A segmental neurofibromatosis case with eruptive seborrheic keratoses

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Abstract

Segmental neurofibromatosis (SNF) is a rare variant of neurofibromatosis (NF) type 1 characterized by a restricted distribution of cafe-au-lait macules, and/or neurofibromas, and rarely freckling to a single dermatomal segment. Patients with NF type 1 have an associated increased risk for benign or malignant tumours. The prevalence of typical NF type 1 complications including malignancies in SNF is much lower than the generalized form. Seborrheic keratosis is one of the more common benign epidermal tumour which can be a paraneoplastic syndrome when it arises with an eruptive appearance. To our knowledge in the literature no case of SNF associated with eruptive seborrheic keratoses has been defined. We report the case of a man, aged 51, who had SNF and abruptly developed eruptive seborrheic keratoses.

Keywords: Neurofibromatosis, Segmental neurofibromatosis, Eruptive seborrheic keratoses.

Introduction

Neurofibromatosis (NF) is a genetic disorder of nervous system that primarily affects the development and growth of the neural tissues. Segmental neurofibromatosis (SNF) is a rare disorder with typical features of NF type 1 localized most often to one region of the body.[1] The median age at onset in SNF is in twenties, with a higher incidence in women.[2] The skin neurofibromas are the most frequent manifestations of SNF.[3] Seborrheic keratosis is a common, benign cutaneous tumour seen in elderly people.[4] To our knowledge, this is the first case of SNF with eruptive seborrheic keratoses published in literature.

Case Report

A 51-year-old man presented with multiple skin-coloured painless nodules on the left lateral side of his lower trunk and multiple, light and dark brown, suddenly arisen papular lesions on his back. The segmentally situated nodules had been present for six years and he did not seek any investigations or treatment. The nodules had increased in number and size over that time in the same area. The papules on his back developed about two years ago suddenly and the number and size had grown gradually. He denied a history of any significant past medical disease. There was no history of other family members with NF. On dermatological examination 12-15 skin-colored, soft, non-tender nodules ranging in size from 5 mm to 1.5 cm in diameter were present on the left lateral side of the lower trunk between dermatomes T10 and T12, without crossing the midline (Figure-1). There was no similar lesions elsewhere. Axillary freckling, cafe-au-lait macules, plexiform neurofibromas or any other skeletal deformities were not present. There was multiple well-circumscribed, pale and dark brown verrucous papular lesions ranging in size from 3mm to 2cm in diameter on his back (Figure-2). In dermoscopic evalution of the lesions comedo-like opening, milia-like cysts and cerebriform structures were seen and there was no pigment network. The papules on the back were diagnosed as seborrheic keratosis with the clinical and dermoscopic features. Physical examination was unremarkable including intelligence, speech and auditory functions. Ophthalmologic examination revealed no Lisch nodules. One of the dermatomally situated nodules was excised and dermal proliferation of spindle-shaped cells consistent with neurofibroma was shown by histopathological examination (Figure-3).

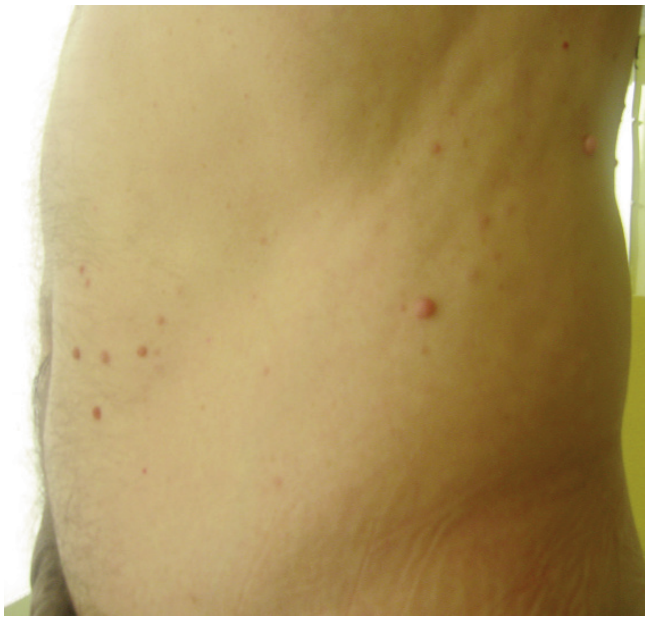

Figure-1: Multiple skin-colored neurofibromas extended in a dermatomal T10 to T12.

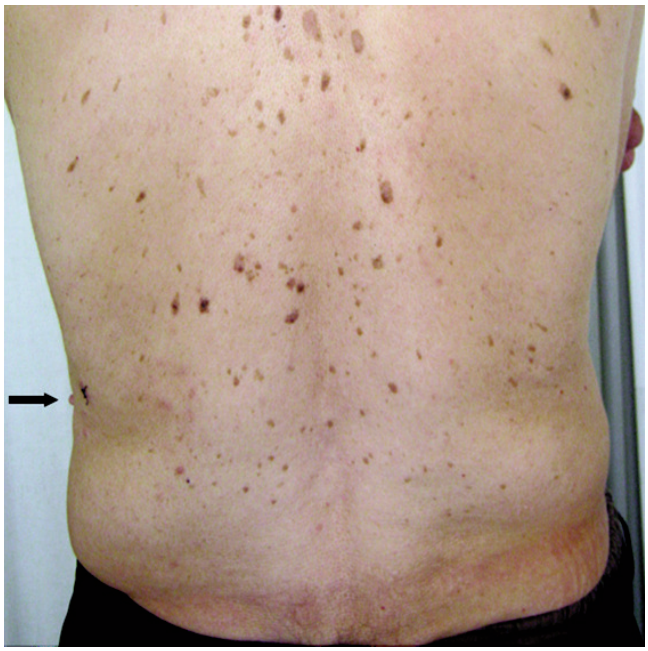

Figure-2: Eruptive seborrheic keratoses on the back. The arrow shows a neurofibroma, and suture material due to the excisional biopsy.

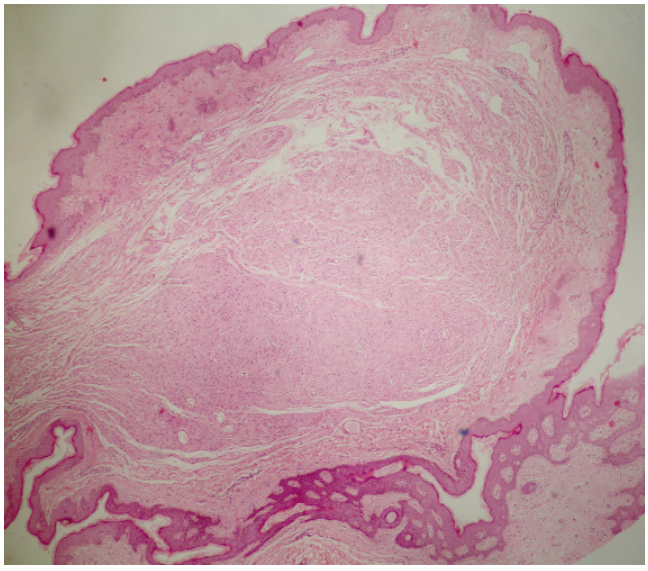

Figure-3: Well circumscribed dermal nodule consisting of spindle cells (Hematoxylin-eosin stain, original magnification ×4).

Immunohistochemically, S-100 protein was positive for tumour cells. The patient was investigated for visceral involvement and internal malignancy in detail. Routine haematological and biochemical investigations, thyroid function tests, tumour markers, peripheral blood smear were within normal limits and occult blood test on stool was negative. Chest X-ray, thyroid ultrasound, oesophageo-gastroduodenoscopy, computerised tomography of the abdomen, and magnetic resonance imaging of the brain were reported as normal. The patient was diagnosed as SNF on grounds of the clinical and histopathological features.

Discussion

Segmental neurofibromatosis is a rare disorder characterized by cafe-au-lait macules and/or neurofibromas following a regional distribution with its prevalence estimated at about 0.0027%.[3] Riccardi established the clinical features of SNF and classified this different presentation first as NF type 5.[5] It has been suggested that SNF is related to postzygotic mutation of the NF type 1 gene, leading to somatic mosaicism. Gonadal mosaicism is thought to be responsible for reports of patients with localized disease having children with generalized NF.[3] Most of the SNF cases do not have a family history of NF.[2] Ruggieri and Huson in 2001 proposed to use the term mosaic localized NF type 1 instead of NF type 5, because of the present understanding of the molecular and genetic aspects of NF.[6] While there is a consensus statement concerning the minimum diagnostic criteria for NF type 1, there is no strict criteria for the diagnosis of SNF although several definitions have been proposed. The diagnosis is essentially based on cafe-au-lait macules, freckling and/or neurofibromas situated dermatomally.[7,8] The prevalence of the disease-associated systemic involvement and complications in SNF is much lower than in the generalized disease.[2,3] There have been reports of SNF associated with visceral neurofibromas, soft tissue hypertrophy, skeletal abnormality, unilateral renal agenesis and renal angiomyolipomas.[3] SNF has been linked to other malignancies rarely such as peripheral nevre sheath tumour, malignant melanoma, bronchoalveolar lung carcinoma, colon cancer, and Hodgkin's lymphoma.[8] Kajimoto et al. presented a bilateral SNF case with gastric carcinoma and they suggested the possibility of SNF as a sign of paraneoplastic process of malignant carcinoma.[9] Seborrheic keratosis is one of the most common benign epidermal tumour in older individuals. The etiology of seborrheic keratosis is unknown, although sun exposure, human papilloma virus, and epidermal growth factors have been suggested as possible etiologies.[4] The eruptive appearance of multiple seborrheic keratoses may be associated with underlying malignant disease that is known as Leser-Trélat paraneoplastic syndrome. Even though this sign remains controversial, it has been described during a wide range of malignancies.[4] Also the acute eruption of seborrheic keratoses in association with erythroderma secondary to an inflammatory dermatose like psoriasis has been reported.[10] In this case the diagnosis of SNF was established by the presence of multiple neurofibromas localized on the trunk dermatomally without an affected family member or systemic involvement. The patient underwent a diagnostic programme

to exclude malignant diseases or visceral involvement of SNF and all the results were within normal limits.

Conclusion

To the best of our knowledge, to date, no case of SNF accompanied by an eruptive seborrheic keratosis has been reported in the literature. It is uncertain whether seborrheic keratosis coexists incidentally or results from a genetic defect associated with SNF. Although it is controversial, eruptive seborrheic keratoses is accepted as a paraneoplastic syndrome by some authorities. Recently SNF has been reported and speculated as a paraneoplastic process. In the presented case, both of the disorders that could raise the suspicion of a paraneoplastic process could not detect any underlying malignancy. We suggest that coexistence of SNF and eruptive seborrheic keratosis is likely to be coincidental. Long term follow up is necessary due to the existing malignancy risk.

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