Angiosarcoma of the Scalp and Paraneoplastic Encephalopathy: Multidisciplinary Approach to Diagnosis and Treatment

Zachary Wendland[1,2*], Noah Goldfarb[1,2], Monica Rani[3], and Elisabeth Hurliman[2,4,5]
[1]Department of Dermatology, Minneapolis VA Medical Center, Minneapolis, Minnesota, US
[2]Department of Dermatology, University of Minnesota, Minneapolis, Minnesota, US
[3]Advanced Dermatology and Aesthetic Medicine, Chicago, Illinois,US
[4]Lakes Dermatology, Burnsville and Minnetonka, Minnesota,US
[5]Ridgeview Medical Center, Waconia, Minnesota,US

*Corresponding Author**

Zachary Wendland
Department of Dermatology, Minneapolis VA Medical Center, Minneapolis, Minnesota, US
E-mail: zach.wendland@gmail.com

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Abstract

A diagnosis of synchronous cancers within the same individual poses a multitude of diagnostic and treatment-related challenges. Many of these challenges pertain to the vast heterogeneity in cancers and presentations, patient ineligibility for clinical trials, lack of standardized guidelines to direct management and an incomplete understanding of the molecular mechanisms that contribute to the development of these cancers. We present a case of concurrent diagnoses of Pancreatic Ductal Adenocarcinoma (PDAC) and Acute Myeloid Leukemia (AML) with a comprehensive mutational analysis of the pancreatic tumor, AML blasts, and germline DNA collected from cultured skin fibroblast samples. In addition to some commonly detected mutations (e.g. KRAS Gly12Asp in PDAC and TP53 Met237Ile in AML), the genetic testing revealed the presence of DDX41 and MUTYH gene mutations in both germline DNA and tumor tissue specimens. This case underscores the importance of addressing the interplay of genetic, lifestyle and environmental factors in the development of synchronous cancers in an individual, and only by doing so, evidence-based guidelines for early detection and management may be developed.

Keywords: Angiosarcoma • Paraneoplastic • Onconeuronal antibody

Introduction

Angiosarcoma is a rare and aggressive malignancy, often presenting with subtle cutaneous signs and oftentimes metastasizing by the time of diagnosis. While commonly affecting the scalp in elderly males, neurological symptoms from Paraneoplastic Syndromes (PNS) are rare and can complicate early detection.

We report the case of a 75-years-old man initially diagnosed with steroid-responsive encephalopathy, later found to have cutaneous angiosarcoma. His neurological symptoms preceded the discovery of scalp lesions, suggesting PNS. This case highlights the importance of considering malignancy in elderly patients with new neurological symptoms and the value of multidisciplinary collaboration for timely diagnosis and management.

Case Presentation

A 75-years-old man presented with daily persistent frontal headaches that rapidly progressed to acute confusion, agitation, and anomic aphasia within three weeks of initial presentation. Infectious workup and Electroencephalography (EEG) were unremarkable. He was successfully treated with a brief course of high-dose steroids and discharged with a diagnosis of steroid-responsive Hashimoto encephalitis. Several attempts were made to taper his prednisone; however, his neurological symptoms re-emerged on every occasion the dose was lowered. Thus, he was maintained on prednisone 20 mg daily. After six months, the patient again deteriorated with cognitive and motor abnormalities and was referred to the inpatient neurology at our academic center, at which time two scalp lesions were identified. The Department of Dermatology was subsequently consulted. On skin exam, the parietal scalp lesion presented as a 1 cm violaceous indented, bound-down plaque with telangiectasias, irregular edges and surrounding adjacent pallor. The vertex scalp lesion exhibited a 1 cm pale plaque with a small central indentation.

Serum studies for antibodies associated with steroid-responsive Hashimoto encephalopathy (thyroid stimulating immunoglobulin, thyroid peroxidase antibody, and thyroglobulin antibody) were negative. EEG demonstrated moderate nonspecific encephalopathy. No acute intracranial pathology was noted on imaging (Figure 1). Biopsy of the midline vertex lesion was consistent with angiosarcoma (Figure 2). A standard paraneoplastic autoantibody panel (antineuronal type 1-3, antiglial nuclear, purkinje cell cytoplasmic, amphiphysin, CRMP-5 IgG, striational, P/Q calcium channel, N-type calcium channel, ACH receptor muscle binding, AChR ganglionic neuronal and neuronal V-G potassium channel) was negative. The patient responded to high-dose IV steroids for 3 days and was transitioned to oral prednisone 60 mg daily. Outpatient oncological workup was negative for additional malignancies.

After his diagnosis of angiosarcoma of the scalp in December 2011, the patient developed subsequent scattered lymph node involvement in the right neck, and was started on a chemotherapeutic regimen with infusional taxol [1,2]. Despite this, his disease progressed, and the regimen was changed to Pegylated-Liposomal Doxorubicin (PLD) three months later and he received 15 monthly cycles. After completion of PLD, he underwent radiation therapy to the scalp and right neck with a total of 6000 cGy in 200 cGy fractions. He initially responded well, and had improved neurologic function, but developed lung metastases 11 months after completion of radiotherapy, documented by a wedge resection. Around this time, his chronic benign anal/rectal fistula, present for 4 years, became symptomatic and a left perianal skin biopsy showed an invasive well to moderately differentiated squamous cell carcinoma, which occurred after the initial development of angiosarcoma. MRI scan of the pelvis showed a

transsphincteric fistula posteriorly, with no evidence of pelvic lymphadenopathy. He also developed a spontaneous pneumothorax secondary to a necrotic right lung due to metastatic pulmonary angiosarcoma and required a chest tube. Therapy with PLD was reinitiated and 5-fluorouracil/mitomycin with concurrent radiation was added. His neurologic findings worsened with vision changes and confusion. Repeat MRI was negative for any structural central nervous system pathology.

Due to the incomplete response of his metastatic angiosarcoma to treatment, his concomitant re-emerging neurologic disease and development of localized anal squamous cell carcinoma, his care was transitioned to hospice. The patient passed away three years after initial diagnosis (Figures 1 and 2).

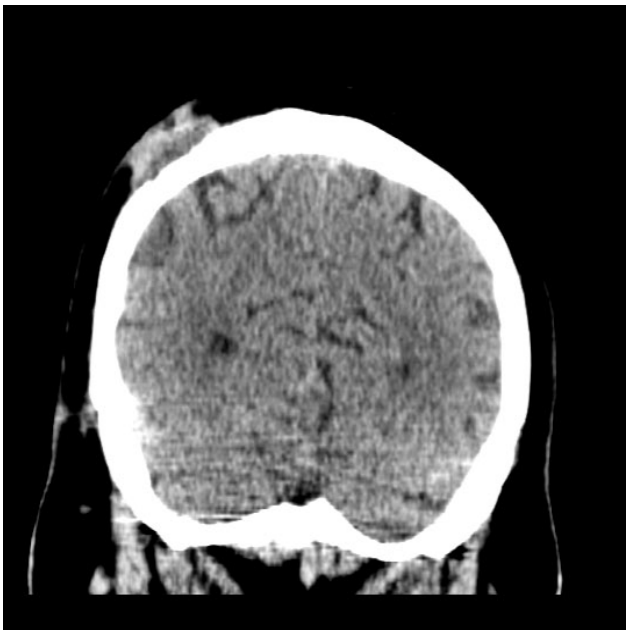

Figure 1. CT Head image showing a 2.3 cm x 1.6 cm non-enhancing right parietal subcutaneous soft tissue mass eroding the outer and inner tables of the underlying parietal bone without extension into the dura. A second soft tissue lesion was seen in the subcutaneous tissue overlying the vertex scalp, without bony involvement.

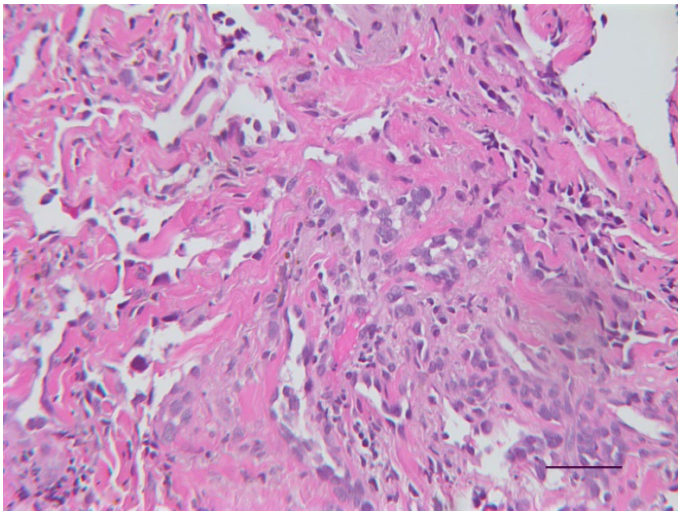

Figure 2. Angiosarcoma histopathology showing multiple slit-like vascular spaces lined by atypical endothelial cells in a background of dense collagen (Hematoxylin and eosin stain; scale bar pathology image=50 micrometers).

Discussion

Cutaneous angiosarcomas of the scalp have an insidious onset, and aggressive course [3]. At the time of diagnosis, local or more distant metastases are present in 50% of cases and intracranial invasion, although rare, can occur [4]. Affected patients are most commonly elderly males [5,6]. While the prognosis of angiosarcomas is generally guarded, they are often responsive to chemotherapy, including paclitaxel and PLD [1,2,7]. Recent studies have found PD-1 inhibitors may also have significant efficacy in angiosarcoma [8,9].

There are three methods by which diagnostic criteria for paraneoplastic neurological syndrome can be attended: with a classical neurologic syndrome such as limbic encephalitis in the presence of tumor with onconeuronal antibodies either present or absent, with a nonclassical neurologic presentation with tumor present and with onconeural antibodies present, or with a nonclassical neurologic presentation with tumor present and with improvement after cancer therapy in the absence of onconeural antibodies [1-3]. The third classification category is emphasized in our case, which pertains to the temporal correlation between the patient's neurological symptoms and their confirmed cancer, the waxing and waning course correlating to their angiosarcoma progression. Of note, such routine paraneoplastic panels often have limited ability to identify antibodies related to paraneoplastic syndromes [10]. Paraneoplastic syndromes have been noted in various dermatologic malignancies including melanoma, and Merkle cell carcinoma [11-15]. Here, we add to the growing literature with a case of paraneoplastic neurologic syndrome in cutaneous angiosarcoma.

Conclusion

This case highlights the importance of multidisciplinary collaboration in the diagnosis and management of these complex patient presentations. As in this case, neurologic symptoms could be the first symptoms observed during presentation, and early diagnosis before the appearance of significant cutaneous involvement suggesting biopsy, could enhance prognosis. As treatment continues to advance, early identification and intervention will be crucial. Further studies are needed to evaluate specific markers or antibodies that could be linked to various dermatologic malignancies in general and angiosarcomas in particular.

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