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Reflectance confocal microscopy features of facial angiofibromas

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ABSTRACT Facial angiofibromas are benign tumors presenting as firm, dome-shaped, flesh-colored to pink papules, typically on the nose and adjoining central face. Clinically and dermoscopically they can mimic melanocytic nevi or basal cell carcinomas (BCC). Reflectance confocal microscopy (RCM) is a non-invasive imaging tool that is useful in diagnosing melanocytic and non-melanocytic facial lesions. To date no studies have described the RCM features of facial angiofibromas. Herein, we present two cases of facial angiofibromas that were imaged with RCM and revealed tumor island-like structures that mimicked BCC, leading to skin biopsy.

Cases

Two women in their fifties presented with a bleeding lesion on their nose. At clinical examination, they presented as small pink papules; one was soft and one was firm on palpation. Polarized dermoscopy revealed a structureless whitish-pink background in both lesions, and an erosion was present in one case (Figure 1A). Due to the curvature of the face, a handheld reflectance confocal microscope (Vivascope 3000, Caliber I.D., Rochester, NY) was used. An adhesive paper ring was placed surrounding the lesion to guide RCM navigation [1]. The indication for RCM was to exclude BCC due to occasional bleeding. Other differential diagnoses included irritated angiofibroma, intradermal nevus, and adnexal neoplasm.

Reflectance confocal microscopy (RCM) showed a regular epidermal honeycombed pattern with BCC-like structures identified at the dermal-epidermal junction and papillary dermis (Figure 1C). These structures varied in size and shape and had increased cellular density compared to hair follicles. Many had clefting (dark signal-void region) around them. In the papillary dermis, abundant thick collagen bundles were identified mainly around hair follicles (Figure 1C). Addition-

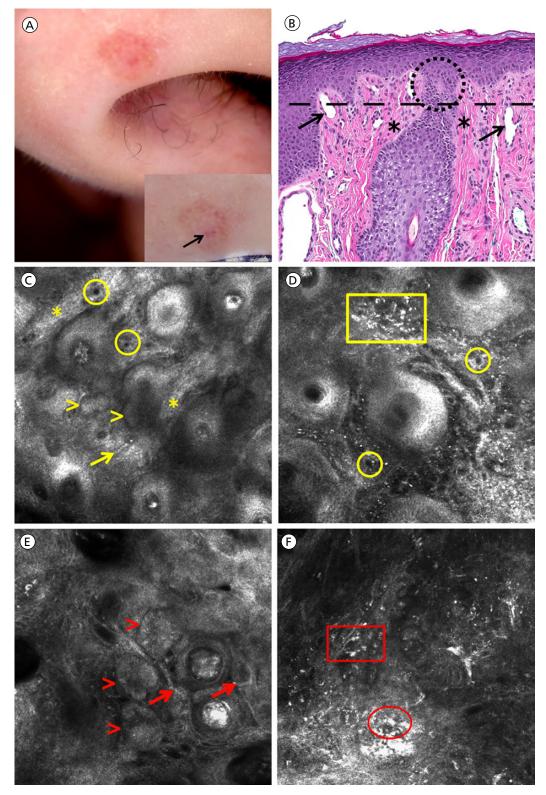


Figure 1. Clinical image of an irritated angiofibroma located on the nose (panel A) showing a superficial erosion and a whitish-reddish background on dermoscopy (arrow, inset). Corresponding hematoxylin and eosin stained histology (panel B; 20X) of angiofibroma showing dilated vessels (arrows), and abundant thick collagen bundles surrounding hair follicles (asterisks) and inflammatory cells (histiocytes and lymphocytes) in the stroma. The area encircled in panel B shows the superficial portion of external root sheath of hair follicle surrounded by thickened collagen (asterisks), which could have been the source of BCC-like nodular structures. RCM images of angiofibroma (panels C and D; ~0.75 mm x 0.75 mm) taken at dermoepidermal junction (corresponding to the level of black dashed line on panel b) shows BCC-like nodular structures with clefting but no palisading (yellow arrowheads, panel C), thick collagen bundles surrounding hair follicles (asterisks, panel C), horizontal linear vessels (arrow, panel C), numerous vertical round vessels (circles, panels C and D), and numerous small bright cells and angulated cells corresponding to lymphocytes and histiocytes, respectively (yellow rectangle, panel D). Conversely, RCM images of basal cell carcinoma (panels E and F; ~0.75 mm x 0.75 mm; taken from a separate case) show tumor nodules with clefting and palisading (red arrowheads, panel E), horizontal canalicular vessels (red arrows, panel E), and an inflammatory stroma with numerous small bright cells (red rectangle, panel F) and plump bright cells (red ellipse, panel F). [Copyright: ©2017 Millán-Cayetano et al.]

		Angiofibroma		Basal cell carcinoma	
		Reflectance confocal microscopy	Histopathology	Reflectance confocal microscopy	Histopathology
Epidermis		• Normal epidermis with regular honeycomb pattern	• Normal epidermis	 Epidermal streaming Variable epidermal disarray 	 Keratinocytes focally elongated along the same axis Variable epidermal pleomorphism
DEJ and superficial dermis	Aggregates	• Nodules with increased cellular density and occasional clefting (BCClike structures)	• Epidermal invagination in the papillary dermis or superficial portion of external root sheath of hair follicle	 Tumor islands Cordlike structures with palisading Clefting Dark silhouettes 	 Tumor nodules comprised of atypical basaloid cells with peripheral palisading Cords of atypical basaloid cells Peritumoral mucin/clefting Aggregates of tumor cells
	Vascularization	• Small round to linear and canalicular vessels	• Increased vascularization with variablysized dilated blood vessels	• Horizontal "enface" canalicular vessels with leukocyte rolling/trafficking	• Prominent, dilated and enlarged blood vessels
	Collagen	• Thickened collagen bundles surrounding hair follicles and BCClike structures	• Thickened collagen bundles arranged around hair follicles	 Gossamer like stroma wrapping around tumor islands 	• Myxoid stroma wrapping around tumor nodules
	Stroma	• Small bright round cells	• Lymphocytes	 Numerous large plump cells Dendritic cells Small bright round cells 	 Melanophages Langerhans cells Melanocytes Lymphocytes

TABLE 1. Reflectance confocal microscopy features observed in angiofibromas, comparing to those observed in BCC and histopathological correlation.

Abbreviations: DEJ, dermal-epidermal junction; BCC, basal cell carcinoma

ally, numerous small round (vertical) to linear and canalicular (horizontal) dilated blood vessels were seen (Figure 1C and D), as well as small bright round cells (inflammatory cells) and angulated bright cells (Figure 1D). Large plump cells (melanophages) and palisading were not identified. These findings were correlated with histopathology (Table 1).

Conclusions

Facial angiofibromas can sometimes mimic melanocytic nevi or basal cell carcinomas (BCC) under clinical and dermoscopic evaluation [2]. Reflectance confocal microscopy is useful in diagnosing melanocytic and non-melanocytic facial lesions [3,4] and can be helpful in diagnosing facial angiofibromas that are diagnostically challenging. Favia et al have previously described the *ex vivo* confocal findings of a gingival angiofibroma in a patient with tuberous sclerosis [5]. They reported the presence of variably sized vessels with dilated lumina and collagen fibers with random orientation [5].

In our cases, we found structures mimicking BCC due to increased cellular density and clefting. However, unlike BCC, peripheral palisading (Figure 1E) was absent. Using vertical stacks (going from the dermis to the epidermis) we identified continuation between some BCC-like structures and hair follicles. Further, the stroma of angiofibromas lacked typical BCC features such as gossamer collagen, numerous horizontal vessels with leukocyte trafficking, and melanophages (Figure 1F). Histologically, angiofibromas are dermal proliferations containing dilated vessels, fibrosis surrounding hair follicles, stellate fibrocytes and distorted hair follicles (Figure 1B) [6,7]. We speculate that the BCC-like structures on RCM represent the base of a rete ridge, a portion of a hair follicle or another adnexal structure that due to the intense perifollicular collagen proliferation could show clefting. We also identified angulated large bright cells, which appeared smaller than melanophages and could correspond to stellate/ spindled fibrocytes [7]. The density of inflammatory cells (bright small round cells) could have been a result of irritation. A comparison between the RCM and histologic features present in our angiofibroma cases and the BCC features are summarized in Table 1.

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