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A quiz from Manaus, Brazil

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Citation: de Miranda MFR, Schettini APM, Lobato LC, da Silva Jr RC, de Morais PM, Bittencourt MJS. A quiz from Manaus, Brazil. Dermatol Pract Concept 2015;5(4):5. doi: 10.5826/dpc.0504a05

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The patient

An otherwise healthy 34-year-old Brazilian male presented with an asymptomatic, slow-growing lesion on his left malar region for six months. No previous personal or familial similar findings were known. On examination, there was a well-circumscribed, raised, pink, telangiectatic, smooth nodule of hard consistency, measuring 1.2 x 1.2 cm in its base (Figure 1A). An excisional biopsy with clear margins was carried out. Additional select histopathologic pictures are depicted (Figures 1B, 2A-G, 3).

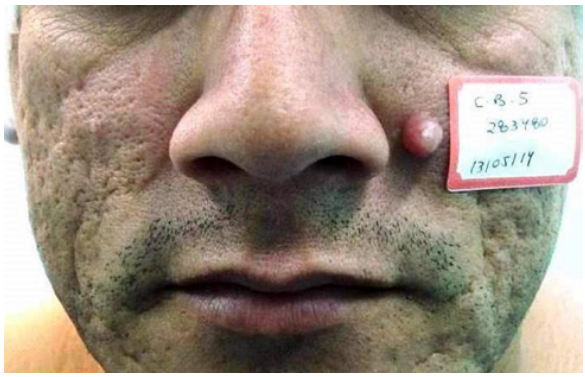

Figure 1A. Nodular lesion over a background of acne scars. [Copyright: ©2015 Miranda et al.]

What is your diagnosis?

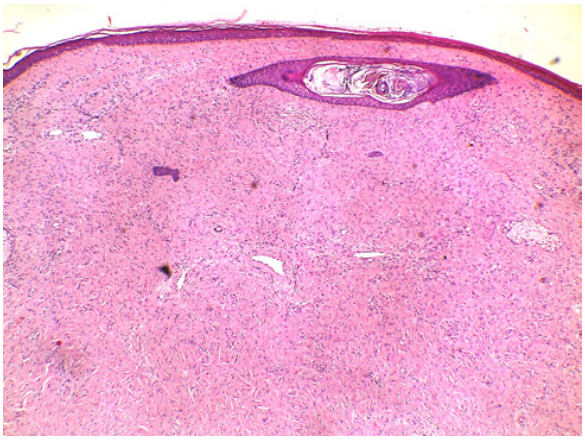

Figure 1B. Hyper- (top) and hypocellular (bottom) areas with clefts. Note atrophic epidermis, Grenz zone and a dilated entrapped follicle (H&E x40). [Copyright: ©2015 Miranda et al.]

Answer and explanation

Sclerotic fibroma

A sharply circumscribed, mostly hypocellular, non-encapsulated, spindle cell proliferation, expanded to the deep dermis, along with hyalinized collagen and clefts, arranged in a storiform/whorled (so-called "plywood"-like) pattern is in concert

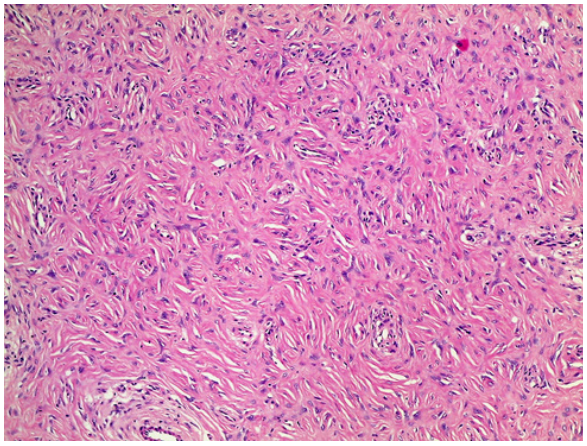

Figure 2A. Stromal clefts and spindle cells in storiform and whorled fashions (H&E x100). [Copyright: ©2015 Miranda et al.]

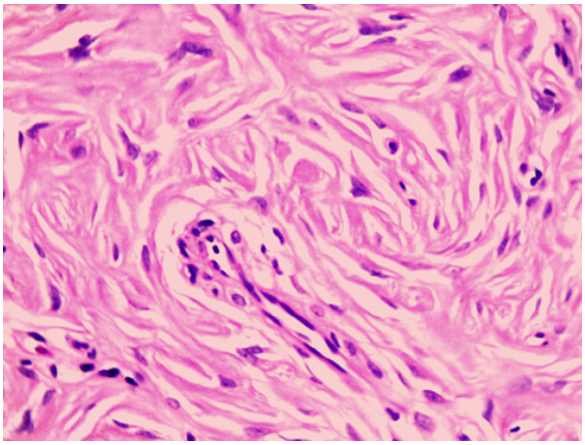

Figure 2B. Hypocellular area with fusiform and stellate-shaped neoplastic cells in sclerotic collagen (H&E x400). [Copyright: ©2015 Miranda et al.]

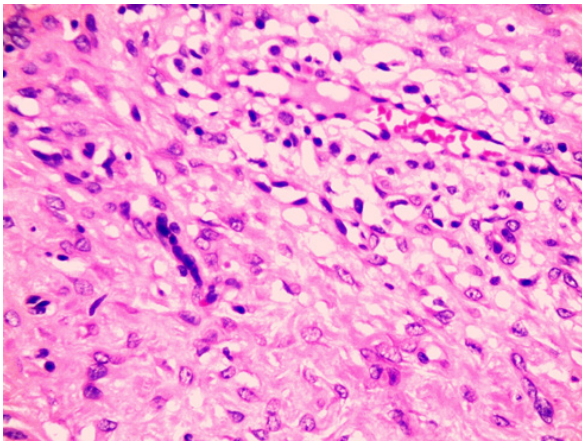

Figure 2C. Histiocytoid cells with plump nuclei, some showing multinucleation, are seen in the uppermost part of the lesion (H&E x400). [Copyright: ©2015 Miranda et al.]

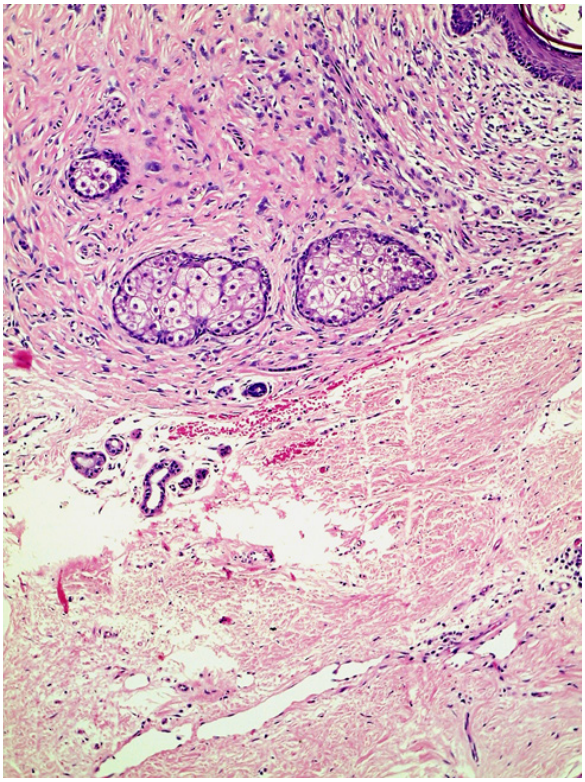

Figure 2D. Sharp demarcation of the lesion from the surrounding dermal tissue (H&E x40). [Copyright: ©2015 Miranda et al.]

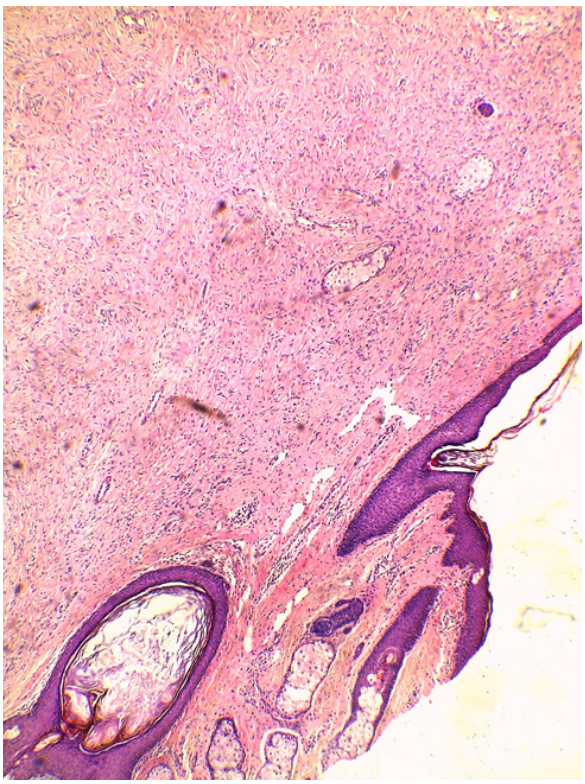

Figure 2E. Epidermal collarette (H&E x40). [Copyright: ©2015 Miranda et al.]

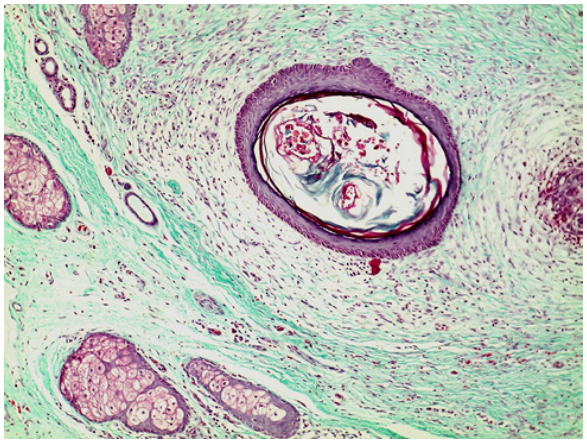

Figure 2F. Discrete condensation of the surround collagen and presence of a dilated follicular structure included in the neoplastic proliferation, in which vellus hair shafts are seen (Gomori's trichrome stain x100). [Copyright: ©2015 Miranda et al.]

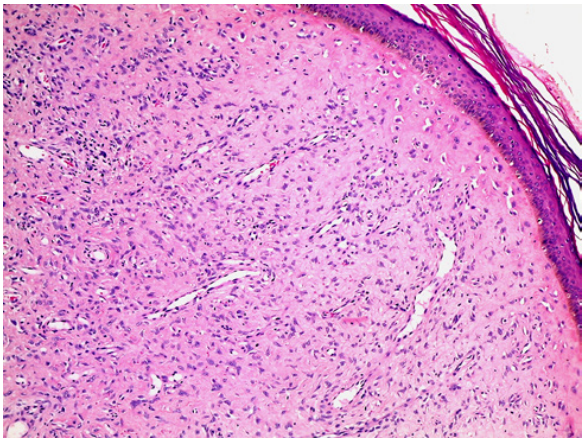

Figure 2G. Spindle and histiocytoid cell proliferation in a sclerotic stroma along with ectatic vessels (H&E x100). [Copyright: ©2015 Miranda et al.]

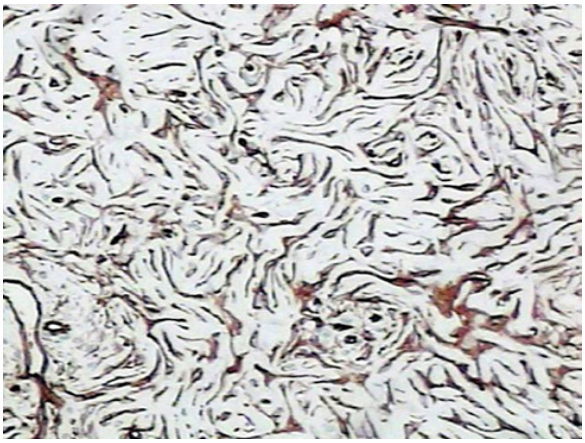

Figure 3. Diffuse CD34 expression by neoplastic cells (immunoperoxidase x100). [Copyright: ©2015 Miranda et al.]

with **sclerotic fibroma** (SF) [1-3]. Immunohistochemically the neoplastic cells showed diffuse reactivity to CD34 (Figure 3), but negative staining with S-100 protein, desmin, smooth muscle actin and D2-40. Taking into account morphologic and immunohistochemical features observed in our case, dermatofibroma, fibrous papule/angiofibroma, scar, keloid, dermatofibrosarcoma protuberans, giant cell fibroblastoma, solitary fibrous tumor, hemangiopericytoma, Kaposi's sarcoma, sclerosing perineurioma, dermal lipoma, end-stage of an inflammatory condition, pleomorphic fibroma and sclerotic fibroma have been considered in the differential diagnosis.

Dermatofibroma (DF) may exhibit hyaline and hypocellular areas. According to some authors, SF could represent an ancient or degenerated stage of DF [4,5], but lacks other classical architectural signs of it, as preferential limb location, hyperplastic epidermis, infiltrative growth pattern, sometimes basaloid follicular induction and basal hyperpigmentation. In contrast to DF, SF affects mainly the face, shows an expansile growth pattern and a sharp circumscription, but no acanthosis or basaloid follicular induction [2]. Besides DF, an involutional sclerotic stage of other pre-existing inflammatory, hamartomatous or neoplastic lesion such as angiofibroma, neurofibroma, melanocytic nevus, lipoma, tendon sheath fibroma (which is never dermal), giant cell collagenoma, erythema elevatum diutinum, solitary myofibroma and chronic folliculitis had been also considered [6,7]. In addition, although some of the above-mentioned SF attributes may be observed in DF, CD34 staining is usually absent in the latter [2,8,9].

Multinucleated and stellate-shaped cells, dilated vessels and collagen bundles oriented around hair follicles are seen in **fibrous papules/angiofibromas**, but hyalinization and cleft formation are not expected features [10].

As fibrosis was not oriented in parallel to the epidermis in this case, a scar has easily been excluded. Although the hyalinizing process seen in keloids share striking similarities with SF, these sclerosing lesions lacked the "plywood"-like pattern characteristic of SF [11].

Dermatofibrosarcoma protuberans (DFSP) is a malignant mesenchymal neoplasm of low metastatic potential. In contrast to SF, it shows infiltration of the subcutis and poor circumscribed margins. Moreover, hyalinized areas are usually absent, and one observes a denser cellularity. Expression of CD34 is used as an ancillary help to the differential diagnosis of DFSP with other cutaneous spindle cell neoplasms [8]. **Giant cell fibroblastoma** (GCF) is closely related to DFSP sharing the same cytogenetic abnormality involving genes COLIA1 on chromosome 17 and PDGFB on chromosome 22 [8]. GCF primarily affects children, presenting as a subcutaneous mass composed of a hypocellular proliferation of spindle-shaped cells and scattered giant cells with multiple

nuclei conglomerated toward the center or arranged peripherally. The stroma may vary from myxoid to collagenous to sclerotic. Angioectoid lymphangioma-like spaces and immunoreactivity with CD34 are also seen [12].

Solitary fibrous tumor (SFT) of the skin is a very uncommon lesion consisting of alternating hypercellular and hypocellular areas of bland spindle cells, arranged in a combination of fascicular, storiform and hemangiopericytoma-like vascular patterns in thick hyalinized collagen. Like SF, SFT is diffusely CD34 positive. Subsets of **hemangiopericytoma** (HP) and SFT are closely related neoplasms (HP/SFT family). HP may present with either positive or negative D2-40 immunostaining [13].

Areas of diffuse proliferation of spindle cells intermingled with vessels, as observed in the present case (Figure 2G), also recommended the exclusion of **Kaposi's sarcoma** (KS), in which a typical morphology and D2-40 positivity would be expected to occur [14]. KS is also often positive to anti-HHV8.

Sclerosing perineurioma (SP), like SF, show hypocellular areas, however, usually occurs on hands and feet, and does not react with CD34 [15]. **Dermal lipoma** with prominent sclerosis may simulate a SF, but mature adipocytes are always demonstrated in the former lesion [16]. Focal changes simulating SF may also be seen in inflammatory conditions such as **erythema elevatum diutinum** and **folliculitis** [17].

Many histological and immunohistochemical features present in a **pleomorphic fibroma** (PF), as dermal circumscription, epidermal atrophy, expansile growth pattern, and prominent clefted "plywood" appearance, were focally seen in one series [1]. The term "pleomorphic SF" (PSF) was further coined for lesions presenting histological features of PF in the superficial portion of the dermal nodule, SF features in the deeper portion, and positive or negative CD34 immunolabeling. Based on these findings, it has been proposed that PF, PSF and SF are components of one spectrum [1,10].

SF—also known as storiform collagenoma, hypocellular fibroma and "plywood" fibroma—is an uncommon benign neoplasm with fibroblastic/dermal dendrocytic differentiation first described in association with Cowden's disease, an autosomal-dominant familial cancer syndrome (multiple hamartoma and neoplasia syndrome) involving the PTEN tumor suppressor gene on chromosome 10q; in such cases, SF often occurs as multiple papules or nodules either on the oral mucosa or the skin [4,10,16,17]. Clinically SF is an asymptomatic, dome-shaped and well-circumscribed lesion of hard consistency [17]. Further SF cases, mostly solitary and on the skin, were observed in patients not affected by Cowden's disease [9].

In conclusion, we believe our patient has fulfilled chief histopathological criteria, including CD34 reactivity (Figure 3) [1,8], for a diagnosis of SF to be made. We also speculate our case could be inserted into the mid-portion of the spectrum PF/PSF/SF. The presence of follicle remnants [18] seen in the histopathologic picture (Figures 1B, 2F), a finding in general not referred for SF [6], cannot rule out the role of an eventual previous inflammatory trigger for this case, such as acne or folliculitis.

Acknowledgments

The authors wish to acknowledge Consultoria em Patologia staff, Botucatu, SP, Brazil, for their excellent technical assistance in performing immunohistochemical stains.

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