Segmental neurofibromatosis: A rare variant of a common genodermatosis

P. Morais, O. Ferreira, H. Bettencourt, and F. Azevedo

SUMMARY

Segmental neurofibromatosis is a rare disorder characterized by features of neurofibromatosis type 1 circumscribed to a particular body segment. This entity is considered to be the result of a somatic mosaicism and is still under-diagnosed. We report a case of segmental neurofibromatosis and give a brief and up-to-date overview of the disease.

KEY WORDS

segmental neurofibromatosis, type V neurofibromatosis, mosaic-localized neurofibromatosis type 1

Introduction

Type V, segmental, or mosaic-localized neurofibromatosis is a rare condition that occurs 10 to 20 times less frequently than neurofibromatosis type 1 (NF-1; 1, 2). It is characterized by *café-au-lait* macules, freckles, and/or cutaneous neurofibromas, and it is limited to a circumscribed body segment (3). The first descriptions of this disorder were those of Gammel in 1931 (4) and Crowe et al. in 1956 (5). Miller and Sparkes proposed the term *segmental neurofibromatosis* (SN) in 1977 (6) and, five years later, Riccardi proposed a classification of NF that included eight different types, including the segmental form (type V; 3). In 1987, Roth et al. proposed a subclassification of SN into four categories: true segmental (type V Riccardi), localized with deep involvement, hereditary, and bilateral (7). Here we report a case of SN located in the thoraco-lumbar region.

Case report

A 64-year-old Caucasian woman presented with a 5-year history of multiple, soft-to-firm, dome-shaped, and flesh-colored papules and nodules grouped over the left thoraco-lumbar transition in a dermatomal distribution (Fig. 1). They had gradually increased in size over time and were slightly painful. There was no history of seizures or other neurologic disorders, *café-au-lait* macules, or axillary freckling. Her past medical history and family history were non-contributory. The patient was married and had two apparently healthy children. Laboratory evaluation was within normal limits. Craniospinal magnetic resonance imaging, abdominal ultrasound, and ophthalmological examination were normal. A histology of one of the nodules revealed a dermal well-circumscribed spindle-cell neoplasm whose cells had wavy nuclei, inconspicuous nucleoli, and scant cytoplasm interspersed with a stroma composed of fibrillary collagen (Fig. 2). The clinical and histopathological findings were suggestive of neurofibromas in a segmental distribution.

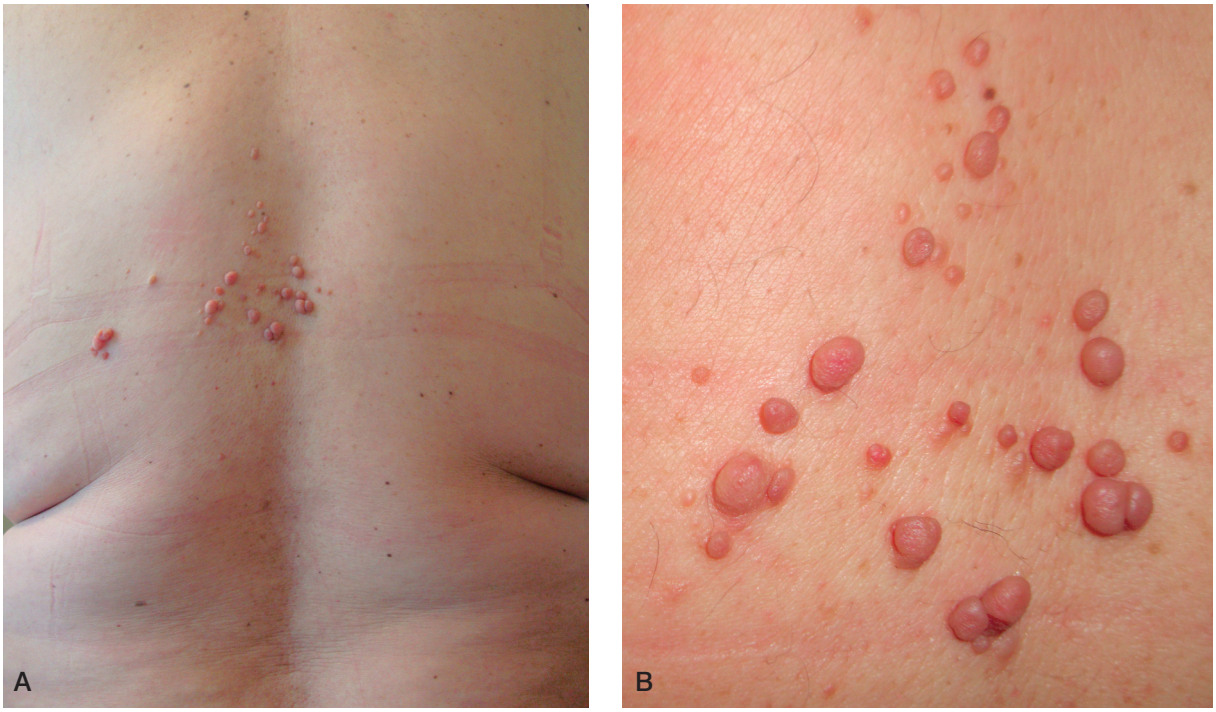

Figure 1. Clinical appearance of patient (A); close-up showing flesh-colored papules and nodules grouped over the left thoraco-lumbar region (B).

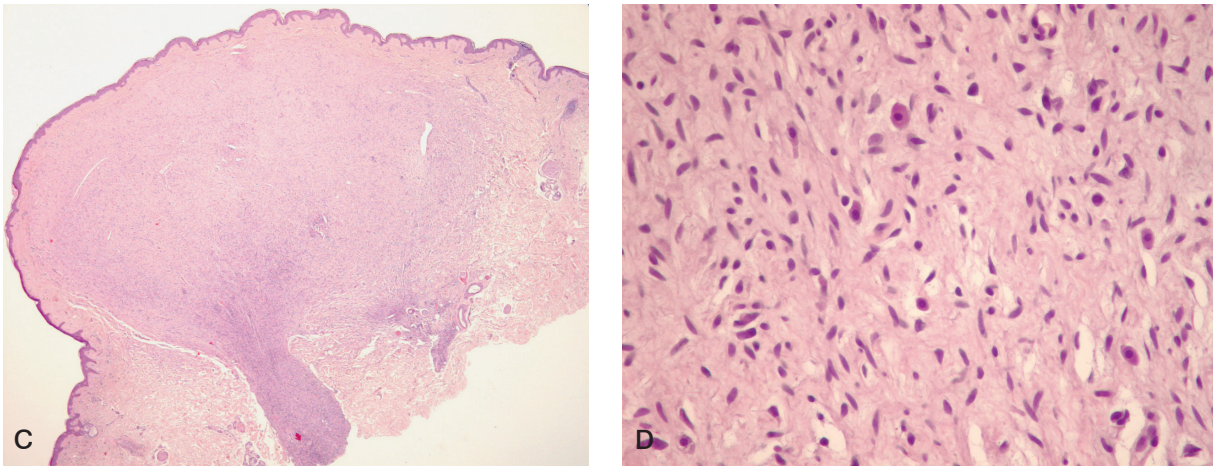

Figure 2. Histopathology of one of the lesions revealing dermal proliferation of spindle cells with wavy nuclei, interspersed in a stroma composed of fibrillary collagen. Nuclear pleomorphism, mitoses, and hypercellularity are absent (A, H&E 2×); close-up (B, H&E 40×).

Discussion

This case exhibited features consistent with the true segmental type of NF. SN primarily affects Caucasians, and females are affected twice as often as males, with bimodal peaks of onset at 10 to 30 years and 50 to 70 years. Skin lesions are most commonly found in a unilateral distribution over the cervico-thoracic region (2, 8, 9). In patients with neurofibromas alone, the tumors are usually dermatomal in distribution (8). The phenotype of SN includes localized manifestations of all of the common complications of NF-1, including pseudarthroses and Lisch nodules (1, 10). To match the diagnosis of SN, Lisch nodules should be unilateral and homolateral to the involved dermatome. If they are bilateral, it would suggest NF-1, which has a high risk of genetic transmission to offspring (1, 2, 8, 10). Therefore, patients with suspected SN should undergo a systematic physical examination and, if neces-

sary, genetic counseling can be offered. SN is thought to arise from a postzygotic mutation in the *NF1* gene leading to somatic mosaicism. If a somatic mutation occurs early enough, it will result in a generalized disorder, whereas mutations occurring late in embryonic development result in a single region or organ involvement (localized disease). Therefore, it seems more appropriate to use the terms "mosaic-generalized" and "mosaic-localized" to describe NF-1 and SN respectively. These two disorders arise at different stages of embryogenesis from mutations in the same gene (1, 2, 8, 10). Genetic counseling with such patients is difficult because gonadal mosaicism for *NF1* has been demonstrated and patients with SN have had offspring with either typical NF-1 or SN (10).

SN is an overlooked disorder and probably more common than previously reported, as the majority of such patients are asymptomatic and seek medical attention only for cosmetic concerns. In others, the condition is incidentally diagnosed while the patient is being examined for a different concern. SF needs to be differentiated from regular NF-1, benign tumors (trichoepithelioma, leiomyoma), malignancies (carcinomas, lymphomas), sarcoidosis, granuloma annulare, epidermal nevus, nevus lipomatosus cutaneous superficialis, agminated lentiginosis, and xanthomas (2). Although no specific guidelines exist regarding management of these patients, accurate diagnosis is important for the detection of systemic complications and, when indicated, to offer adequate genetic counseling.

REFERENCES

1. Ruggieri M, Huson SM. The clinical and diagnostic implications of mosaicism in the neurofibromatoses. Neurology. 2001;56:1433–43.

2. Hager CM, Cohen PR, Tschen JA. Segmental neurofibromatosis: case reports and review. Am J Acad Dermatol. 1997;37:864–9.

3. Riccardi VM. Neurofibromatosis: clinical heterogeneity. Curr Probl Cancer. 1982;7:1–34.

4. Gammel JA. Localized neurofibromatosis. Arch Dermatol Syph. 1931;24:712–5.

5. Crowe FW, Schull WJ, Neel JV. Clinical, pathological, and genetic study of multiple neurofibromatosis. Springfield (IL): Charles C Thomas; 1956. 181 p.

6. Miller RM, Sparkes RS. Segmental neurofibromatosis. Arch Dermatol. 1977;123:837–8.

7. Roth RR, Martines R, James WD. Segmental neurofibromatosis. Arch Dermatol. 1987;123:917–20.

8. Gonzalez G, Russi ME, Lodeiros A. Bilateral segmental neurofibromatosis: a case report and review. Pediatr Neurol. 2007;36:51–3.

9. Niiyama S, Satoh K, Kaneko S, Aiba S, Mukai H. Segmental neurofibromatosis. Acta Derm Venereol. 2005;85:448–9.

10. Listernick R, Mancini AJ, Charrow J. Segmental neurofibromatosis in childhood. Am J Med Genet. 2003;121A:132–5.

AUTHORS' ADDRESS

Paulo Morais, Department of Dermatovenereology, S. João Hospital, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal, corresponding author, E-mail: paulo@med.up.pt

Olga Ferreira, Department of Dermatovenereology, same address

Herberto Bettencourt, Department of Pathology, same address

Filomena Azevedo, Department of Dermatovenereology, same address