benign tumor that undergoes a slow and spontaneous involution with subsequent regression within 5 to 7 years
	Histologically characterized by endothelial hypercellularity and increased mitotic activity during the proliferation phase, and by fibrosis and fat deposition during the involution phase
Kaposi sarcoma	Produces pink, purple, or brown tumors
	Rare form of cancer until the 1980s when it began to present in patients with AIDS
	Typical histologic findings include proliferation of spindle cells, prominent slitlike vascular spaces, and extravasated red blood cells
	Cytologic atypia is less prominent than angiosarcoma and there is no endothelial multilayering
Malignant melanoma	Malignancy of pigment-producing cells (melanocytes)
	Accounts for only 4% of all skin cancers; however, it causes the greatest number of skin cancer-related deaths worldwide
Metastasis	Tumor of unknown origin
	Well-differentiated and moderately-differentiated adenocarcinomas are the most common tumors found on biopsy specimens, followed by poorly-differentiated adenocarcinomas, undifferentiated carcinomas, and squamous cell carcinomas, and poorly differentiated neoplasms
Vascular venous malformation	Benign abnormality that occurs in infancy
	Normal rate of endothelial cell turnover
	Enlarge proportionately with the growth of the child
	Does not undergo spontaneous involution

*AIDS indicates acquired immunodeficiency syndrome.

Several differential diagnoses should be considered on pathology.[20] Unlike benign vascular lesions, the well-differentiated angiomatous areas in angiosarcoma display cytologic atypia; multilayering, papillary structures; and irregular anastomosing blood vessels. In Kaposi sarcoma, cytologic atypia is less prominent and there is no endothelial multilayering.[20]

The optimal treatment of cutaneous angiosarcoma has not been defined.[21] Generally, radical surgery and postoperative radiotherapy are advocated to treat patients with these tumors. In many patients, surgery often is not feasible because of the tumor's multifocal nature and local spread pattern.[21] Therefore, the results have been poor. In a study by Mark et al,[22] only 1 of 12 patients had the disease locally controlled. Holden et al[23] reported 1 cure in 7 patients treated with surgery alone.

The surgical aim is to resect all clinically identifiable disease.[24] In areas of doubt, microscopic control of surgical margins may have a role in guiding the extent of resection. Achieving a negative margin frequently is difficult in angiosarcoma patients because of the extensive microscopic spread that is so common in this disease. Therefore, in trying to achieve a negative margin, a wound is created that almost never can be closed primarily. The reconstructive surgeon has a number of options for initial temporary coverage, as well as definitive reconstruction, including homograft skin, autologous skin graft, rotation flaps, and free flaps.[24]

Angiosarcomas usually respond to radiotherapy to some degree and most studies suggest that a combination of surgery and radiotherapy offers the best chance for long-term control.[3,21] In 1 series of 28 angiosarcomas of the head and neck, Mark et al[22] reported better survival after a median 32 months with combined surgery and radiotherapy compared with surgery alone. In cases unsuited for surgery, radiotherapy alone may be considered; however, usually only partial responses are achieved. Morrison et al[21] suggested that moderate doses of radiation could control subclinical disease.

Because angiosarcoma is a systemic disease, chemotherapy may be useful in its management.[25] The efficacy of chemotherapy is undefined, with some studies reporting a beneficial effect and others suggesting no survival benefit. Chemotherapeutic agents used have included doxorubicin, cyclophosphamide, dacarbazine, actinomycin D, methotrexate, and vincristine.[25] Systemic paclitaxel therapy has been used with encouraging results in 3 patients with angiosarcoma with regression of the lesions.[26] Spieth and colleagues[27] reported the effectiveness of 13-*cis*-retinoic acid and interferon alfa-2a combination therapy in a patient with recurring cutaneous angiosarcoma of the head after radical radiation treatment. There is no optimal treatment for angiosarcoma and the search for effective systemic treatment is needed.

The prognosis in angiosarcoma is poor because of its high potential for metastasis.[28] The 5-year survival rate is about 12%. Prognostic factors include the size of the tumor and mitotic counts, with tumors less than 10 cm in diameter and those with low mitotic counts having a better prognosis.[28]

Conclusion

Angiosarcomas are rare, aggressive tumors of vascular origin. They occur most often in areas of long-term sun-exposed skin in elderly patients, patients with longstanding lymphedema, or patients who have completed radiation therapy. The prognosis is poor and radical surgery is often required. In addition, radiation or chemotherapy may be considered as therapeutic options.

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