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Case presentation

Post-radiation atypical vascular proliferation on the head of a young woman: a diagnostic challenge

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Abstract

With improved outcomes associated with radiotherapy (RT), post-irradiation tumors are increasingly seen in long-term cancer survivors. We report a case of a young woman who presented with a three-year history of a vascular lesion on the temple, previously irradiated for a childhood brain tumor. The history of radiation, the clinical appearance, and the biopsy findings of an atypical vascular proliferation in the dermis, were worrisome for a malignant vascular neoplasm and prompted surgical excision. However, further tissue analysis of the excised specimen confirmed a benign atypical vascular lesion (AVL) overlying a banal pilar cyst. Distinguishing post-radiation benign from malignant vascular lesions can be difficult because they share overlapping clinical and histopathologic features. Thus, any vascular lesion that occurs in a previously irradiated field should be excised completely with tumor-free margins and examined histologically.

Introduction

Atypical vascular lesions (AVL) and angiosarcoma (AS) are known complications of radiation therapy (RT). Angiosarcoma is an aggressive malignancy with poor survival [1], whereas AVLs are reportedly benign vascular proliferations [2,3]. The majority of reported cases of AVL occur on the chest of women following RT for breast carcinoma and exhibit heterogeneous clinical and histopathologic features [3,4,5]. Distinguishing an AVL from a well-differentiated AS can be a significant diagnostic challenge because these entities share overlapping histologic features. Furthermore, large excision specimens for AS frequently harbor areas characteristic of AVL and AS has been reported to arise in patients with pre-existing AVL [3,6,7]. In contrast to the benign course of an AVL, AS frequently is metastatic with a grim median survival of 18 months [1]. Accurate diagnosis is therefore paramount. We present a case of a diagnostically challenging post-RT AVL on the temple of a young woman that was clinically and histopathologically concerning for AS. However, further tissue analysis following staged excision confirmed an AVL overlying a banal pilar cyst.

Case synopsis

A 23-year-old woman presented to the dermatology clinic with a painful nodule overlying the right temple. She reported that the lesion started as a red “pimple” three years prior; over the past year it had grown in size and would occasionally bleed. She denied a history of trauma to the area. Clinical examination revealed a solitary 2 cm erythematous to violet nodule with a central heme-crusted erosion on the right temple (Figure 1)

Her medical history was significant for a hypothalamic pilocytic astrocytoma, which developed in early childhood and was treated with 50 Gy of radiation. In her early 20s she developed a recurrent grade 3 astrocytoma, which was treated with chemotherapy and again with RT. Three and a half months after treatment she developed the painful cutaneous nodule in the area of radiation.

In light of the history of prior RT, and appearance of the lesion, a biopsy was performed to rule out a vascular neoplasm. A punch biopsy was performed, which revealed a vascular proliferation in the dermis composed of anastamosing and focally dilated vascular spaces (Figure 2A). The endothelial cells were hyperchromatic with focal "hobnail" features (Figure 2B). Multi-layering was not identified. ERG, CD34, and D240 (Figure 2C) stains highlighted the atypical cells, and Ki-67 marked less than 5% of the endothelial cells. These findings were consistent with an atypical vascular proliferation. A staged excision was performed and the deeper nodule removed proved to be a pilar cyst with a small focus of an atypical vascular proliferation at the border. Lateral and deep margins were negative for any residual atypical vascular proliferation.

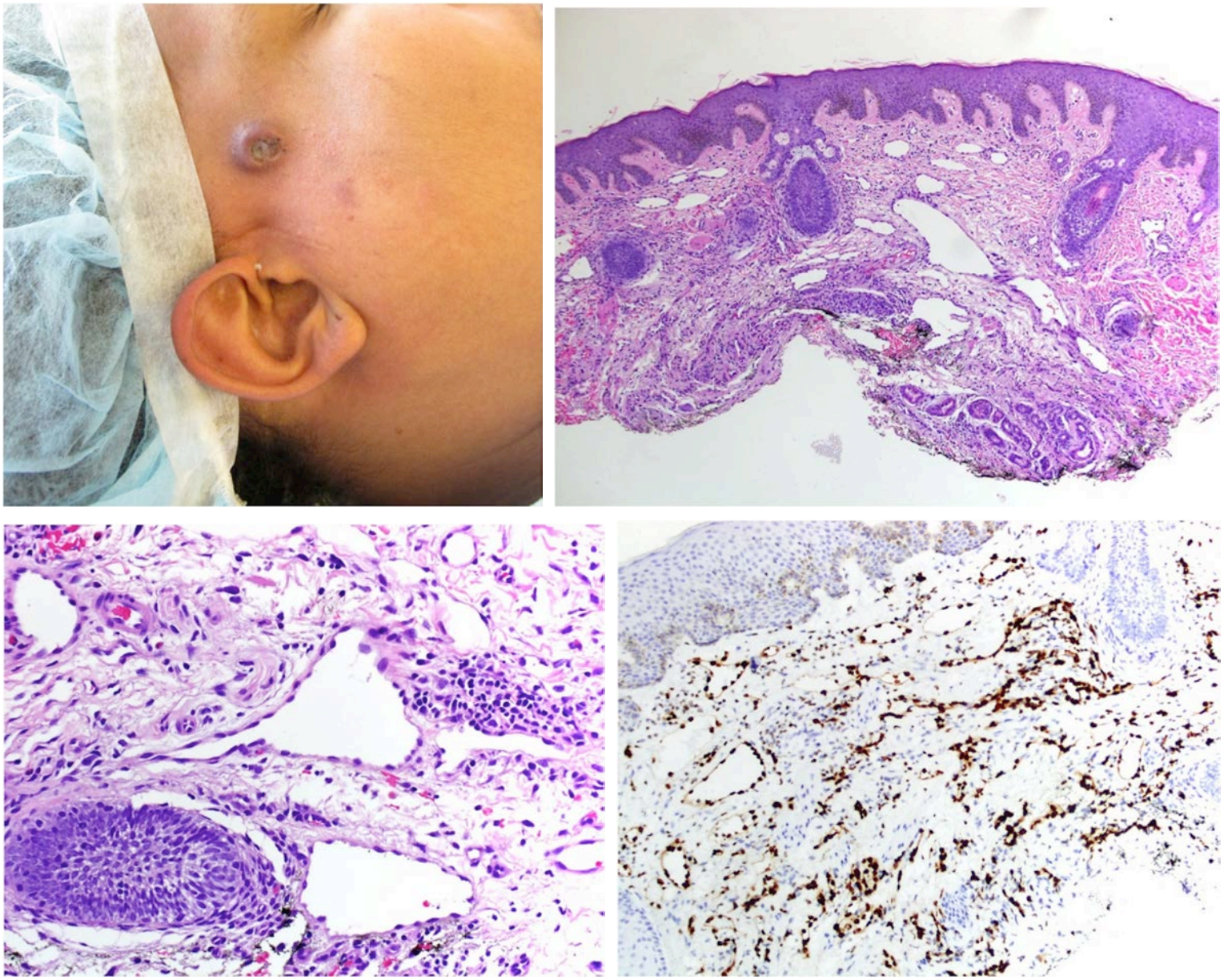

Figure 1. An erythematous nodule occurring on the temple after radiation therapy: A solitary 2 cm erythematous to violet nodule with a central heme-crusted erosion on the right temple. **Figure 2.** A vascular proliferation in the dermis: A, There is a vascular proliferation in the dermis composed of anastamosing and focally dilated vascular spaces (hematoxylin-eosin, original magnification ×50). B, The endothelial cells were hyperchromatic with focal "hobnail" features. Muti-layering was not identified (hematoxylin-eosin, original magnification ×200). C, D240 stains highlighted the atypical cells, and Ki-67 marked less than 5% of the endothelial cells (original magnification ×100).

Discussion

Cutaneous vascular lesions are well-established complications of RT [3,5,8,9,10]. The spectrum of postradiation vascular lesions ranges from benign AVLs to frank AS. With improved outcomes associated with RT, the incidence of post-radiation sarcomas and cutaneous vascular lesions in long-term cancer survivors is on the rise [2,7]. These lesions share overlapping clinical and histopathologic features. Therefore, dermatologists and pathologists must be cognizant of the challenges and pitfalls involved in distinguishing these.

The majority of cases of post-radiation AVLs are on the chest of women following RT for breast carcinoma. There are scattered reports following RT for gynecologic malignancy, multiple myeloma, bladder rhabodmyosarcoma, and tonsillar squamous cell carcinoma. To date, there have been no reports of AVLs on the head following RT for a pediatric brain tumor. Brain tumors constitute the second most common pediatric cancer and occur most commonly in the first decade of life. Radiation for pilocytic astroctyoma may be used in cases not amenable to surgery or for recurrent tumors, but once treated this pediatric brain tumor has an excellent overall survival [11]. Irradiated patients surviving into adulthood are at risk for developing AS and, as our case highlights, post-radiation AVLs.

The median age of onset of AS is 70 years [1,9], whereas patients diagnosed with AVL are on average at least one decade younger [3,4,5,12,13]. The skin of the chest wall is the most frequent site for both post-radiation AVLs and AS; both lesions are associated with a similar median radiation dosage of 40-60 Gy. Atypical vascular lesions have a median onset of three years after RT and they present as small, brown-to-erythematous papules or nodules that can occur singly or as multiple lesions [2,3,14]. In contrast, AS presents as large erythematous to violaceous plaques and arise with a later median interval of 6 years [5]. Our patient had received a median radiation dosage of around 50 Gy. The time course from prior radiation is difficult to say in this case because the area had been previously irradiated once for the primary tumor and again over a decade later for the recurrent tumor.

Atypical vascular lesions share several histologic features with AS. They exhibit an anastomosing growth pattern of vascular channels within the dermis with focal dissection of dermal collagen [2]. Unlike AS, they are well-circumscribed, somewhat wedge-shaped, confined to the mid to superficial dermis, and without extension into the subcutaneous tissue. Endothelial cell nuclei can be prominent and hyperchromatic, but there is no significant cytologic atypia or multi-layering. Mitoses, necrosis, and “blood lakes” are also absent. Although these features are helpful in distinguishing AVLs from AS, there are no absolute diagnostic features because both entities show varying degrees of morphologic overlap.

In a study of 56 post-radiation vascular lesions, Gengler et al reported that all lesions had a benign clinical course. They concluded that although they are morphologically similar, AVLs are distinct from AS [13]. Whereas most studies report post-radiation AVLs as benign, there are scattered cases of patients developing additional lesions within the radiation field, as well as of local recurrences and even progression to AS [5,7,12]. In their series of 32 post-radiation AVLs, Patton et al report that one lesion progressed over 5 yeas to a well-differentiated AS and one patient developed an aggressive AS after 14 months [12].

Irrespective of the true course of AVLs, distinguishing them from AS can pose quiet a challenge. In a study of cases diagnosed as AVL on initial biopsy, approximately half were reclassified as AS on re-excision [14]. Furthermore, both AVLs and AS can co-localize to the same irradiated field and their boundaries may overlap [5,12]. Therefore, any vascular lesion that occurs in a previously irradiated field should be completely excised with tumor-free margins for a histologic examination and diagnosis.

In light of the degree of clinical and histologic overlap between AVLs and AS, new methods to distinguish these entities are warranted. Amplification of c-myc is of interest because secondary AS demonstrates high levels of amplification, whereas post-radiation AVLs do not [15]. In patients who had an AVL and secondary AS adjacent to one another in the same irradiated field, FISH results were negative in the AVLs, but positive in the AS [15]. In our case, it was clear from the excision specimen that the lesion in question was an AVL, rather than an AS. However, had it not been clear with the excision specimen, we may have proceeded with c-myc analysis to help determine the diagnosis.

There are no standard guidelines for the management of AVLs. Characterization of the true nature of these lesions remains limited to small case series and reports. Therefore, dermatologists and pathologists should exercise caution when evaluating a vascular lesion arising on irradiated skin. Complete excision with negative margins is a prudent approach, with careful pathological evaluation to exclude a focus of AS. Patients should be followed clinically with re-biopsy of any recurrent or new lesions within the radiation field.

Conclusion

In summary, our case is important because it is the first we could find of an AVL occurring on the head following irradiation for a pediatric brain cancer. The diagnosis was not definitive on the initial biopsy specimen and thus underscores the need for a complete excision specimen when evaluating vascular lesions that arise on irradiated skin. Patients treated with RT are at risk for developing AVLs and AS. As pediatric cancer survivors enter adulthood, clinicians and pathologists must remain cognizant of this risk and the pitfalls of relying on partial biopsy alone for an accurate diagnosis.

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