FIBROUS PAPULE OF THE NOSE: A CLINICOPATHOLOGICAL STUDY*

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The usual history of a patient with a fibrous papule of the nose is that of a middle-aged person who consults a physician because of recent color changes in the lesion or to request removal for cosmetic reasons. These dome-shaped papules are often interpreted clinically as cellular nevi; but their configuration, firm consistency, and vascularity may cause confusion with fibrous proliferations and vascular lesions.

The purpose of this paper is to report our clinicopathological observations of a distinct isolated fibrous papule of the nose, stressing histogenesis, pathogenesis, histochemical characteristics, and possible relationship to cellular nevi of the nasal region.

MATERIALS AND METHODS

The study was conducted on 42 fibrous papules of the nose removed from 40 patients. The material from 6 of the 40 patients was from The Armed Forces Institute of Pathology (AFIP). The files of the AFIP include case material from military, veterans administration and civilian sources. Clinical and pathological observations were supplemented by clinical records, surgical reports, questionnaires, and/or personal interview and examination of the patient. Follow-up data was obtained from 34 patients. For comparative purposes, 70 cellular nevi removed from the nose of 65 patients were studied. For purposes of this paper, the term cellular nevus is used to indicate a nevus cell nevus. All specimens were fixed in 10% neutral buffered formalin and the tissue was processed for routine paraffin-blocked sections. Multiple sections stained with hematoxylin and eosin were examined in all cases. Sections from 15 fibrous papules and 10 cellular nevi were prepared by the following methods: periodic acid-Schiff (PAS) reaction, with and without diastase digestion; colloidal iron reaction (1), with and without bovine testicular hyaluronidase and ribonuclease digestion; Feulgen reaction; Fontana-Masson stain for argentaffin granules (melanin); Snook's reticulum stain; Movat's pentachrome I stain (2); Bodian's method for nerve fibers and nerve endings; Gomori's iron reaction; Gomori's aldehyde-fuchsin technic; and the alcian blue method. The pH of the working solutions, and the methods used in the aldehyde-fuchsin and alcian blue techniques and detailed interpretation of the results were similar to those described by Johnson and Helwig (3), and Johnson, Graham and Helwig (4). Formalin-fixed tissue from 3 fibrous papules and 2 cellular nevi was used for preparing frozen sections for the following fat stains: oil red O; osmium tetroxide; sudan black B; and the nile blue sulfate stain for neutral fats and fatty acids. With the exceptions given, the procedures were carried out as outlined in the "Manual of Histologic and Special Staining Techniques" (5).

CLINICAL DATA

Fibrous papule.—The fibrous papule occurred predominantly in the Caucasian race. Twenty-two patients were men, and 18 were women. The only Negro patients were 2 men. The median age of the 40 patients at first biopsy or treatment was 41 years. The youngest was 14, and the oldest 65 years. The duration of 28 lesions in 26 patients from stated onset to time of biopsy removal or treatment varied from 3 months to 16 years. The median duration was 3 years, i.e. half of the patients had a biopsy diagnosis established within 3 years after recognized onset.

The fibrous papule usually appeared dome-shaped and was flesh-colored, pigmented or angiomatous (Fig. 1). A few of the lesions were sessile, polypoid or papillomatous. The majority of the lesions were firm and indurated, but a few were soft. The size of the lesions varied from 1 to 5 mm in diameter; the median was 3 mm. Most patients stated the lesion was asymptomatic, although a few mentioned episodes of erosion and bleeding usually associated with trauma. Forty-two lesions from 40 patients involved the nose as illustrated in

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Figure 2. The majority of the lesions were located on the ala nasi. Thirty-eight patients had a single lesion and the other 2 patients had 2 lesions each.

The initial clinical diagnosis in 18 patients was cellular nevus. Other diagnoses were: fibrous papule, 7; fibroma, 2; telangiectasia, 2; hemangioma, 2; and keratosis, epithelioma, neurofibroma, verruca, granuloma pyogenicum, ulceration, epidermoid cyst, papilloma, and milia, 1 each.

Family history was not significant. Six patients had cellular nevi of the head and neck region confirmed by biopsy examination. One patient had a primary malignant melanoma of the scalp. This latter patient and 1 other had basal cell carcinoma of the skin.

Treatment of the fibrous papule was by surgical excision in 34 patients, excision and desiccation of the base of the lesion in 5, and desiccation and curettage in 1. Surgical excision was by sharp blade removal of the lesion flush with the surface of the surrounding skin.

The follow-up period for 34 patients, from the first biopsy diagnosis of the fibrous papule to the last known status, ranged from 2 months to 9.3 years. The median was 17 months. None of the patients have had recurrences. Only 1 patient is known to be dead and death was caused by malignant melanoma with widespread metastasis. Six of the 40 patients in the study were lost to follow-up.

Cellular nevi.—Cellular nevi of the nose occurred predominantly in the Caucasian race. Only 5 of the 65 patients were Negro. Forty-two patients were women, and 23 were men. The median age of the 65 patients at the time of first biopsy or treatment was 37 years. The youngest patient was 13, and the oldest 84 years. The duration of 44 lesions in 41 patients from stated onset to biopsy examination varied from 3 weeks to 78 years; the median was 5 years.

Clinically, the majority of the 70 cellular nevi of the nose appeared dome-shaped, smooth, and flesh-colored to brown. A few of the nevi were sessile, polypoid, or papillomatous. The consistency of the lesions varied from firm to soft. The size of the lesions varied from 1 to 9 mm in diameter; the median was 4 mm.

**HISTOPATHOLOGIC AND HISTOCHEMICAL OBSERVATIONS**

*Fibrous papule:* In hematoxylin- and eosin-stained preparations, the fibrous papules showed a
dome-shaped or papular to polypoid configuration, fibrosis and vascular ectasia (Fig. 3). Hyperkeratosis and acanthosis was seen in some examples, and a few lesions showed superficial erosion of the epidermis. Variable numbers of vacuolated cells were seen in the epidermis in 34 of the 42 lesions (Fig. 4). An increased amount of melanin pigment was present in the basal layer of the epidermis in many specimens. Melanocytes were located at the dermoepidermal junction, and in several specimens these cells were increased in number (Fig. 4). The melanocytes in some areas were grouped in small clusters and others showed nuclei arranged in a peripheral ring about a central mass of cytoplasm. Sections from 5 of the lesions showed single theques of nevus cells at the dermoepidermal junction (Fig. 4), and 1 showed changes resembling senile lentigo. A few lesions showed areas of an indistinct basement membrane at the dermoepidermal junction associated with incontinence of melanin pigment. Focal areas of inflammation were present in the corium and composed of variable numbers of lymphocytes, histiocytes, and plasma cells (Fig. 4a). Thirty-six of the lesions contained multinucleated giant cells. Most of these giant cells showed a peripheral ring of nuclei arranged about a distinct mass of cytoplasm, but others varied in size and shape, and appeared stellate, fusiform, spindled or dendritic (Figs. 5, 7b and 7c). These giant cells were seen most often in the papillary corium, but were observed at all levels in the fibrous stroma. Lanugo hairs were observed in 33 of the lesions and fibrosis was striking, because the proliferation was arranged about these structures in a unique concentric or laminated pattern (Figs. 6 and 7a). In a few lesions, the perifollicular fibrosis was associated with atrophy of the lanugo hairs (Figs. 6 and 7a). In the upper corium, the fibrous proliferation showed a tendency to run in wavy fibrillar strands at right angles to the overlying epidermis (Figs. 3 and 4a). A few of the lesions showed myxomatous features as a part of the fibrous proliferation. Sebaceous glands were present in 29 of the lesions, and these often appeared rudimentary and compressed by the surrounding fibrosis. All of the lesions showed dilated vessels (Figs. 3, 4a, and 6), and in some examples there were focal areas of capillary-endothelial proliferation and extravasated red blood cells.

Results of histochemical studies were as follows: The Fontana-Masson stain for melanin showed an abundance of pigment in the basal layer of the epidermis and in the lanugo hair follicles (Fig. 6). In the corium, the melanin granules were free, within giant cells and/or melanophages (Fig. 5). The colloidal iron reaction demonstrated reactive material in the large cutaneous nerves, cytoplasm of the giant cells, interfibrillar ground substance, outer root sheath and dermal papilla of lanugo hair follicles, mast cells, and particulate granules in the epidermis and corium. The majority of the reactive substance in the cutaneous nerves, interfibrillar ground substance and outer root sheath of the hair follicles was hyaluronidase-labile, and interpreted as hyaluronic acid. The various colloidal iron reactive sites were Feulgen negative and were not altered by ribonuclease digestion. There is a possibility that the acid substance in the giant cells and about particulate

Fig. 3. Fibrous papule showing dome-shaped configuration, fibrosis and vascular ectasia. H & E, X 38.
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Fig. 4. Fibrous papule. a. Dome-shaped configuration, vascular ectasia, and melanocytes and a theque of nevus cells (arrow) at the dermoepidermal junction. H & E, × 120. b. Higher magnification of a. illustrates the theque of nevus cells at the tip of a rete ridge. Melanocytes are present along the sides of the rete ridge. H & E, × 430.

granules in the epidermis and corium represents ribonuclease resistant nucleic acid complexes associated with the tyrosine-tyrosinase reaction of melanin synthesis. Mast cells and the dermal hair papillae are known sites of sulfated acid mucopolysaccharides and this accounts for the resistance to hyaluronidase and ribonuclease digestion. The mast cells and dermal hair papillae were positive with aldehyde-fuchsin at pH 1.7 and 0.4, and with alcian blue at pH 2.5 and 0.4. These results verify the presence of sulfated acid mucopolysaccharides in the mast cells and dermal hair papillae since at low pH values (0.4) only strongly acid substances such as the sulfated acid mucopolysaccharides will yield a positive reaction. The mast cell population was increased and as high as 25–30 per high power field in several examples of the fibrous papule. The hyaluronic acid in the interfibrillar ground substance was aldehyde-fuchsin negative at pH 1.7 and 0.4, but reacted with alcian blue at pH 2.5. Since iron compounds in the tissue may produce a false positive colloidal iron reaction, Gomori's reaction for iron was used as a control. Iron was absent in the corium.

The vacuolated cells in the epidermis were PAS negative, whereas some melanocytes at the dermoepidermal junction and giant cells in the corium contained PAS-positive diastase-resistant material in the cytoplasm. The exact nature of this positive material is not known, but it may represent a reaction of nucleic acid complexes associated with melanin or melanin synthesis. Variable amounts of PAS-positive diastase-labile material (glycogen) was present in the outer root sheath of the lanugo hairs.

Bodian's method for nerve fibers and nerve endings demonstrated a network of fine nerve fibrils
Fig. 5. Fibrous papule. a. Multinucleated giant cells and melanin pigment in the corium. One of the giant cells has a dendritic process intimately associated with it. Fontana-Masson stain, × 395. b. High power magnification showing melanin pigment free and within a giant cell. Fontana-Masson stain, × 635.

Fig. 6. Fibrous papule showing melanin in the epidermis and hair follicles. Fibrous proliferation about lanugo hairs is arranged in a concentric pattern. Outlines of atrophic follicles are present. Fontana-Masson stain, × 66.
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Fig. 7. Fibrous papule. a. Reticular fibers surround lanugo hairs and outline atrophic follicles. Snook's reticulum stain, \( \times 115 \). b. A dense network of reticular fibers are located about individual giant cells and inflammatory cells. Snook's reticulum stain, \( \times 305 \). c. No elastic fibers are present in the corium. Several giant cells are present. Pentachrome 1 stain, \( \times 305 \).

ramifying the fibrous stroma and showing an intimate relationship to the giant cells.

Elastic tissue stains demonstrated a decreased to absence of elastic fibers (Fig. 7c). The pentachrome stain showed thickened collagen bundles and an associated fibrocytic proliferation. In areas of inflammation, about giant cells, lanugo hairs, and blood vessels there was a prominent proliferation of reticular fibers (Figs. 7a and 7b).

The giant cells failed to react to the various fat stains.

Cellular nevi: Of the 70 lesions studied, 42 were histologically classified as intradermal cellular nevi and 28 as compound cellular nevi. Many of the latter group would ordinarily be classified as intradermal cellular nevi, but multiple sections invariably demonstrated a single or only a few theques of nevus cells at the dermoepidermal junction.

Variable amounts of melanin pigment was present in the basal layer of the epidermis. In many of the lesions, the number of melanocytes was increased along the dermoepidermal junction and an occasional nevus giant cell was observed. In general, a grenz zone of connective tissue separated the epidermis from nests and strands of nevus cells located in the corium. Often the nevus cells were arranged at right angles to the epidermis. Nevus giant cells were common and observed at all levels of the corium, but were more concentrated in the upper corium. These giant cells were of 2 morphological types; 1 type appeared as clusters of nevus cells and the second type showed a peripheral ring of nuclei arranged
about a mass of cytoplasm. Intermediate forms of the 2 types were observed. Dilated vessels, nerve trunks, lanugo hairs, and sebaceous glands were seen in the majority of the lesions. Evidence of regression with thinning out of nevus cells was observed in several nevi. The changes of regression included fibrosis, inflammation, and fat infiltration. The nevus giant cells showed some distortion, but were still intact in regressing lesions. The fibrous proliferation about nevus cells in some areas was dense and appeared to be "choking the nevus cells." Lanugo hair follicles were surrounded and compressed by connective tissue fibers arranged in a laminated configuration (Fig. 8). In one of the nevi showing changes of regression, multiple sections revealed 2 theques of nevus cells at the junction of the dermis and outer root sheath of a rudimentary pilosebaceous follicle located in the deeper corium.

Special histochemical studies showed the following significant results: The Fontana-Masson stain for melanin demonstrated an abundance of pigment in the epidermis, nevus cells, nevus giant cells, melanophages, and free in the corium.

The nevus cells and nevus giant cells contained cytoplasmic colloidal iron positive material which was: hyaluronidase and ribonuclease resistant; Feulgen negative; aldehyde-fuchsin negative; and alcian blue reactive at pH 2.5 and negative at pH 0.4. An occasional nevus cell and nevus giant cell contained PAS-positive diastase-labile material in the cytoplasm. Mast cells were observed in increased numbers and scattered throughout the nests and strands of nevus cells. The substance demonstrated in the nevus cells and nevus giant cells probably represents nucleic acid complexes associated with the production of melanin.

The Bodian stain showed fine argyrophilic nerve fibers ramifying and intimately associated with the nests and strands of nevus cells.

The pentachrome stain showed thinning or absence of elastic and collagen fibers in areas occupied by the nevus cells. Elastic fibers appeared normal or hypertrophic beneath and lateral to the nests and strands of nevus cells. Reticular fibers surrounded and separated the aggregates of nevus cells.

Some of the nevus cells and nevus giant cells contained lipid material and this was demonstrated by all the fat stains utilized.

**DISCUSSION**

Zackheim and Pinkus (6), in 1960, reported 5 patients with papular lesions of the skin under the title of "perifollicular fibromas." They (6) described the lesion as showing pathological changes of a benign fibroma with a striking perifollicular arrangement of collagen fibers. In their (6) review of the literature, the report of 1 case by Burnier and Rejsek (7)

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Fig. 8. Intradermal cellular nevus of the nose showing regression changes. Fibrotic connective tissue is "choking" the nevus cells and is arranged about a lanugo hair in a concentric pattern. H & E, X 103.
was considered as showing the pathologic
changes of a fibroma with a perifollicular pat-
tern. Zackheim and Pinkus (6) considered peri-
follicular fibromas as a relatively rare condi-
tion, and described the lesions clinically as
small firm papules, either flesh-colored or pink,
and located on the face and neck. They (6)
mentioned the clinical appearance was not dis-
tinctive, but suggested a nevus, trichoepithelioma
or related condition. Zackheim and Pinkus (6)
concluded that perifollicular fibromas either
constituted a true nevoid condition, falling in
the broad category of adnexal tumors, or simply
represented a fibroblastic response to previous
follicular inflammation. Nickel and Reed (8),
in 1962, reviewed 74 biopsies from the skin of
38 patients with tuberous sclerosis and stressed
the fibrous and vascular changes in the cutane-
ous hamartomas of this disease. Percival,
Montgomery and Dodds (9), in 1962, illustrated
the histopathology of a soft fibroma in figure 377.
They stated, “Numerous hair follicles may be
present in those which develop and enlarge on
the face in middle-aged females.” The gross
morphology of the fibrous papule is not en-
tirely distinctive, but there is a good possibility
that the clinical photograph illustrated in
figure 32 by Conway (10) represents an ex-
ample. Conway (10) referred to a dome-shaped
lesion of the tip of the nose as representative
of fibroma durum. Microscopically, there is a
resemblance between the facial angiofibromas
(8) of adenoma sebaceum, perifollicular fi-
bromas (6), soft fibromas (9), and what we
have reported as fibrous papules of the nose.
The microscopic changes of a lesion from the
face of a 34 year old woman illustrated in
figure 6 in the report by Nickel and Reed (8)
shows features identical with those seen in
fibrous papules of the nose. The soft fibroma
illustrated by Percival et al. (9) also appears
identical with the lesion we are reporting. It
would appear that at least 4 of the cases with
perifollicular fibromas (6) are identical to the
lesions from our patients with fibrous papules of
the nose. Cases 2 and 5 had perifollicular fibro-
mas (6) located on the nose, and case 3 had
papules on the cheeks, chin and nose, but the
exact location of the lesion removed for biopsy
was not recorded.

There is considerable evidence supporting
origin of the fibrous papule from a pre-existing
cellular nevus. Clinically, 18 of the 40 patients
had their lesions diagnosed as cellular nevi, and
6 patients had histological evidence of nevi
involving the head and neck region. Compari-
sion of clinical data from patients with fibrous
papules and cellular nevi of the nose show a
striking similarity.

Histologic evidence supporting origin of the
fibrous papule from a cellular nevus include:
configuration of the lesion; abundance of
melanin pigment; 5 lesions with theques of
nevus cells at the dermoepidermal junction;
increased numbers of melanocytes at the
dermoepidermal junction; 1 lesion with epi-
dermal changes resembling senile lentigo;
vacuolated cells in the epidermis; fibrosis with
a tendency for the fibers to run at right
angles to the epidermis; vascular ectasia;
lanugo hairs; giant cells resembling nevus
giant cells; colloidal iron positive material in
the giant cells; melanin pigment in the giant
cells; intimate relationship of nerve fibers to
the giant cells; thinning or absence of elastic
fibers; and a proliferation of reticular fibers
about the giant cells.

The natural regression of cellular nevi has
been reported in detail by Unna (11), Lund
and Stobbe (12), and Stegmaier (13, 14).
Stegmaier (13, 14) lists inflammation (halo
nevus phenomenon), development of skin tags,
fibrosis, and fat degeneration as changes in-
volved in the pathogenesis of regression and
disappearance of cellular nevi. Stegmaier (13)
states that all regressing nevi show evidence of
fibrosis, except for the very superficial, imma-
ture nevi with junctional proliferation.

Our histopathologic observations in cellular
nevii of the nose indicate a general sparsity of
collagen in areas of the corium occupied by
nests and strands of nevus cells. As the nevus
cells disappear, the void is replaced by fibrous
proliferation and this change appears to play
a role in the involution of the nevus cells. The
reason for a persistent fibrous papule as a
residual of a regressed cellular nevus is difficult
to answer, but anatomical location may be an
important factor. Replacement of the nevus
cells in the corium by dense fibrosis could
maintain and accentuate the dome-shaped
contour initially present in a cellular nevus
located on the nose.

Absence or thinning of elastic tissue in the
fibrous papules and cellular nevi that we studied
is supported by the observations of Unna (11), and Mehregan and Stariceco (15). Unna (11) observed that wherever nevus cells are numerous, all the elastic tissue between them perishes, but close to the margin of the nevus the elastic tissue remains unaffected. Mehregan and Stariceco (15) studied intradermal nevi and observed that the elastic fibers in the upper portions of the tumor showed a tendency to become gradually finer and thinner.

The network of nerve fibers demonstrated in fibrous papules and cellular nevi of our study are supported by the observations of Shelley and Arthur (16). They (16) reported that intradermal cellular nevi regularly possess an extremely dense network of fine nerve fibers, and these filaments arise from large mixed nerve trunks and penetrate virtually between every nevus cell.

Fibrous papule appears to be a common lesion of the nose, although they undoubtedly occur on other areas of the head and neck region. In reviewing lesions coded as fibrosis, fibroma, fibrous polyps, and fibroepithelial polyps, in over 20,000 accessions, we accepted 5 lesions as clinically and microscopically similar to the fibrous papule of the nose. These 5 lesions were located on the lower eyelid near the inner canthus, preauricular region, chin, nasolabial fold, and forehead. Only the lesion from the chin showed completely characteristic changes of the fibrous papule of the nose. This was a 3 mm papule from a 44 year old Negro man who stated the lesion had been present for 10 years.

We also studied biopsy material from a few patients with multiple facial lesions of adenoma sebaceum, and solitary hamartomas from the head and neck region of children. The microscopic changes in the lesions from these 2 groups of patients show a similarity to the fibrous papule of the nose. Follow-up information from 34 of our patients did not suggest the diagnosis of adenoma sebaceum in any of the group or in other members of their family.

From our observations, we believe that the fibrous papule usually located on the ala nasi is a common lesion, and because of the clinical resemblance, is frequently diagnosed as a cellular nevus. Because the lesions are small, asymptomatic and often inconspicuous, it is possible that only a minority of patients seek medical attention.

**SUMMARY**

A clinicopathological study of 40 patients with a distinct isolated fibrous papule of the nose is reported. The histogenesis and pathogenesis of this unique tumor indicates the lesion probably represents the residual of a cellular nevus in which stromal elements persist because of the anatomical location. There is a microscopic similarity of the fibrous papule to facial lesions of adenoma sebaceum and solitary hamartomas. For this reason the possibility that the lesion could represent a hamartoma or unusual type of neural end organ tumor can not definitely be ruled out. We propose the name of fibrous papule for this benign dome-shaped tumor of the nose. Excision of the lesion flush with the surrounding skin is adequate treatment and allows for excellent cosmetic results.

**REFERENCES**


