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Case Report

Segmental neurofibromatosis: report of two cases of this rare entity and brief review of the literature

Loknath Ghoshal*, Suchibrata Das*, Saumen Nandi, Jayanta Kumar Barua†**

* Department of Dermatology, Venereology and Leprology, NRS Medical College, Kolkata
** Department of Chest Medicine, NRS Medical College, Kolkata
† Department of Dermatology, Venereology and Leprology, Malda Medical College

Abstract Neurofibromatosis (NF) is a group of rare genetic disorder of neural crest derived cells of which neurofibromatosis type-1 is the most common. Riccardi classified NF into eight subtypes (NF-I to NF-VIII), of which NF-V is segmental neurofibromatosis (SNF). SNF is rare and facial involvement is even rarer. A 52-year-old man presented with complaints of numerous swellings on the right side of his face for the last 20 years. On examination, there were many papules and papulo-nodules only on the right cheek. The swellings were non-tender, firm on palpation and measured from 3 mm to 12 mm in diameter. A biopsy was taken from one of the nodules; the slide revealed non-encapsulated but well circumscribed proliferation of spindle cells with wavy, buckled nuclei arranged in wavy fascicles in myxoid background. This case of facial SNF is described not only for its extreme rarity, but also as an important differential diagnosis for facial tumor-like papules. We have also reviewed the literature briefly.

Key words
Segmental neuofibromatosis, postzygotic somatic mutation, neural crest cells.

Introduction

Neurofibromatosis (NF) is a group of rare genetic disorder of neural crest derived cells designated as neurofibromatosis type 1 (NF 1), neurofibromatosis type 2 and schwannomatosis. Neurofibromatosis type 1 is the most common of these disorders (affecting 1:3500 individuals worldwide) characterized by café-au-late macules, axillary freckling, multiple neurofibromas, Lisch nodules, and bone abnormalities.[1,2]

Riccardi[3] classified NF into eight subtypes (NF-I to NF-VIII), of which NF-V is segmental neurofibromatosis (SNF). SNF is rare and is characterized by neurofibromas and/ or café-au-lait macules limited to an area or segment with no crossing of the midline, no familial history, and no systemic involvement.[4] It is an example of mosaicism in which localized disease results from a post-zygotic NF1 gene mutation located on the proximal long arm of chromosome 17. Facial involvement is rarer.

Two cases of SNF are described; a case of facial SNF not only for its extreme rarity, but also as an important differential diagnosis for facial tumor-like papules. The second case affected arm. We also review the literature briefly.

Address for correspondence
Dr. Loknath Ghoshal
Department of Dermatology,
NRS Medical College,
138, AJC Bose Road, Kolkata 700014
E-mail - loknathghoshal@yahoo.co.in

Case reports

Case 1

A 52-year-old man presented to the clinic with complaints of numerous swellings on the right

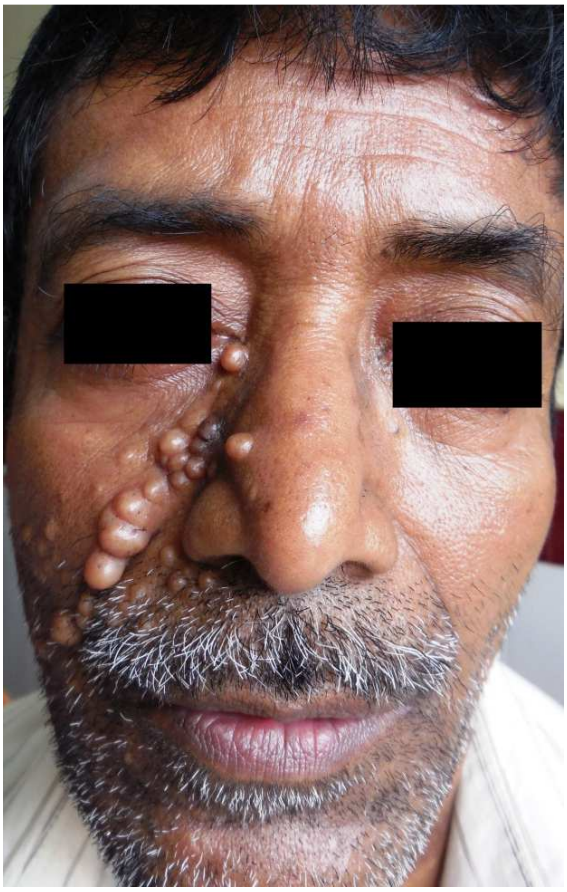

Figure 1 Skin-colored papules and papulonodules on the right cheek.

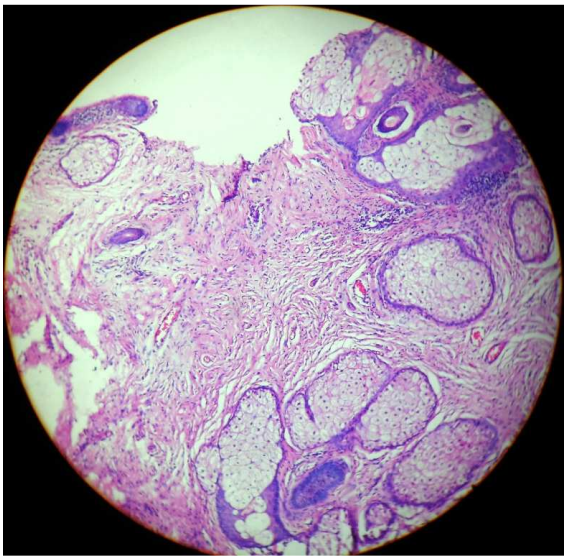

Figure 2 Non-encapsulated but well circumscribed proliferation of spindle cells with wavy, buckled nuclei arranged in wavy fascicles in myxoid background (H & E, 400X).

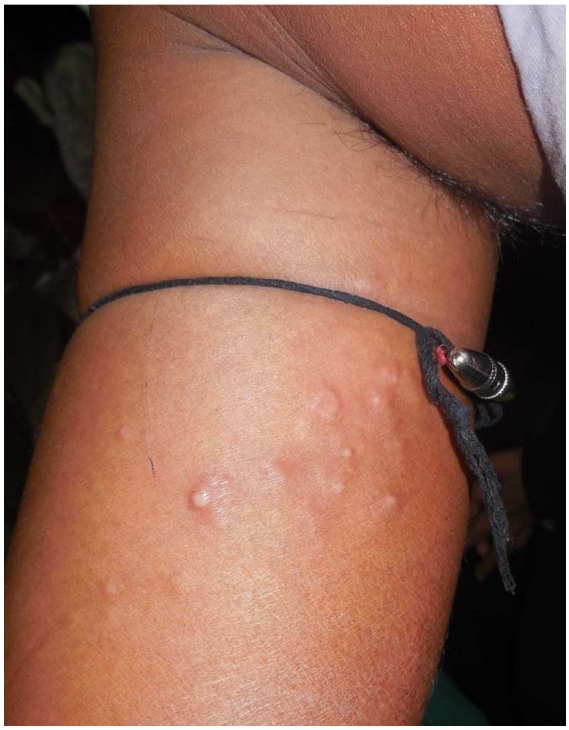

Figure 3 Few soft swellings on the right arm near the axilla.

side of his face **(Figure 1)** for the last 20 years. Otherwise he was asymptomatic, but he had grown curious about the nature and significance of these swellings. On examination, there were many (approximately 30) skin colored papules and papulonodules only on the right cheek, especially on the nasolabial furrow, where there was a linear pattern of distribution. The swellings were non-tender, firm on palpation and measured from 3 mm to 12 mm in diameter. He could not recall any of his family members having such swellings on the body.

No other abnormalities were found on examination of the rest of his body. General physical examination was normal including intelligence, speech, and hearing. Neurological examination was non-contributory, and so was slit lamp examination of the eyes. Imaging did not reveal any osseous abnormality.

A biopsy was taken from one of the nodules and sent for histopathological examination. The slide

revealed non-encapsulated but well circumscribed proliferation of spindle cells with wavy, buckled nuclei arranged in wavy fascicles in myxoid background (**Figure 3**). No features of malignancy were noted.

Based on the history, clinical findings and investigations, a diagnosis of segmental neurofibromatosis (SNF) was made.

The patient was explained about the disorder and counseled that he would need no treatment; also, since there were no complications associated there was no subsequent risk.

Case 2

A 26-year-old man presented with few soft swellings on the right arm near the axilla **(Figure 3)** for the previous 12 years. Though he had no symptoms, he was simply inquisitive about what those swellings were, and whether they needed any treatment. He also could not recollect any of his family members having such swellings on their bodies.

Examination revealed about 15 soft nodules on the right upper arm along the distribution of the first thoracic (D_1) nerve extending till above the elbow. Some of the nodules exhibited the 'button hole' sign. Examination of the rest of his body revealed no significant abnormalities. General physical examination including intelligence, speech, and hearing was again non-contributory. Neurological examination yielded normal findings, and so did slit lamp examination of the eyes. Again, imaging did not reveal any osseous abnormality.

A scalpel biopsy was taken excising one of the nodules and sent for processing. The stained slide once again showed spindle shaped cells in a myxoid background with wavy delicate nuclei suggestive of neurofibroma, much similar to **Figure 2**.

The patient was explained about the innocuous nature of the condition and that also he needed to cease worrying.

Discussion

This patient had localized distribution of neurofibromas in the distribution of the right trigeminal nerve. There was no involvement of other areas of the body, neither was any positive family history. Thus the patient has SNF according to Riccardi's classification.

Four subtypes occur in SNF, described as a true segmental type (Riccardi´s neurofibromatosis 5), a localized type with deep involvement, a hereditary type, and a bilateral type.[2]

Though neurofibromatosis is exceptionally variable in presentation, in most (90%) cases generalized expression of the disease develops. Rarely cases present with localized neurofibromas or café-au-lait spots.[3] This was first described by Crowe *et al.*[5] as sectorial NF, who proposed that such neurofibromatosis limited to a distinct sector of the body, without genetic transmission of the trait could be explained by somatic mutation. Also, Riccardi assumed that a postzygotic somatic mutation, occurring in primitive neural crest cells, is the most likely pathogenesis and thus the lesion should be strictly non-inherited.

Ingordo *et al.*[6] reviewed 11 cases of NF, with relative frequency of 0.020%. During the same period, only one case of SNF was observed (relative frequency 0.0018%). From these observations, the authors concluded that SNFs are probably not under-diagnosed but are 10 times more infrequent than other forms of NF.

Ruggieri *et al.*[7] estimated the prevalence of SNF to lie between 0.0014 and 0.002%.

Clinical findings develop with café-au-lait macules appearing in childhood and neurofibromas in adulthood. The most common presentation is neurofibromas alone ranging from 0.1 cm to several centimeters in diameter. Most often these occur are in a dermatomal distribution, of which the most commonly involved segment is cervical, followed by thoracic, lumbar, and sacral. Most cases present with unilateral disease although there are reports of bilateral disease.[8]

From the above, it is clear that the diagnosis of SNF may be a tentative one. The patient may, in course of time develop lesions in other areas of the body or a family member is subsequently detected to have neurofibromatosis, the patient subsequently may have to be assigned to a different subgroup.

Thus, extensive evaluation of the patient and relatives is necessary at the onset and subsequent follow up is also essential to maintain the diagnosis of SNF.

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