

Case presentation

A fibrous papule with abundant CD34-immunoreactive ganglion-like multinucleated giant cells: a case report and review of the literature

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Dermatology Online Journal 21 (7): 14

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Abstract

Fibrous papules present clinically as benign, asymptomatic, dome-shaped, flesh colored papules on the face. Histologically, fibrous papules are characterized by fibrous stroma with fibroblasts and dilated blood vessels. Multiple variants of fibrous papules have been reported. Although scattered multinucleated cells in fibrous papules have been well described, we report a fibrous papule with abundant multinucleated ganglion-like giant cells that were immunoreactive with CD34. Recognition of such fibrous papule variants is important to avoid misdiagnosis as potentially more worrisome and/or aggressive melanocytic, soft tissue, or neural lesions that may require more aggressive treatment. Indeed, fibrous papules do not commonly appear on the differential diagnosis for lesions with multinucleated giant cells or ganglion-like cells and consideration should be given to their inclusion in the appropriate clinical setting.

Keywords: fibrous papule, multinucleated giant cells, ganglion-like, CD34

Introduction

Fibrous papules typically appear clinically as individual, asymptomatic, dome-shaped, flesh-colored papules. These lesions occur most commonly on the face, particularly on the nose of middle-aged adults [1]. Histologically, fibrous papules are most commonly characterized by fibrous stroma with plump fibroblasts and dilated blood vessels [1, 2]. Fibrous papules are currently classified as angiofibromas along with adenoma sebaceum, acral fibrokeratomas, pearly penile papules, and familial myxovascular fibromas [1].

Although most fibrous papules can be readily identified, multiple histologic variants have been reported including granular-cell, hypercellular, pigmented, pleomorphic, inflammatory, epithelioid, and clear-cell fibrous papules [1, 3]. Recognition of these variants is important to prevent misdiagnosis and overly aggressive treatment of a benign lesion. Although the presence of occasional multinucleated cells within fibrous papules is well described [1, 2, 4], here we report a case of a fibrous papule with abundant ganglion-like giant cells that were immunoreactive with CD34.

Case synopsis

A 33-year-old healthy man presented for dermatologic evaluation after complaining of a mildly pruritic growth on the nose. The lesion first appeared 3 years prior to presentation and had been slowly increasing in size since. The patient stated that two years prior to his presentation for evaluation, he had had two similar appearing lesions removed from his nose while in the military. Both prior lesions were treated with excisional shave biopsies followed by liquid nitrogen destruction. He was unsure as to the pathologic diagnoses rendered at the time. On physical exam, the patient was found to have a 5 mm smooth, violaceous to red papule on the left nasal alar crease (Figure 1). He was also noted to have two small, well-healed depressed scars on the nasal bridge and nasal tip without evidence of nodularity or color changes. Excisional shave biopsy of the lesion was performed.



Figure 1. Clinical photograph.

Methods

The biopsy specimen was fixed in 10% buffered formalin and processed and embedded in paraffin using standard histologic methods. Four-micrometer-thick sections were stained with hematoxylin and eosin (H&E). Immunohistochemical studies were performed using standard avidin–biotin immunoperoxidase techniques. The following antibodies were used: CD34 (Clone QBEnd/10, Cell Marque), S100 (Polyclonal, Dako), CK7 (Clone OV-TL 12/30, Dako), synaptophysin (Clone MRQ-40, Ventana), GFAP (Clone 6F2, Dako), Factor XIIIa (Clone AC-1A1, Cell Marque), CD68 (Clone PG-M1, Dako), Melan-A (Clone A103, Dako), and desmin (Clone D33, Cell Marque).

Results

Histologic sections of the shave biopsy showed a dermal proliferation of fibrous tissue with dilated vessels. Additionally present were numerous multinucleated giant cells with granular basophilic cytoplasm resembling Nissl substance that gave the cytoplasm of the giant cells a distinct ganglion cell-like appearance (Figures 2-4). Many cells contained multiple peripheral nuclei, while some contained a single nucleus. A number of cells contained prominent nucleoli.

An immunohistochemical stain for factor XIIIa highlighted multiple cells within the dermis, however, the large multinucleate cells were not highlighted (Figure 5). These large cells showed strong staining with an immunohistochemical stain for CD34 (Figure 6). S100 and Melan-A stains highlighted background melanocytes, but were negative within the lesion. Stains for CD68, desmin, CK7, synaptophysin, and GFAP were also negative.

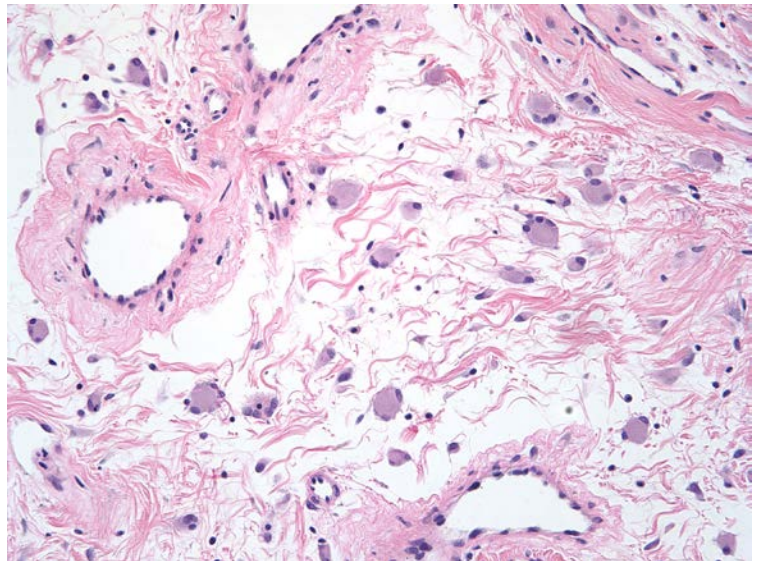
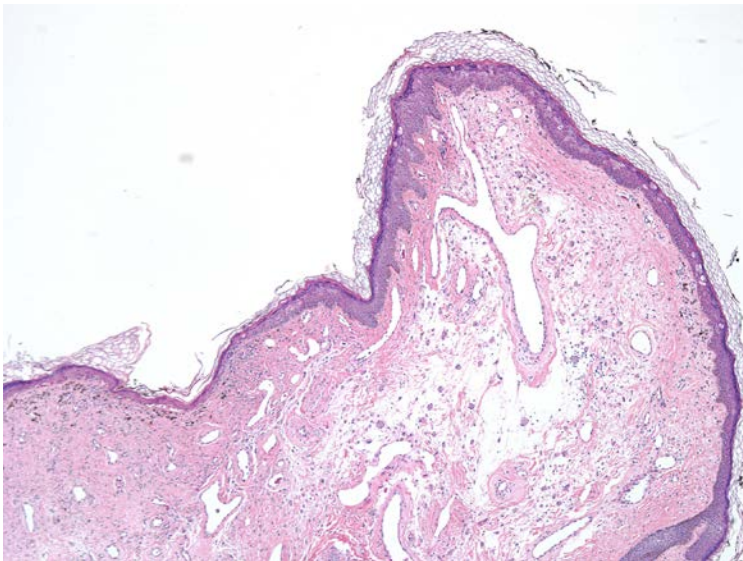


Figure 2. Fibrous papule (4 X). Note the numerous dilated blood vessels. **Figure 3.** Fibrous papule (20 X). Note the numerous plump giant cells in a cluster.

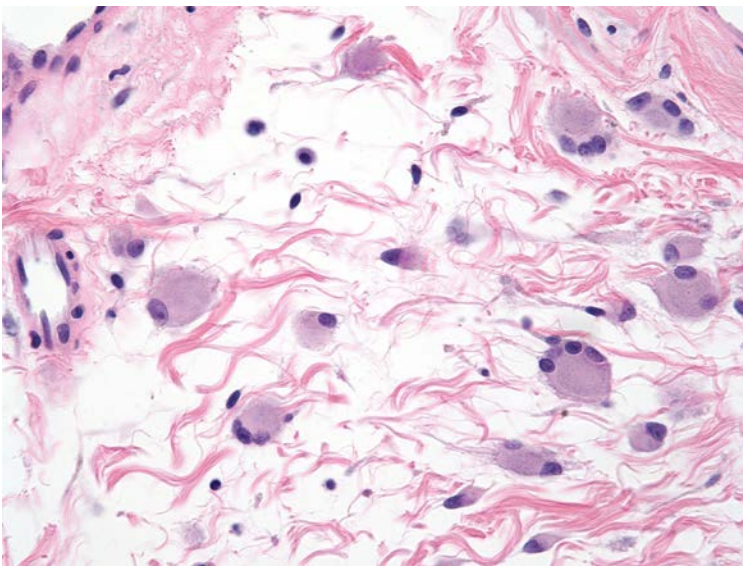


Figure 4. Fibrous papule (40 X). Note the multinucleation of several of the giant cells and basophilic cytoplasm resembling Nissl substance.

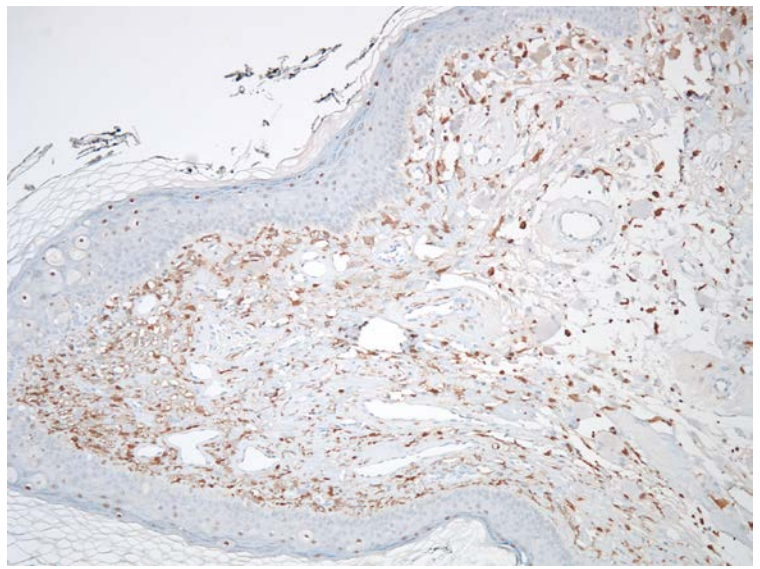


Figure 5. Immunohistochemical stain for Factor XIIIa (10x). Note the staining of small spindled cells but not of the multinucleated cells.

Discussion

Originally described as “perifollicular fibromas” by Zackheim and Pinkus in 1960 [5], fibrous papules were given their current popular title by Graham in 1965 [4]. Fibrous papules present clinically as asymptomatic, dome-shaped, flesh colored papules on the face that are common, affect both sexes equally, and follow a benign course. Clinically, these lesions can resemble basal cell carcinomas, adnexal tumors, pyrogenic granulomas, and nevocellular nevi [1-3].

Histologically, fibrous papules are characterized by a proliferation of fibrous tissue, fibroblasts, and dilated blood vessels [1, 2]. Scattered vellus hairs may be present [2]. Although these constituents are fairly constant allowing for rapid diagnosis in the majority of cases, several variants of fibrous papules have been described that include granular-cell, hypercellular, pigmented, pleomorphic, inflammatory, epithelioid, and clear-cell fibrous papules [1, 3, 6].

The pathogenesis of fibrous papules has been somewhat controversial with various etiologies having been proposed including a resolving melanocytic nevus, a hair follicle connective sheath fibroma, and a proliferation of periadnexal dermal cells and related blood vessels [2, 4, 5]. Indeed, the increase in melanocytes within the basal layer of the epidermis and resemblance of the dermal cells to the spindle cell component of a Spitz nevus can lead to diagnostic confusion with a melanocytic process [7]. Nonetheless, multiple studies have shown an absence of S-100 protein within fibrous papules lending no support to a melanocytic origin [8, 9]. Instead, these lesions have been proposed to arise from dermal dendrocytes given immunohistochemical staining with factor XIIIa [9, 10].

In addition to possibly being confused pathologically for a melanocytic process, the presence of rare lesions with CD34 immunohistochemical staining may also lead to such a lesion being misdiagnosed as a solitary fibrous tumor, dermatofibrosarcoma protuberans, epithelioid fibrous histiocytoma, epithelioid sarcoma, neurofibroma, or meningioma [11-13]. Indeed, similar multinucleated giant cells can be seen in orbital solitary fibrous tumors, alternatively known as giant cell angiofibromas, allowing for potential histologic overlap and diagnostic confusion given the location on the face [14]. Somewhat comparable multinucleated cells can also be seen in epithelioid fibrous histiocytomas [12, 15].

The stromal cells in fibrous papules have been observed to have several morphologies including stellate, spindled, or plump and can have single or multiple nuclei [2, 3, 16-18]. These cells may also have dark round inclusion bodies [19]. Here, we present a case of a fibrous papule with abundant plump, multinucleated stromal cells with basophilic cytoplasm resembling Nissl substance giving the cells a “ganglion-like” or “floret-like” appearance. These cells did not stain with immunohistochemical stains for

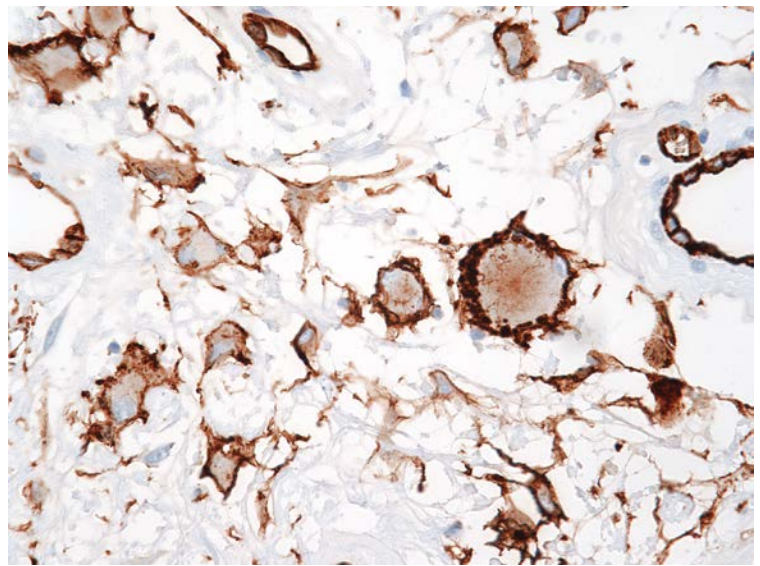


Figure 6. Immunohistochemical stain for CD34 (40x). Note the staining of the multinucleated giant cells. The background blood vessels also show strong staining.

synaptophysin or S100 thereby showing no evidence of a true ganglion cell immunophenotype. Instead, these cells stained with CD34, an antigen expressed normally on hematopoietic stem cells, endothelial cells, periadnexal cells, and a subset of dermal interstitial cells [11]. The background small spindle cells stained with factor XIIIa as is commonly seen in fibrous papules. All other performed immunohistochemical stains, including S100, Melan-A, GFAP, CD68, desmin, and CK7, were negative within the dermal proliferation lending no support to a neural, melanocytic, histiocytic, or muscular process.

The presence of CD34 immunohistochemical staining within the large multinucleated cells of a fibrous papule, to our knowledge, has not been previously reported. Instead, a previous report of CD34 staining in a fibrous papule focused on the background spindle cell population [11]. Although novel, this finding is perhaps not entirely unexpected as the presence of CD34 expression in the multinucleated floret-like cells of other lesions including dermal pleomorphic lipomas and a pleomorphic onychomatricoma have been reported [20-23]. Prior ultrastructural studies of similar large multinucleated cells in fibrous papules have shown that the cells have abundant rough endoplasmic reticulum [24, 25]. As such, it is readily apparent why these cells resemble ganglion cells on routine histologic analysis as the Nissl substance in ganglion cells is also composed of abundant rough endoplasmic reticulum [26].

Given the expression of CD34 and prominent unusual cells, consideration could be given to the diagnosis of a pleomorphic fibroma, which can have similarly dilated blood vessels [27]. However, although multinucleated and floret-like, the cells we observe do not have hyperchromatic or vesicular chromatin, multilobated nuclei, or any other prominent atypia typical of pleomorphic fibromas [28-30]. Also absent was the typical dense collagenous stroma.

The presence of abundant ganglion-like giant cells as seen in this lesion could easily lead the histopathologist toward a ganglion cell differential diagnosis to entities including ganglioneuroma and proliferative fasciitis [31]. Although rare cells similar to these giant cells have been reported previously including in many of the original descriptions of fibrous papules [2, 4, 16-18], the presence of abundant ganglion-like giant cells has not been reported. In point of fact, fibrous papules do not often appear on the differential diagnosis for lesions with multinucleated giant cells or ganglion-like cells [31, 32], and consideration should be given to their inclusion given the commonality of fibrous papules and their various appearances.

In conclusion, we have described a case of a fibrous papule with abundant multinucleated ganglion-like giant cells that were immunoreactive with CD34. Recognition of such fibrous papule variants is important to avoid misdiagnosis as potentially more aggressive melanocytic, soft tissue, or neural lesions that may require more aggressive treatment.

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