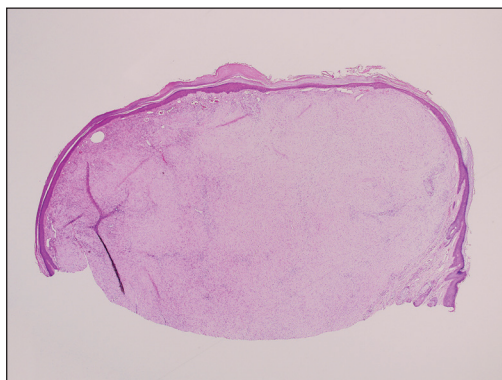


# Solitary Papule on the Nose

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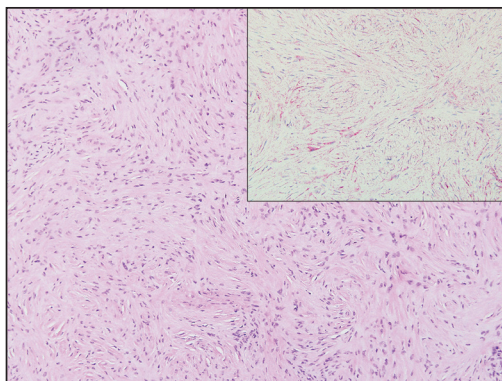
H&E, original magnification  $\times 20$ .

A 25-year-old man presented with a flesh-colored papule on the left side of the nose of 2 years' duration.

## THE BEST DIAGNOSIS IS:

- desmoplastic nevus
- fibrous papule
- palisaded encapsulated neuroma
- sclerosing perineurioma
- sclerotic fibroma

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H&E, original magnification  $\times 100$  (epithelial membrane antigen, original magnification  $\times 200$  [inset]).

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The authors report no conflict of interest.

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## THE DIAGNOSIS: Sclerosing Perineurioma

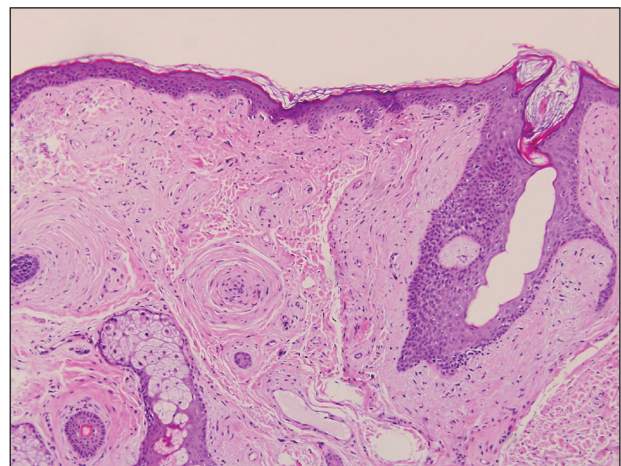
Sclerosing perineurioma, first described in 1997 by Fetsch and Miettinen,<sup>1</sup> is a subtype of perineurioma with a strong predilection for the fingers and palms of young adults. Rare cases involving extra-acral sites including the forearm, elbow, axilla, back, neck, lower leg, thigh, knee, lips, nose, and mouth have been reported.<sup>2-4</sup> Perineurioma is a relatively uncommon and benign peripheral nerve sheath tumor with exclusive perineurial differentiation.<sup>5</sup> Perineurioma is divided into intraneural and extraneural types; the latter are further subclassified into soft tissue, sclerosing, reticular, and plexiform types. Other rare forms include the sclerosing, Pacinian corpuscle-like perineurioma, lipomatous perineurioma, perineurioma with xanthomatous areas, and perineurioma with granular cells.<sup>6,7</sup>

Clinically, sclerosing perineurioma usually presents as a solitary lesion; however, rare cases of multiple lesions have been reported.<sup>8</sup> Our patient presented with a solitary papule on the nose. Histopathologically, sclerosing perineurioma demonstrates slender spindle cells in a whorled growth pattern (onion skin) embedded in a hyalinized, lamellar, and dense collagenous stroma with intervening cleftlike spaces. Immunohistochemically, the spindle cells of our case stained positive for epithelial membrane antigen (quiz images). Other positive immunostains for perineurioma include claudin-1 and glucose transporter 1 (GLUT1). Perineurioma lacks expression of S-100 but can express CD34.<sup>2</sup> As a benign tumor, the prognosis of sclerosing perineurioma is excellent. Complete local excision is considered curative.<sup>1</sup>

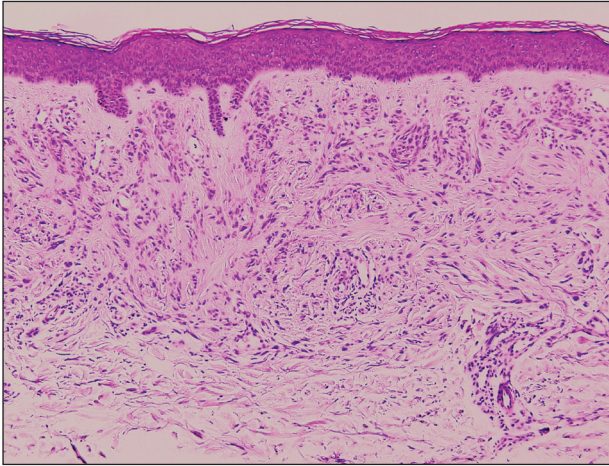
Angiofibroma, also known as fibrous papule, is a common and benign lesion located primarily on or in close proximity to the nose.<sup>9</sup> Angiofibromas can be associated with genodermatoses such as tuberous sclerosis, multiple endocrine neoplasia type 1, or Birt-Hogg-Dubé syndrome. When angiofibromas involve the penis, they are called pearly penile papules. Ungual angiofibroma, also known as Koenen tumor, occurs underneath the nail.<sup>10-12</sup> Both facial angiofibromas ( $\geq 3$ ) and unguinal angiofibromas ( $\geq 2$ ) are independent major criteria for tuberous sclerosis.<sup>13</sup> Clinically, angiofibroma presents as a small, dome-shaped, pink papule arising on the lower portion of the nose or nearby area of the central face. Histopathologically, angiofibromas classically demonstrate increased dilated vessels and fibrosis in the dermis. Stellate, plump, spindle-shaped, and multinucleated cells can be seen in the collagenous stroma. The collagen fibers around hair follicles are arranged concentrically, resulting in an onion skin-like appearance. The epidermal rete ridges can be effaced (Figure 1). Increased numbers of single-unit melanocytes

along the dermoepidermal junction can be seen in some cases. Immunohistochemically, a variable number of spindled and multinucleated cells in the dermis stain with factor XIIIa. There are at least 7 histologic variants of angiofibroma including hypercellular, pigmented, inflammatory, pleomorphic, clear cell, granular cell, and epithelioid.<sup>9,14</sup>

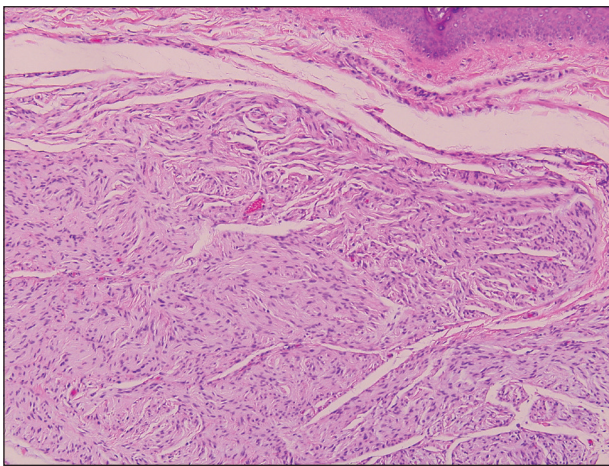
Desmoplastic nevus (DN) is a benign melanocytic neoplasm characterized by predominantly spindle-shaped nevus cells embedded within a fibrotic stroma. Although it can resemble a Spitz nevus, it is recognized as a distinct entity.<sup>15-17</sup> Clinically, DN presents as a small and flesh-colored, erythematous or slightly pigmented papule or nodule that usually occurs on the arms and legs of young adults. Histopathologically, DN demonstrates a dermal-based proliferation of spindled melanocytes embedded in a dense collagenous stroma with sparse or absent melanin deposition. The collagen bundles often show artifactual clefts and onion skin-like accentuation around vessels. Melanocytes may be epithelioid (Figure 2).<sup>16</sup> Immunohistochemically, DN expresses melanocytic markers such as S-100, Melan-A, and human melanoma black 45, but epithelial membrane antigen is negative. Human melanoma black 45 demonstrates maturation with stronger staining in superficial portions of the lesion and diminution of staining with increasing dermal depth.<sup>18</sup> Many other melanocytic tumors share histologic similarities to DN including blue nevus and desmoplastic melanoma.<sup>17,19,20</sup>



**FIGURE 1.** Fibrous papule. Increased dilated vessels and fibrosis in the dermis with an onion skin-like appearance around hair follicles. Scattered stellate, spindled, and multinucleated cells can be seen (H&E, original magnification  $\times 100$ ).

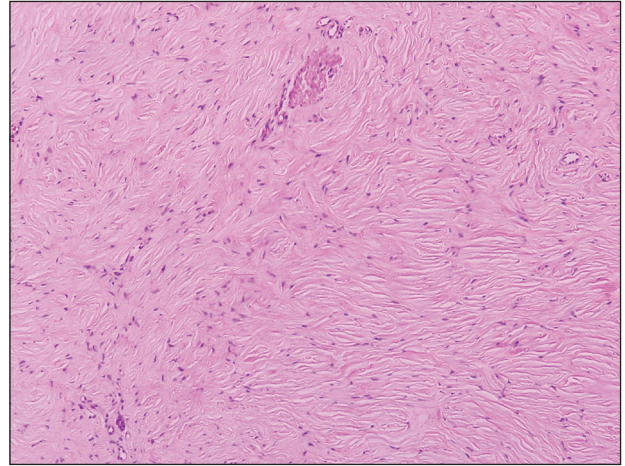


**FIGURE 2.** Desmoplastic nevus. A proliferation of spindled and epithelioid melanocytes embedded in a dense collagenous stroma. Clefts within sclerotic collagen bundles can be seen (H&E, original magnification  $\times 100$ ).



**FIGURE 3.** Palisaded encapsulated neuroma. A partially encapsulated nodule composed of interweaving fascicles of spindle cells with prominent clefts can be seen (H&E, original magnification  $\times 100$ ).

Palisaded encapsulated neuroma, also referred to as solitary circumscribed neuroma, was first described by Reed et al<sup>21</sup> in 1972. It is a benign and solitary, firm, dome-shaped, flesh-colored papule that occurs in middle-aged adults, predominately near mucocutaneous junctions of the face. Other locations include the oral mucosa, eyelid, nasal fossa, shoulder, arm, hand, foot, and glans penis.<sup>22,23</sup> Histopathologically, palisaded encapsulated neuroma demonstrates a solitary, well-circumscribed, partially encapsulated, intradermal nodule composed of interweaving fascicles of spindle cells with prominent clefts (Figure 3). Rarely, palisaded encapsulated neuroma may have a plexiform or multinodular architecture.<sup>24</sup> Immunohistochemically, tumor cells stain positively for S-100 protein, type IV collagen, and vimentin. The capsule, composed of perineural cells, stains positive for



**FIGURE 4.** Sclerotic fibroma. Sclerotic collagen bundles with scattered spindled cells and clefts resembling Vincent van Gogh's *Starry Night* (H&E, original magnification  $\times 100$ ).

epithelial membrane antigen. A neurofilament stain will highlight axons within the tumor.<sup>24,25</sup> Currently, palisaded encapsulated neuroma does not have a well-established link to known neurocutaneous or inherited syndromes. Excision is curative with a low risk of recurrence.<sup>26</sup>

Sclerotic fibromas (SFs) were first reported by Weary et al<sup>27</sup> as multiple tumors involving the tongues of patients with Cowden syndrome. Sporadic or solitary SFs of the skin in patients without Cowden syndrome have been reported, and both multiple and solitary SFs present with similar pathologic changes.<sup>28-30</sup> Clinically, the solitary variant manifests as a well-demarcated, flesh-colored to erythematous, waxy papule or nodule with no site or sex predilection.<sup>30,31</sup> Histologically, SF demonstrates a well-demarcated, nonencapsulated dermal nodule composed of hypocellular and sclerotic collagen bundles with scattered spindled cells and prominent clefts resembling Vincent van Gogh's *Starry Night* or plywood (Figure 4). Immunohistochemically, the spindled cells strongly express CD34. Factor XIIIa and markers of melanocytic, neural, and muscular differentiation are negative. When rendering a diagnosis in a patient with multiple SFs, a comment regarding the possibility of Cowden syndrome should be mentioned.<sup>32</sup>

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