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A Case of Solitary Fibrofolliculoma Over Nasal Bridge in a 46-year-old Woman

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Abstract

Fibrofolliculoma is a hallmark clinical manifestation of Birt-Hogg-Dubé syndrome, typically presenting as multiple skin lesions. To date, only 14 cases of solitary fibrofolliculoma have been documented worldwide. Here, we present a case of solitary fibrofolliculoma that is the third recorded to have occurred on the nose. Histopathology showed dilated hair follicles containing keratinous material and follicular epithelium extended out into the fibrotic stroma to rejoin the follicle. The diagnosis of fibrofolliculoma was confirmed by histopathological examination. The patient underwent excision of the lesion and local advancement of the skin flap. Here, we report typical clinical and histopathological findings in solitary Fibrofolliculoma. This report details the typical clinical features and histopathological findings of solitary fibrofolliculoma, contributing to the limited literature on this rare entity.

Keywords

Solitary fibrofolliculoma; nasal tumor; folliculin

1. Introduction

Fibrofolliculoma is a rare benign connective tissue tumor that forms in the hair follicle area. It appears as a small raised whitish bump that usually occurs on the face, ear, neck, and chest. Fibrofolliculoma tends to grow slowly but can increase in size and number with time. Fibrofolliculomas often occur in persons who have an inherited condition called Brit Hogg-Dubé syndrome that results from a mutation in the folliculin gene [1]. This gene may function as a tumor suppressor. Birt-Hogg-Dubé (BHD) syndrome typically presents with fibrofolliculomas on the skin, pulmonary cysts, renal cell carcinoma, and spontaneous pneumothorax. Fibrofolliculoma has rarely presented as a solitary lesion since being reported first in 1984 [2]. We present the clinical features and surgical treatment of a rare, solitary fibrofolliculoma located over the left lateral aspect of the nasal bridge in a 46-year-old woman.

2. Case Report

A 46-year-old woman presented with an asymptomatic flesh colored lesion on the left lateral aspect of the nasal bridge. She had a two-year history of a single nasal pimple on the aforementioned site, which was approximately the size of a rice grain and appeared as a yellow-white papule without any other obvious symptoms, diagnosis, or treatment. The papule gradually increased to 5 mm × 6 mm with a central depression. There was no history of bleeding, rupture, or any associated systemic features. No similar lesion was found elsewhere on her body. She was healthy with no previous medical history or family history of such dermatological findings. Since the onset of the disease, she had a normal appetite, sleep, urination, and defecation, and no weight change.

On her dermatological examination, there was a single, yellow- white, solid papule of diameter approximately 0.6 cm over the left lateral aspect of the nasal bridge. The swelling had clear boundaries with a slight peripheral rise, a central umbilication, and a smooth surface without scale, erosion, or crusting (Figure 1). There was no tenderness on palpation. The patient's physical examination showed good general condition without any superficial lymphadenopathy related to swelling. The other systemic examinations were normal.

Figure 1. A solitary yellowish-white, well-demarcated margin, smooth surface lesion with central umbilication over the left lateral aspect of the nasal bridge.

We took a biopsy sample from the mass. The histopathology showed hyperkeratosis of the epidermis, multiple twisted follicle-like structures in mid-dermis with dilated central infundibulum composed of keratinized debris on the hair shaft. The cord of tumor cells was composed of basal-like cells radiating from the infundibulum and interweaving into a network surrounded by pink fibrous stroma, which showed a gap between the fibrous interstitium and surrounding normal dermal connective tissue (Figure 2).

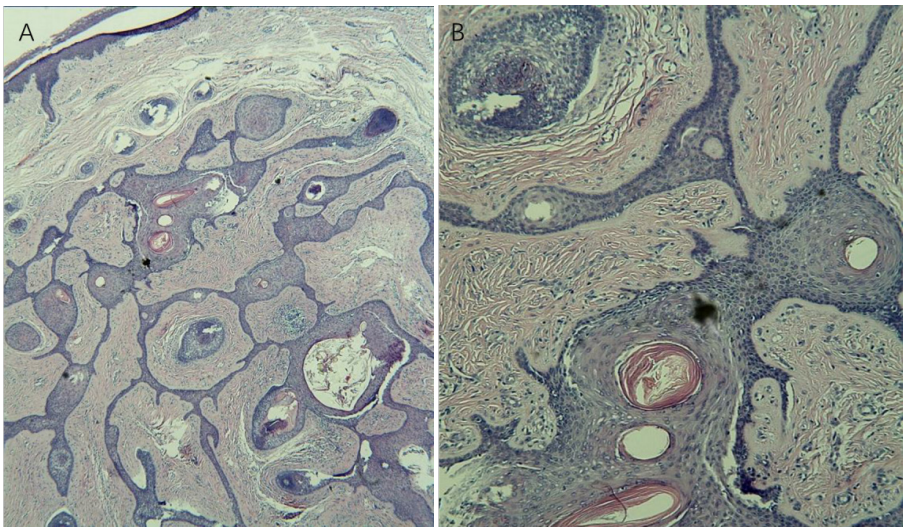

Figure 2. Histopathological photomicrograph of solitary fibrofolliculoma. A. Multiple twisted follicular structures are seen in the middle layer of the dermis, and strips of tumor cells composed of basaloid cells intertwine and anastomose into a meshwork [hematoxylin and eosin (HE) *50]. B. Fibrous stroma containing mucin, surrounding the hair follicle were found [hematoxylin and eosin (HE) *100].

Ultrasound showed that both kidneys of the patient were normal, and no abnormalities in the CT-scanning of the chest. Based on these findings, we made a diagnosis of solitary fibrofolliculoma.

The patient opted for excision of the lesion. Under local anesthesia, an elliptical excision was made, including an incision of 1 mm of extra tissue from the edge of the lesion. We did not find invasion of the mass into cartilage or other tissue, and no adhesion to the periphery. Thus, we concluded that the mass was completely excised, and the defect of the nasal bridge was repaired using a local advancement skin flap. A gray line split was performed on the cut ends of skin defects, and then the skin defects were sutured directly. The stitches were removed one week after surgery, and the patient had no particular discomfort. A follow-up was completed after six months. There was no recurrence or new lesions.

3. Discussion

Fibrofolliculoma is a type of benign tumor that originates from both epithelial and mesenchymal layers [3]. It is usually found in Birt-Hogg-Dubé (BHD) syndrome, which affects the skin, lungs and kidneys. The skin

manifestations of BHD syndrome are multiple fibrofolliculomas, acrochordons, and trichodiscomas. BDH is inherited as an autosomal dominant; about 60% to 80% of persons with BHD syndrome have mutations in the susceptibility gene, folliculin, localized to 17p11.2 and 17p12-q11.2 [4, 5]. As a tumor suppressor gene, folliculin is expressed in many tissues, including stromal cells, the distal nephron, type I pneumocytes, the skin, and skin appendages. Most fibrofolliculomas are clinically asymptomatic, dome-shaped, skin-colored, 2-4 mm-sized soft papules. Fibrofolliculoma often occurs as multiple lesions in adults in diverse locations such as the scalp, forehead, face, and neck [6]. The histopathological characteristics of fibrofolliculoma have minor variations [2]. The center of the lesion appears as dilated hair follicles surrounded by a moderately well-circumscribed thick mantle of fibrous tissue containing keratinous material. The thin bands of follicular epithelium extend out into the fibrotic stroma, rejoin the follicle, or anastomose with one another. Solitary fibrofolliculoma presents no heritability and is unassociated with other cutaneous abnormalities.

Solitary fibrofolliculoma occurs more often in scalp and face and may be associated with an abundance of hair follicles and a propensity for trauma in these locations [7]. After injury, multipotent stem cells resident in the hair follicle bulge can form epidermis, hair follicles, and sebaceous glands to reconstruct the epidermis [8]. Noriyuki et al. reported that fibrofolliculoma may be caused by abnormal function of hair follicle bulge cells. They presented immunohistochemical features of fibrofolliculoma and expression patterns of CD34, factor XIIIa, nestin, and c-kit in the stromal cells, as well as abnormal CK15 expression in the hair follicles [9]. Nestin is present in almost every tissue and has important functions in tissue development and tissue regeneration [10]. CK15 is the best marker for bulge stem cells in human hair and is expressed throughout all stages of the hair cycle in different types of follicles. The classical proto-oncogene c-*kit* responds to stem cell factor. Overexpression or mutations in c-*kit* disturb c-KIT function and promote tumor development and progression in various neoplasms [8].

Table 1. Summary of reported cases of solitary fibrofolliculoma

Author	Case	Age(yr.)/Sex	Location	Tumor Size	Mass Appearance
Scully et al.[2] Starink and Brownsteinc[18]	1	65/F	Chin	5mm in diameter	Skin-to-pink colored, dome-shaped papule
	2	49/M	Chin	5 mm in diameter	Yellowish nodule
	3	20/F	Nose		Skin-colored papule
	4	50/M	Cheek		Skin-colored Papule
	5	60/F	Ear		Dome-shaped papule
	6	52/M	Eyebrow	3 mm in diameter	
				6x4 mm	
Hong et al.[19]	7	40/F	Scalp	7x6x5 mm	Skin-to-pink-colored papule
Chang et al.[6]	8	37/F	Eyelid	5x5 mm	Skin-colored papule
Cesinaro et al.[20]	9	63/F	Nose	12x10 mm	Skin-colored papule
Cho et al.[7]	10	45/M	Ear	12x10x8 mm	Flesh-colored mass
Criscito et al.[11]	11	72/F	Cheek	4 mm in diameter	Flesh-coloured, dome-shaped papule
Sohn et al.[21]	12	50/M	Posterior Auricular Region	10x12 mm	Flesh-colored papule
Wang and Cheng[3]	13	68/F	Eyelid	5x5x4 mm	Flesh-colored papule
Mishra et al.[22]	14	50/M	Eyelid	3x3x2 cm	

Cases of solitary fibrofolliculoma are rare; only 14 cases have been reported since the first in 1984. On reviewing published cases, we observed that most lesions were on the face, with two lesions around the eye, one on the eyelid, one on the eyebrow, and two on the nasal region (Table 1). Tumor prevalence is greater among women; the mean age of presentation is 45-50 years. The duration of the lesion varies from several months to many years, mostly being asymptomatic. Our patient was a 46-year-old woman with a skin lesion involving the nasal bridge. It arose as a yellow-white papule without any other obvious symptoms. Although dermoscopy can provide some clues to diagnosing solitary fibrofolliculoma, sonography and reflectance confocal microscopy are the gold standard is histopathological examination. For this case, on dermoscopy, the papule exhibited hypopigmented globules and curvilinear vessels often connecting red dots and globules [11]. Sonography of the lesion showed a hypoechoic, well-defined lesion with hyperechoic areas and increased peripheral vascularization [12]. In the last couple of years, reflectance

confocal microscopy has been used widely for diagnostic decisions, especially for benign and malignant skin neoplasms. Because reflectance confocal microscopy is a noninvasive imaging technique, the image of fibrofolliculoma is a follicular structure through which a cord of refractive cells emanates, evident from the superficial dermis to the depth; bright stroma is arranged in bundles [13].

Our case was confirmed pathologically as a fibrofolliculoma after excisional biopsy. Histologically, fibrofolliculoma reveals multiple twisted follicles in the mid-dermis. Dilated hair follicles containing keratinous material surrounded by a well-circumscribed proliferation of connective tissue composed of fibers. The infundibular follicular epithelium extends out into this fibrous mantle, forming epithelial cords and strands. The thin strands of follicular epithelium anastomose and intertwine into a network, embedded in the peripheral boundary and lobulated interstitial lining. The perifollicular connective tissue is rich in acidic mucopolysaccharides, is alkaline mucus-like, and there are fissures between it and the surrounding normal connective tissue.

Because solitary fibrofolliculoma is rare and asymptomatic, it is definitively diagnosed only by histopathological examination; otherwise, it can be easily missed or misdiagnosed. In the spectrum of benign follicular tumors, perifollicular fibroma (purely of mesodermal origin) is at one end of the spectrum, trichofolliculoma (purely of epithelial origin) is at the other, and fibrofolliculoma is at the middle.[2] Fibrofolliculoma has both an epithelial and a mesenchymal origin, so we should distinguish it from other follicular neoplasms that involve mesenchymal proliferation, such as trichodiscoma, perifollicular fibroma, tricofolliculoma, and angiofibroma. The difference between trichodiscoma and fibrofolliculoma is the proportions and disposition of the stromal and epithelial components. Trichodiscoma shows a generally horizontal orientation of the lesion, a more peripheral disposition of the epithelial component, and more pronounced mature sebaceous content. Perifollicular fibromas show fibrous tissue surrounding normal follicular structures without a twisted follicle, which often contains a keratotic plug. Tricofolliculoma has a similar stroma to fibrofolliculoma, a dilated follicle connected to the skin surface, numerous mature or dystrophic vellus hair follicles, and retraction clefts in connective tissue. Angiofibroma shows an angiomatous component that is prominent and capillary hyperplasia with perivascular fibrosis.

The lesion described in this report was on the nasal bridge, which also should be included as a differential diagnosis of malignant conditions like melanoma, squamous cell carcinoma, and basal cell carcinoma. Basal cell carcinoma appears as a translucent, waxy papule with a rolled, pearly border with telangiectasia. As it enlarges, central ulceration usually develops. Squamous cell carcinoma appears as a painless, elevated, nodular, or plaque-like lesion with chronic scaling and fissuring of the skin. Its characteristic features also include pearly, irregular borders and a tendency to develop ulceration with irregular rolled edges.

Surgical excision is the treatment of choice for a skin solitary fibrofolliculoma. A CO_2 laser, erbium-doped YAG laser, and electrodesiccation at a low setting are devices of choice for the excision of multiple lesions [14-16]. Topical use of the mTOR inhibitor rapamycin for angiofibromas in tuberous sclerosis is successful, but it failed for fibrofolliculomas in BHD [17]. For patients, further screening for other cutaneous and extracutaneous features is necessary.

We have presented a rare case of a flesh-colored, dome-shaped lesion on the left lateral aspect of the nasal bridge that showed histologic features of solitary fibrofolliculoma. Because of the asymptomatic nature of solitary fibrofolliculoma, it is easily misdiagnosed and underdiagnosed by a doctor's naked eye and experience. The biopsy and histological examination are important to confirm the diagnosis and treatment method. The operation should excise a 1-mm margin of normal tissue around the tumor, and the cosmetic aspect should be considered. This report highlights both the clinical and histopathological features of the tumor that are important for diagnosis, treatment, and prognosis.

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