doi:10.36849/JDD9348

Pembrolizumab as an Off-Label Treatment of Facial Angiosarcoma: A Case Report

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ABSTRACT

Summary of Case: We report an atypical case of cutaneous angiosarcoma presenting as unilateral nasal swelling in an elderly male. The lesion was unresponsive to topical and antibiotic therapy. Diagnosis was confirmed after surgical excision, and disease control was ultimately achieved through radiation and off-label use of pembrolizumab.

Patient Info: A 79-year-old male with a history of squamous cell carcinoma presented with a 1–2 month history of erythematous, scaly swelling of the left nasal tip and ala. Family history was notable for nonmelanoma skin cancer.

Diagnosis: Initial differential diagnoses included contact dermatitis, rosacea, and rhinophyma. A shave biopsy revealed actinic damage but no malignancy. Following persistent symptoms and referral to plastic surgery, debulking surgery was performed. Histopathology confirmed cutaneous angiosarcoma.

Treatment: The patient declined wide local excision and instead underwent a 4-week course of hypofractionated radiation. Subsequent imaging showed regional lymph node recurrence. He declined biopsy and surgery, and was started on off-label pembrolizumab immunotherapy for disease control.

Outcome: Following immunotherapy, the patient experienced sustained remission with no clinical or radiographic evidence of disease four years post-treatment.

Discussion: Cutaneous angiosarcoma is a rare, aggressive malignancy with a poor prognosis. This case illustrates the importance of considering angiosarcoma in atypical facial lesions and demonstrates disease control using a non-traditional, patient-centered treatment strategy. Immunotherapy with pembrolizumab may offer a promising option in select patients, particularly those with contraindications to extensive surgery.

J Drugs Dermatol. 2026;25(5):471-473. doi:10.36849/JDD.9348

INTRODUCTION

Cutaneous angiosarcoma is a rare, aggressive malignant neoplasm of vascular endothelial cell origin with a poor prognosis, due to its rapid growth and propensity for local recurrence and distant metastasis.[1,2] The typical presentation of cutaneous angiosarcoma involves a progressive, bruise-like lesion on the head or neck.[2] In most cases, the scalp is the predominant site affected, while other less commonly affected areas include the trunk and extremities. Cutaneous angiosarcoma, despite its poor prognosis, is extremely rare accounting for less than 1% of all sarcomas.[3] The incidence rate is approximately 3.3 cases per 1,000,000 person-years, with higher prevalence in those over 70 years of age.[3] As Wagner et al (2024) highlight, the increase in cases within a 20-year period emphasizes the need for early detection and treatment. Current treatment for cutaneous angiosarcoma includes a multimodal approach due to its aggressive nature and high recurrence rate. Treatment plans usually include wide local excision, radiation therapy, and chemotherapy.[4]

We present an atypical case of facial angiosarcoma arising as an asymmetric, non-purpuric swelling of the left nasal tip and ala, treated unconventionally with debulking surgery, radiation therapy, and off-label pembrolizumab immunotherapy. These treatment paradigms aligned with the patient's goals as they navigated concerns of wide local excision due to cosmesis and quality of life. The patient is doing well four years later and will resume surgery or radiation if needed for any recurrence.

Case Presentation

A 79-year-old male with a history of squamous cell carcinoma presented to the dermatology department with a chief concern of "swelling" on the left side of the nose for the past 1–2 months. He reported his symptoms on the left side of the nose as "red", "swollen", "somewhat scaly", and "not itchy". The patient has a family history of nonmelanoma skin cancer. The dermatologic exam revealed an erythematous, ill-circumscribed nodule at the left nasal tip, eliminating the left alar groove, positive for

FIGURE 1. Initial presentation. Smooth, pink nodularity to the left nasal tip and ala.

FIGURE 2. After tangential excision of the tumor. Angiosarcoma is widely positive at the base of the lesion.

overlying scales. (Figure 1) The differential included dermatitis, rosacea, or unilateral rhinophyma. The initial treatment was fluocinonide 0.05 % topical ointment two times a day for two weeks. After the treatment course was complete, the patient returned two weeks later, and the dermatologic exam revealed bulbous erythematous swelling of the left side of the nose with a small central ulcer. The differential diagnosis was expanded to include basal cell carcinoma and rhinophyma. A shave biopsy of the lesion was obtained and revealed actinic damage but no skin malignancy. There were no improvements with the initial treatment of fluocinonide, so the patient was prescribed doxycycline 100 mg two times a day, mupirocin 2% ointment applied twice daily for 2 weeks, and referred to the Head and Neck Surgery (HNS) department for further evaluation and management.

The HNS department agreed with the possible differential of actinic keratosis or rhinophyma, with recommended monitoring. In the next follow-up appointment, the plan was to refer the patient to the Plastic Surgery department for surgical excision. The excision from the Plastic Surgery department was sent to pathology, and the result revealed angiosarcoma transected at the base. The recommendations included surgery and radiation, but the patient declined the surgery and chose to move forward with a hypofractionated 4-week course of radiation therapy. The patient underwent the full course of radiation therapy with expected side effects of fatigue, dermatitis, and nasal cavity mucositis. A follow-up PET scan showed decreased hypermetabolic activity in the nose and nasal cavity compared to the prior exam. After treatment completion, a PET scan was performed four months later, and

FIGURE 3. Angiosarcoma after surgical excision with positive margins, radiation therapy, and pembrolizumab immunotherapy.

the results revealed the suspicion of regional recurrence of the nasal angiosarcoma in the left submandibular lymph nodes and left parotid lymph node, which prompted a CT-guided biopsy for confirmation. The patient refused biopsy and surgery, which led the team to consider palliative radiation therapy. The care team concluded that the use of pembrolizumab for palliation of the recurrent angiosarcomas would be a systemic approach to addressing the recurrent angiosarcoma. The course treatment of pembrolizumab led to no current evidence of angiosarcoma.

DISCUSSION

Angiosarcoma of the head and neck is a rare vascular sarcoma associated with high rates of local recurrence, distant metastasis, and a poor prognosis. However, several studies comparing face and scalp angiosarcomas have shown improved prognosis when angiosarcoma occurs on the face.[5] A meta-analysis by Shin et al showed improved prognosis in patients less than 70 years old, tumor size less than 5 cm, treatment with surgical resection (vs radiation or chemotherapy alone), negative surgical margins after resection, and tumor location on the face as opposed to the scalp.[5] Our case mostly supports this trend since the tumor location was on the face, the tumor size was less than 5 cm, and surgical resection was performed.

Angiosarcoma is typically treated with multiple modalities, including surgery, radiotherapy, and chemotherapy. Our patient's angiosarcoma was controlled with debulking surgery, radiation therapy, and pembrolizumab. Pembrolizumab is a humanized antibody that targets the programmed cell death protein 1 (PD-1). PD-1 functions as an immune checkpoint receptor that inhibits the activation of T-cells, inevitably allowing cancer cells to evade immune surveillance.[6,7] (Blay 2023, Ravi 2017) pembrolizumab is used in cancer immunotherapy and is currently FDA approved for a variety of malignancies, including melanoma, non-small cell lung cancer, squamous cell carcinoma, and Merkel cell carcinoma. Although currently being used off-label in angiosarcoma, there are multiple case reports in the literature showing a sustained response of angiosarcoma to PD-1-directed therapy.[7]

It is theorized that PD-1 inhibitors, like pembrolizumab, show efficacy in treating cutaneous angiosarcoma by restoring

the immune system's ability to recognize and destroy cancer cells.[6,7] In conjunction with multimodal treatment, checkpoint inhibitors may serve a beneficial role in controlling disease, especially in cutaneous angiosarcoma, where there is a high recurrence rate and poor prognosis. The following factors must also be considered, such as tumor location, size, age of the patient, and surgical intervention, which have been shown to influence outcomes positively. Our case aligns with existing literature that indicates improved prognosis for angiosarcomas located on the face. Additionally, the use of immunotherapy, specifically pembrolizumab, has shown promise in controlling angiosarcoma, suggesting potential for further research and clinical application in this aggressive malignancy.

DISCLOSURES

The authors have no conflicts of interest to declare or financial disclosures.

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