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Pitfall regarding expression of ETS-related gene (ERG) in fibrohistiocytic neoplasms

Ben J. Friedman

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NOTES AND COMMENTS

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I read with great interest the recent paper entitled "*EWSR1-SMAD3* rearranged fibroblastic tumor: Case series and review," which is the largest case series to date reviewing the histopathological features of this newly described entity.[1] Dermatopathologists should welcome this contribution given the common occurrence of spindled cell tumors that are difficult to precisely classify in clinical practice. Furthermore, the authors provide a nice overview of the differential diagnosis for this tumor in Table 2 and cite two other papers discussing potential mimickers.[2,3]

I find it interesting that none of the groups that have published on *EWSR1-SMAD3* rearranged fibroblastic tumor (ESFT) have included cellular fibrous histiocytoma in the differential diagnosis. Certainly, there appear to be morphological/architectural features which may in some circumstances assist in discriminating the two (notably the zonation with foci of hyalinization) on a complete excision. However, many of the biopsy specimens that dermatopathologists receive are superficial samples and the presence of spindled cells in hypercellular, well-organized, and intersecting fascicles can be seen in cellular fibrous histiocytoma. Moreover, fibrous histiocytoma can arise on acral surfaces, is easily the most commonly biopsied fibrous tumor of the skin, and may not reliably stain for commonly used fibrohistiocytic markers on immunohistochemistry.

The authors emphasize that ETS-related gene (ERG) is uniformly expressed in ESFT in contrast to many of the other entities on the differential diagnosis. There is a paucity of literature regarding ERG expression in fibrohistiocytic proliferations in general, though we recently encountered an acral cellular fibrous histiocytoma at our institution that demonstrated strong and diffuse staining for ERG (Figure 1). Moreover, given the lack of expression of other commonly used markers in this setting (Fac13a, CD34, SMA, CD163, CD68) a next-generation sequencing panel was ordered, which failed to detect the *EWSR1-SMAD3* translocation. There is one published abstract

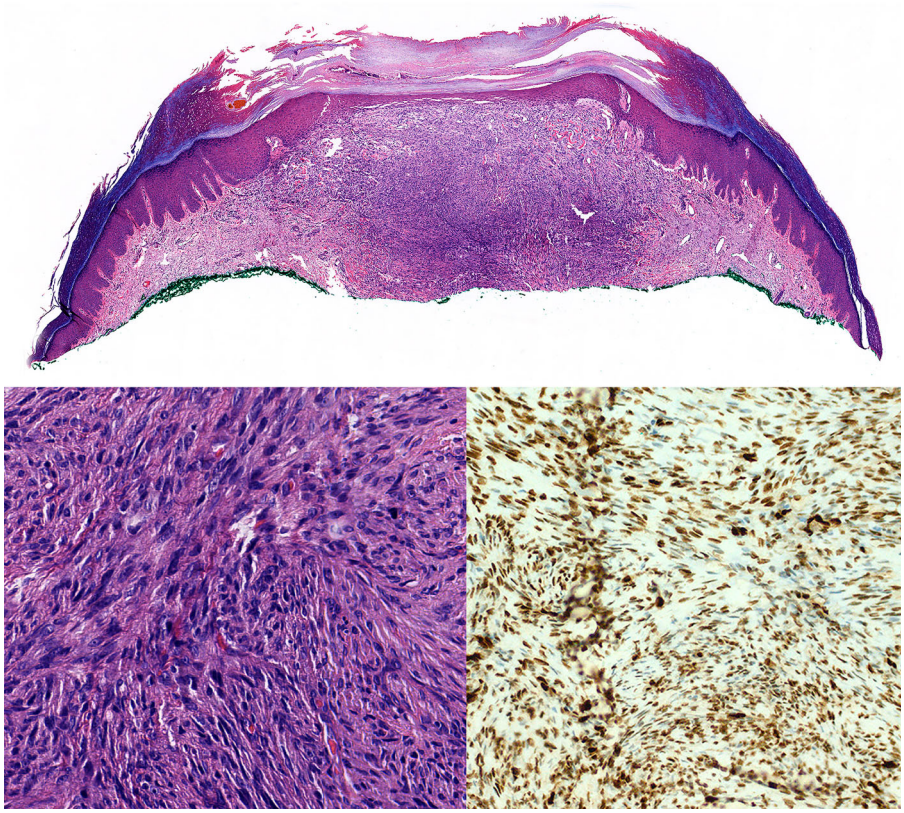

FIGURE 1 Top panel demonstrates a dermal-based proliferation of spindled cells in fascicles pressed up against the epidermis with peripheral collagen trapping (hematoxylin and eosin [H&E], ×40, original magnification). Lower right panel shows relatively monomorphous plump spindled cells in hypercellular fascicles (H&E, ×200, original magnification). Lower left panel shows intense expression of ERG (H&E, ×200, original magnification)

which reported consistent expression of ERG in fibrous histiocytoma and giant cell tumor of the tendon sheath.[4] Moreover, it is well established that some case of epithelioid sarcoma express ERG.[5] If additional neoplasms of fibrohistiocytic origin are found to express ERG, it would become a much less helpful adjunct in this setting. This would be important to establish to mitigate the use of costly sequencing panels.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Ben J. Friedman MD[1,2]

[1]*Department of Dermatology, Henry Ford Health System, Detroit, Michigan*

[2]*Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan*

Correspondence

Ben J. Friedman, MD, Department of Dermatology, Henry Ford Health System, 3031 West Grand Blvd, Ste 800, Detroit, MI 48202, USA.

Email: bfriedm1@hfhs.org

ORCID

Ben J. Friedman https://orcid.org/0000-0002-2266-8197

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