A case of pleomorphic dermal sarcoma with perineural invasion treated with Mohs micrographic surgery and adjuvant radiation therapy

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Abstract

Pleomorphic dermal sarcoma (PDS) was recognized in the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone as a clinical entity with adverse histopathologic features compared to the more superficial and less aggressive atypical fibroxanthoma (AFX). Although the gold standard treatment of AFX is Mohs micrographic surgery (MMS), the optimal treatment for PDS has yet to be determined. We report the case of a 71-year-old man with a PDS with perineural invasion on the scalp, with no recurrence one-year post-treatment with MMS and adjuvant radiation therapy. In contrast to wide local excision, MMS offers complete margin control and tissue preservation, which helps minimize scarring and morbidity. The comparative efficacy of MMS versus wide local excision in the treatment of PDS with and without radiation remains unknown and warrants further investigation.

Keywords: atypical, cutaneous, dermal, fibroxanthoma, Mohs, pleomorphic, radiotherapy, sarcoma

Introduction

Atypical fibroxanthoma (AFX) and pleomorphic dermal sarcoma (PDS) are rare mesenchymal tumors that share many clinical, etiologic, genomic, and immunohistochemical features [1]. The two cutaneous neoplasms are believed to exist along a clinicopathologic spectrum. However, some authors believe that AFX represents a superficial variant of PDS or undifferentiated pleomorphic sarcoma and others consider it a distinct entity [1,2]. Both tumors most frequently occur on sun-damaged skin in elderly men, with a predilection for the scalp [3-5]. They typically present as rapidly-enlarging nodules that ulcerate and bleed [1,6]. Histologically, both AFX and PDS display dense cellularity with sheets of large, pleomorphic, atypical-appearing epithelioid and spindle cells with hyperchromatic nuclei and multiple nucleoli [3,7].

Despite the fact that PDS and AFX appear to be closely related, PDS have a more aggressive clinical and histologic phenotype [4,6]. A diagnosis of AFX requires that the tumor be confined to the dermis and lacks features such as necrosis or vascular invasion [4,8]. Histological criteria used to distinguish PDS from AFX include the following: deep subcutaneous invasion, invasion of fascia or muscle, tumor necrosis, lympho-vascular invasion (LVI), and perineural invasion (PNI), [6,8]. Pleomorphic dermal sarcomas have a greater propensity for local recurrence, distant metastases, and mortality than AFX [1].

Owing to the rarity of PDS, as well as its relatively recent recognition as a distinct clinical entity by the World Health Organization in 2013, there are a paucity of published reports describing PDS variants with aggressive features such as PNI [4,9]. Accordingly, the optimal management and prognosis of PDS with PNI is uncertain [3]. The current consensus is that the primary goal of PDS

treatment is to remove the tumor with clear surgical margins [7]. Wide local excision (WLE) of PDS has yielded varying rates of recurrence [4,5]. In a study of 32 cases of PDS treated with WLE, Miller et al. reported 28% local recurrence and 10% metastatic disease over a median follow-up of 24 months [4]. In a separate case series of 18 patients with PDS treated with WLE, Tardio et al. reported 20% local recurrence and 20% distant metastatic disease over a median follow-up of 33 months [5].

As a result of the high recurrence rates with WLE and the previous success of Mohs micrographic surgery (MMS) in treating closely related tumors such as AFX, MMS has been suggested for the management of PDS [7]. Few studies report the use of MMS for PDS [10]. In 2015, Fosko et al. reported the successful treatment of two cases of AFX with PNI using MMS and staged excision with Mohs-oriented tissue margins to minimize the likelihood of recurrence [11]. Using current histopathologic criteria and nomenclature, these two tumors would now be reclassified as PDS with PNI [4].

Adjuvant radiation therapy (RT) following WLE has also been suggested for the treatment of AFX with PNI, and more recently for the treatment of PDS variants with PNI and LVI involvement [3,12]. The efficacy of different treatment approaches for PDS remains unclear and there is insufficient evidence to provide clear recommendations [1,3]. Herein, we report the successful treatment of a scalp PDS with PNI and LVI using MMS and adjuvant RT.

Case Synopsis

A 71-year-old man with a dermatologic history of hypertrophic actinic keratoses and basal cell carcinomas presented with a 1cm hard, dome-shaped pink nodule on the left frontal scalp and a 1cm crusted plaque on the left lateral scalp (**Figure 1**). Both lesions had been enlarging in the few months prior to presentation, but the patient delayed seeking care due to the COVID-19 pandemic. No lymphadenopathy was present on examination. Shave biopsies of both lesions were performed and showed spindled cells with hyperchromatic and enlarged nuclei, arranged as intersecting fascicles

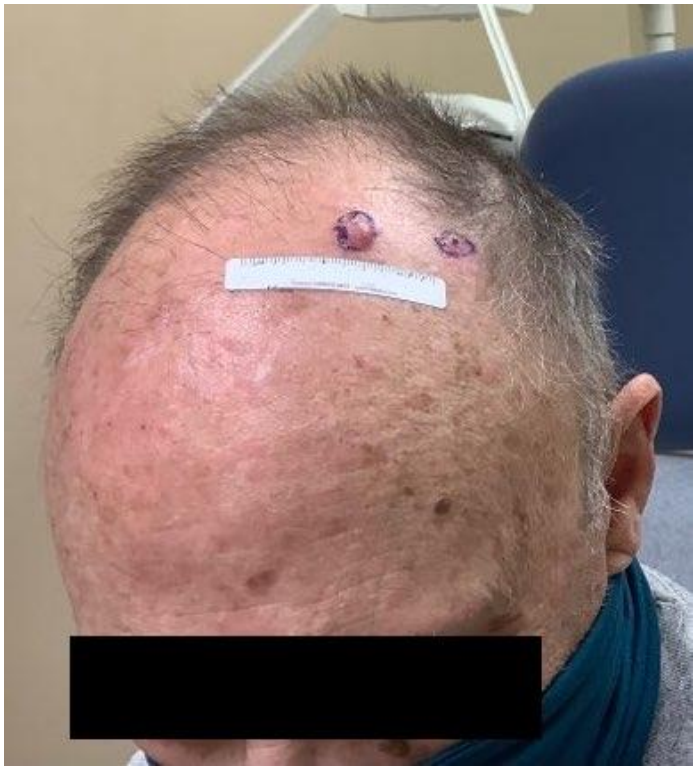

Figure 1. *Presenting lesions included a 1cm hard, dome-shaped pink nodule on the left frontal scalp and a 1cm firm, exophytic plaque on the left lateral scalp.*

consistent with AFX on the left frontal scalp (**Figure 2**), and aggregates of basaloid cells with hyperchromatic nuclei and peripheral palisading consistent with nodular basal cell carcinoma on the left lateral scalp. Both lesions were treated with MMS. Perineural invasion, LVI, and invasion into the subcutis were noted on the first stage of Mohs surgery, which were confirmed with permanent histopathologic sections (**Figure 3A**). Based on the defining criteria for PDS, the diagnosis was upgraded from AFX to PDS. Complete removal of the PDS with clear margins was obtained on the third stage of

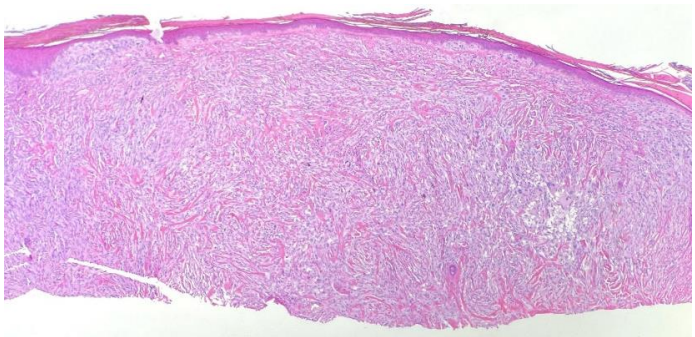

Figure 2. *H&E histopathology consistent with atypical fibroxanthoma, 5×.*

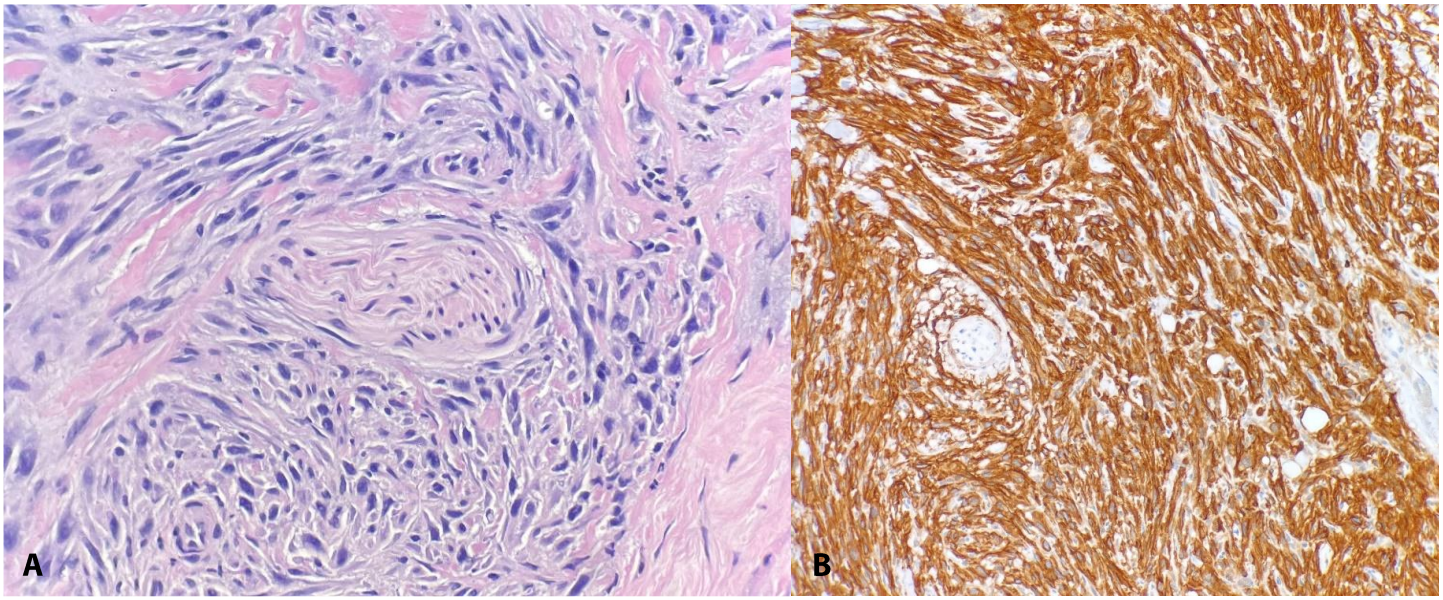

Figure 3. ***A)*** *H&E histopathology consistent with pleomorphic dermal sarcoma. Perineural invasion is noted, 40×.* ***B)*** *Positive immunohistochemical staining for CD10, 20×.*

MMS. Immunoperoxidase studies revealed reactivity for CD10 (**Figure 3B**) and CD68, but not for CK5/6, p63, AE1/AE3, 34bE12, SOX-10, S-100, Melan-A, desmin, or CD34. Computerized tomography scan with and without contrast of the head and neck revealed an intact bony calvarium and no significant lymphadenopathy. Due to the observed PNI and proximity to blood vessels, adjuvant electron beam radiation therapy at a dose of 5000cGy in 20 fractions, with a 1.0cm bolus over the entire field was administered. The radiotherapy was tolerated well by the patient, despite development of radiation dermatitis. Approximately three months after the final RT session, two squamous cell carcinomas (SCC) in situ were diagnosed on the right superior medial forehead and right medial frontal scalp. Both were successfully treated with MMS. One-year post-Mohs and radiation, there has been no evidence of PDS recurrence.

Case Discussion

Diagnostic challenges

Atypical fibroxanthoma and PDS are closely related tumors that can be difficult to differentiate clinically from SCC, basal cell carcinoma (BCC), and melanoma [1,4, 5,13]. Atypical fibroxanthoma and PDS vary in appearance from non-descript papules and plaques to red or pink ulcerated nodules [4,14]. Additionally, history of other skin cancers is relatively common in patients with AFX and PDS, which can bias the clinical assessment [15]. In our case, the patient had a history of basal cell carcinoma and presented with a hard, rapidly enlarging, 1cm dome-shaped nodule with a smooth, shiny pink surface. Given the patient history and prevalence, BCC or SCC were considered to be more likely than the less common AFX or PDS. However, shave biopsy results showed superficial histopathologic findings consistent with AFX. Shave biopsies are limited in their ability to differentiate AFX from more aggressive PDS variants. In clinical practice, more prevalent tumors such as BCC and SCC may be favored in the differential diagnosis of smaller skin lesions that clinically resemble AFX or PDS, resulting in shave biopsies which do not sufficiently differentiate AFX from deeper, more aggressive PDS. Therefore, if there is suspicion for a cutaneous PDS, a deeper biopsy should be favored to facilitate accurate diagnosis and prevent recurrence [4].

In this case, immunohistochemical staining helped to confirm the PDS diagnosis. Immunoperoxidase studies revealed reactivity for CD10 and CD68. The tumor was negative for CK5/6, p63, AE1/AE3, 34bE12, SOX-10, S-100, Melan-A, desmin, and CD34, helping

to exclude SCC, melanoma, leiomyosarcoma, and dermatofibrosarcoma protuberans.

Management challenges

Aggressive PDS variants present a management dilemma for clinicians due to a lack of evidence-based recommendations [3]. We report the successful treatment of a scalp PDS with PNI using MMS and adjuvant RT. Although WLE has been used for the treatment of PDS, it is associated with a relatively high recurrence rate [7]. It has been suggested that treatment with MMS may result in better outcomes [11]. Unlike WLE, MMS offers complete margin control and tissue preservation, resulting in lower recurrence rates and less morbidity when used to treat other cutaneous malignancies. Several studies have demonstrated the advantages of MMS compared to WLE in the treatment of the closely-related AFX. In a study of 91 patients with AFX, MMS resulted in superior tissue preservation, with the median amount of tissue removed with MMS being significantly less than that removed with WLE (0.4 versus 1.0cm), [13]. Further analysis showed that a 2cm margin would be needed to ensure clearance of over 95% of AFX with WLE, an unfavorable margin for tumors of the head and neck. Comparatively, the median margin needed to clear AFX with MMS was 0.4cm [13]. Thus, MMS may reduce tissue loss, scarring, and morbidity in cosmetically sensitive areas [5,12,13]. Further, a systematic review and meta-analysis including 914 cases of AFX reported a recurrence rate of 8.7% for WLE and 2% for MMS [2]. While there are sparse publications detailing the use of MMS for PDS, it is important to note that many tumors previously diagnosed as aggressive AFX and included in prior publications would now be reclassified as PDS according to current diagnostic criteria [1,13,16].

There is insufficient published evidence describing the role of RT in PDS management [3]. Lonie et al. suggested that RT may be useful in the management of PDS [3]. It was reported that PDS recurred in one of 18 patients treated with RT versus one of 9 patients treated without RT [3]. There is only one published report of MMS and adjuvant RT for the treatment of PDS, but the effect was uncertain as RT was discontinued after four sessions due to patient preferences [10]. The efficacy, optimal dosing, fractionation, type, and frequency of adjuvant RT for MMS-treated PDS have not been clearly described in the literature [1]. In our case, the patient received adjuvant RT approximately two months post-MMS. The patient was treated with electron beam therapy with a dose of 5000cGy in 20 fractions, with a 1.0cm bolus over the entire field. The patient tolerated the treatment despite the development of radiation dermatitis. It is unclear if the RT contributed to the development of the SCCs in situ on the forehead and scalp. The risk of nonmelanoma skin cancer is higher in patients who receive RT, with an approximate latency period of 20 years between the first exposure of radiation and the appearance of secondary nonmelanoma cutaneous malignancies [17].

Conclusion

We report the management of PDS with PNI using MMS and adjuvant RT, with no recurrence one-year post treatment. The comparative efficacy of MMS and WLE, alone or in combination with RT in the treatment of aggressive PDS variants warrants further investigation.

Potential conflicts of interest

The authors declare no conflicts of interest.

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