Intriguing Bumps Over Palms and Soles

Bhavana R Doshi, Vasudha A Belgaumkar, Nagbhushan S Chougule

Departments of Dermatology and Ophthalmology, KLE Academy of Higher Education and Research’s JN Medical College, Belagavi, Karnataka, Department of Skin and VD, B J Medical College and Sassoon Hospital, Pune, Maharashtra, India.

E-mail: bhavs1982@gmail.com

Indian J Dermatol 2019;64(3):245-6

Sir,

Neurofibromatosis (NF) is a set of inherited disorders originally designated as neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2), and schwannomatosis occurring as benign tumors of nerve sheath. Cardinal dermatologic features include café au-lait macules, neurofibromas along with the features of axillary, inguinal, and palmoplantar freckles. According to Riccardi’s classification,[1,2] segmental neurofibromatosis (SNF) was initially classified as type V NF, which presents as either multiple café-au-lait macules or neurofibromas in a segmental distribution with no crossing of the midline, no familial history, and no systemic involvement.[2] SNF is further classified as subtypes: True segmental localized with deep involvement, hereditary, and bilateral.[2] Type VIII NF as per Riccardi’s classification includes those cases that are otherwise not specified.

A 23-year-old male born of non-consanguineous marriage presented with multiple skin to red colored asymptomatic fixed, raised lesions over the palms and soles since 4 years with no other skin lesions or underlying systemic diseases. He denied history of trauma, pain in lesions following cold exposure, and similar lesions in siblings or other family members.

On physical examination, multiple skin colored to minimally erythematous papules and nodules were observed over the palmar aspects of both the hands up to the wrist, lateral aspect of fingers and web spaces, [Figure 1a] and along the margins of both the feet and toe web spaces [Figure 1b]. These were of 3 mm to 8 mm size, non-tender, soft to rubbery on palpation with intact overlying dermatoglyphics, and lacked pain on deep pressure. There was no evidence of other cutaneous or mucocutaneous lesions. This prompted a differential diagnosis of granuloma annulare, multiple fibromas, eruptive xanthomas, and appendageal neoplasms.

Hematological investigations were within normal limits. The punch biopsy from papule on the palm showed well-demarcated non-encapsulated nodule in the reticular dermis consisting of numerous cells with spindle shaped tapering nuclei admixed with few mast cells on hematoxylin and eosin stain [Figure 2a and b] consistent with diagnosis of neurofibroma. The patient was normotensive with normal skull x-ray and ultrasonography of abdomen and pelvis. The auditory evaluation along with a thorough ophthalmic slit-lamp and the fundoscopic examination were unremarkable. Thus, co-relating the clinical features and histopathological appearance, a final diagnosis of isolated palmoplantar NF was put forth.

SNF is a rare disorder with prevalence estimated between 0.0014 and 0.002%.[3] Most patients (93%) do not have a family history of NF.[4] SNF may arise from post-zygotic somatic mutation or loss of heterozygosity (LOH). The gene for NF-I is in the pericentric region of chromosome 17 q 11.21. When a patient presents with SNF-I, it is critical to determine if the disorder is a result of mosaicism or LOH. In the latter, the abnormal allele is present throughout the body, with loss of the remaining normal allele in the affected segment.[1] In a patient who presents with SNF along with Lisch nodules or axillary freckling, LOH is likely to account for the segmental presentation. The risk of passing the gene to a child is roughly 50:50 (as in generalized NF-I).[1] Our case lacked presence of Lisch nodules or other ocular manifestations.

Patients with mosaicism from post-zygotic somatic gene mutation may or may not have gonadal mosaicism.[1]

**Figure 1:** (a) Multiple skin colored papules over the palm. (b) Skin colored papules over the sides of foot

**Figure 2:** (a) Biopsy from a palmar papule showed hyperkeratotic epidermis with a well circumscribed non-encapsulated collection of spindle shaped cells with tapering nuclei in reticular dermis (H and E, ×10). (b) On higher magnification, the neural cells with interspersed mast cells can be observed (H and E, ×40)
Gonadal mosaicism is more likely when more than one segment is involved in different parts of the body. According to this theory, it appears that in our case the probability of “gonadal mosaicism” as a pathogenetic mechanism is high because of the involvement of more than one segment. Gonadal mosaicism is thought to be responsible for reports of patients with localized disease having children with generalized NF1.[3,4] Hence, a geneticist should be consulted to discuss the risk of transmission.

SNF-I occurs in all age groups and has a mean onset age of 28 years.[4] In SNF-I, clinically, patients may be divided into four groups: Those with only pigmentary changes, those with only neurofibromas, those with both pigmentary changes and neurofibromas, and those with isolated plexiform neurofibromas. Although the lesions are usually unilateral, there are reports of bilateral SNF-I.[5] In this variant, the affected area can vary in size from a narrow strip to an area encompassing half of the body.

Clinical disease in SNF-I develops in the same course of time as generalized NF. Pigmentary changes, plexiform neurofibromas develop in childhood, and neurofibromas develop in adulthood.[4] Most commonly, patients present with isolated neurofibromas in a dermatomal distribution, most commonly cervical, followed by thoracic, lumbar, and sacral.[4,5] Pigmentary changes include cafe-au-lait macules and axillary freckling, with the cervical dermatomal distribution being more common.[4] However, in our case, the unusual feature is the simultaneous involvement of the cervico-thoracic as well as the sacral dermatome in the absence of any pigmentary changes at the time of presentation.

Localized lesions may be neglected by the patient, and occurrence over unusual sites such as palms and soles with lack of other classical features could be clinically misleading unless the lesions are biopsied. Therefore, increased awareness among the clinician about the atypical manifestations is essential to facilitate a careful investigation and follow-up to monitor disease progression and timely detection of any systemic complications.[2]

To conclude, whether our case with an unusual pattern of distribution of neurofibromas restricted to palm and soles and devoid of other cutaneous features and systemic involvement can be classified as a variant of SNF or a different variant hitherto not mentioned in literature (Riccardi type VIII not otherwise specified) remains a matter of debate.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Theos A. American college of physicians; American physiological society. Pathophysiology of neurofibromatosis type 1. Ann Intern Med 2006;144:842-9.
2. Riccardi VM. Neurofibromatosis: Clinical heterogeneity. Curr Probl Cancer 1982;7:1-34.
3. Victor FC. Segmental neurofibromatosis. Dermatol Online J 2005;11:20-1.
4. Oguzkan S, Cinbis M, Ayter S, Anlar B, Aysun S. Familial segmental neurofibromatosis. J Child Neurol 2004;19:392.
5. Nagaoka Y, Asahin A, Yanos S, Tamaki K. Bilateral segmental neurofibromatosis. Acta Derm Venereol (Stockh) 2002;82:219-20.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

How to cite this article: Doshi BR, Belgaumkar VA, Chougule NS. Intriguing bumps over palms and soles. Indian J Dermatol 2019;64:245-6. Received: December, 2017. Accepted: December, 2018.