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Case Report

Segmental neurofibromatosis (a rare variant of a common genodermatosis): report of two cases

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Abstract Segmental neurofibromatosis is a rare variant of neurofibromatosis in which the lesions are confined to one segment or dermatome of the body. They resemble classical neurofibromas in their morphology, histopathology. However, systemic associations are usually absent. We report two cases representing with segmental distribution of neurofibromas on localized areas of the skin over back and chin respectively. They had negative family history and were lacking any systemic involvement.

Key words
Neurofibromatosis, segmental neurofibromatosis, neurofibroma.

Introduction

Neurofibromatosis (NF) is an autosomal dominant disorder that affects the bone, the nervous system, soft tissue, and the skin. At least 8 different clinical phenotypes of neurofibromatosis have been identified and are linked to at least 2 genetic disorders. Segmental neurofibromatosis (NF type V) is a rare disorder characterized by cafe-lu-lait macules (CAM) and neurofibromas, or only neurofibromas, limited to one region of the body.[1-4] It has been suggested that segmental NF results from a postzygotic NF1 gene mutation. Segmental NF is underdiagnosed as the majority of such patients is asymptomatic and seek medical attention for disfigured appearance of skin. In others, the condition is incidentally diagnosed while being examined for another problem. This is supported by the fact that though the first case of segmental NF was reported in 1937, little more than 100 cases have been reported till date.[5,6] It occurs in all age groups, has a mean age of onset of 28 years, with a slight male preponderance (male: female ratio = 1.14:1).[2,3] Most patients with segmental neurofibromatosis do not have a family history of neurofibromatosis. Cervical and thoracic regions are commonly involved and the disease is unilateral in the majority. Bilateral involvement may be either symmetric or asymmetric.[2-4] Various features of NF such as CALM, axillary freckling and neurofibromas occur at a varying frequency. However, variations seem to depend upon the age of onset of symptoms. In children, pigmentary findings are commoner, while in adults, neurofibromas are more common.[2,7] Lisch nodules are rarely seen, even after thorough ophthalmologic examination. Segmental NF does not evolve to the generalized form. Moreover, severe disease is less likely to

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occur in the segmental form as compared to NF1. Systemic complications typically associated with NF1 are rare and occur in less than 10% of patients.[2-4] Malignancies rarely occur in association with segmental NF[8]. Segmental NF needs to be differentiated from certain similar-appearing lesions, such as epidermal nevus, nevus lipomatosus cutaneous superficialis, and agminated lentiginosis (a condition characterized by numerous lentigines confined to a body segment, with a sharp demarcation at the midline).[9] There is no specific management strategy. However, genetic counseling should be done and the small risk of transmission to the offspring communicated. Careful follow-up is required to monitor disease progression or to detect any systemic complications that may occur in a minority.

Case report

Case 1 A 37-year-old patient reported with a history of multiple soft grouped skin papules over his back on left side. About 13 years ago he noted the development of small multiple papules on the left upper back. These lesions were asymptomatic and progressed slowly. Past medical history was not significant. He was married, having three children and there was no evidence of neurofibromatosis in his family. Multiple, soft, dome-shaped, flesh-colored nodules were located over a circumscribed area on the left upper back (**Figure 1**) Café-au-lait macules and axillary freckling were absent. Hematoxylin and eosin stained sections showed a dermal proliferation of spindle cells with wavy nuclei and inconspicuous nucleoli. The interspersed stroma was composed of fibrillary collagen (**Figure 2**).

Case report 2 A 43-year-old patient reported with a 4 years history of multiple asymptomatic soft grouped skin lesions over his right chin (**Figure 3**). The lesions started insidiously and were slowly progressive. On examination, he did not have any evidence of neurofibromatosis. None of the family members were found to have features of segmental NF. Histology of one of the lesion revealed the diagnosis of neurofibroma (**Figure 4**).

Discussion

Segmental neurofibromatosis has rarely been described in literature and total number of cases (including these two) does not go beyond 150. It may be misdiagnosed as a birthmark or remain undiagnosed for long periods of time, as the patients are often asymptomatic. Moreover, the clinical features are highly variable and range from a small area of skin involvement to involvement over the entire half of the body[2-4]. This variation is explained by the fact that segmental NF is thought to arise from a postzygotic NF1 gene mutation, leading to somatic mosaicism.[4,5,10] By FISH analysis, a whole gene deletion was shown in a percentage of fibroblasts from a café-au-lait spot in the affected skin but not from unaffected skin or blood lymphocytes. NF1 mutations in Schwann cells, but not in fibroblasts, correlate with neurofibroma formation. It is thought that, if a somatic mutation occurs early enough, it will result in generalized disease. Therefore, it seems more appropriate to use the terms “mosaic-generalized” and “mosaic-localized” to describe NF1 and segmental NF, respectively. These two entities arise at different stages of embryonic development

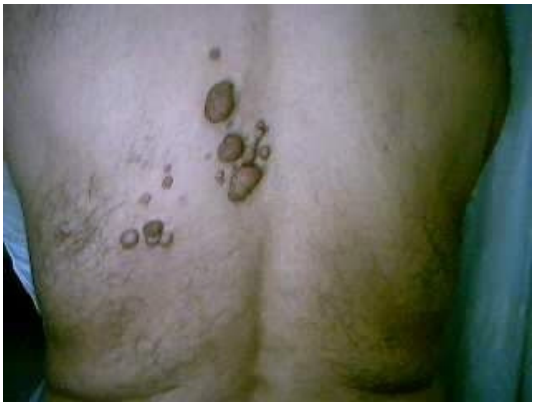

Figure 1 Multipe, small, dome-shaped, feshy skin growths localized over left back of a middle aged patient.

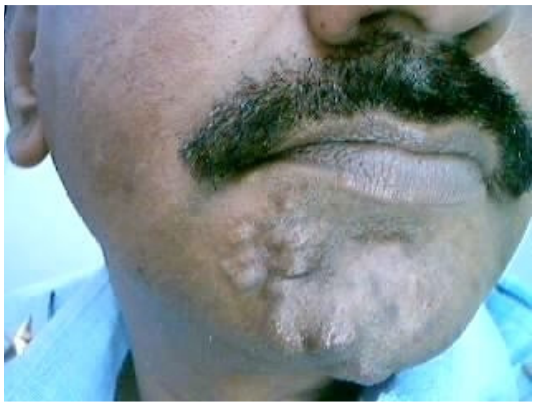

Figure 3 Soft, multiple, closely grouped skin tumours over right side of the chin.

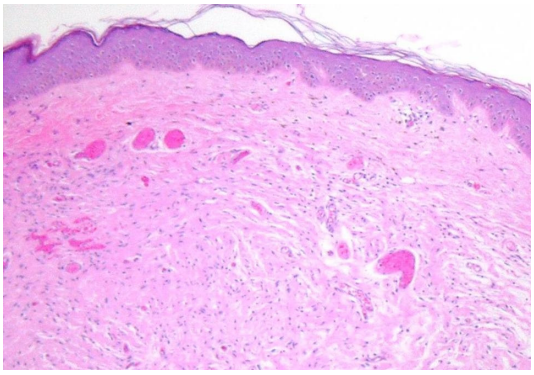

Figure 2 Histopathology of one of the lesions revealing epidermal hyperplasia and dermal proliferation of spindle cells with interspersed wavy collagen in different directions.

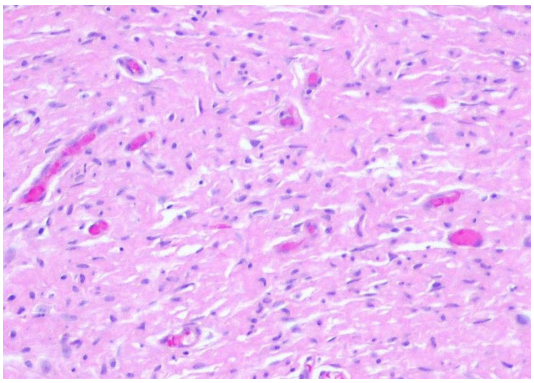

Figure 4 Histopathology shows thin wavy fibers in loosely textured stroma of fibrillary collagen and proliferated spindle cells with wavy nuclei.

from mutations in the same gene.[4,5,10]

Individuals with segmental NF have a low risk of transmitting the disease to their offspring. Moreover, 93% of patients do not have a positive family history.[2,3] In both of our cases, family screening did not reveal any evidence of neurofibromatosis in his children or parents. It was most likely, the somatic mutation that gave rise to the segmental disease in both of our patients. The recognition of this mosaic phenotypes (resulting from post zygotic somatic mutation) is important because individuals with the mosaic form, even with a generalized phenotype (due to early post zygotic mutation), are less likely to have severe disease and they also have lower offspring recurrence risk than individuals with the nonmosaic form.[4,5,10] One of our case had Segmental NF of facial localization and a similar case has recently been reported in literature.[11] Another idea of presenting these cases was to promote the concept that generalized NF1 and the previously termed NF5, or segmental NF, are likely variant expressions of the same disease.

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