

A Case of Late-onset Segmental Neurofibromatosis

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ABSTRACT

Segmental neurofibromatosis (NF5) is a rare variant of neurofibromatosis. To our knowledge, there have been few reports of cases presenting later in life. The recognition of NF5 is important, as there have been reports of paraneoplastic manifestations and transmission to offspring. Here we present the case of a patient who presented with NF5 first appearing in her mid-50s. This case illustrates the subtle nature of NF5, which often leads to misdiagnosis.

INTRODUCTION

Segmental neurofibromatosis (NF5) is a rare variant of neurofibromatosis (NF) with cutaneous lesions typically limited to one body region, and an absence of systemic complications in the majority of patients.^{1,2} The median age of onset is 28 years in men and 27 years in women.² The clinical findings can be subtle, and therefore NF5 is often under- or misdiagnosed. This is an important clinical variant of NF to recognize, since offspring of patients with this condition are at risk of developing NF1, with the possibility of developing oculocutaneous lesions, bony abnormalities, seizures, and learning difficulties.¹⁻⁴

CASE PRESENTATION

A 59-year-old white woman was seen in dermatology clinic for evaluation of small skin-colored bumps on her right shoulder that had been present for approximately 4 years (Figure A,B). The lesions were completely asymptomatic, but she was bothered by their cosmetic appearance. She had no family history of similar lesions and reported no history of skin lesions in her children.

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A skin exam revealed firm, grouped skin-colored papules 3-10 mm in size, with a positive buttonhole sign (easy manual invagination of lesion) in a dermatomal distribution on the right shoulder. She did not have any other ocular, bony, or cutaneous features of type I neurofibromatosis, including Lisch nodules, kyphoscoliosis, diffuse or plexiform neurofibromas, café au lait macules or axillary/inguinal freckling.

There is a fairly narrow differential diagnosis for segmental cutaneous neoplasms (Table), and given the clinical appearance of her lesions, our clinical suspicion for segmental NF was high. Despite this, a biopsy of one of the lesions on the shoulder was obtained. Histologic examination of the tissue by a dermatopathologist demonstrated spindle and s-shaped cells within a delicate stroma. There was no significant atypia or melanocytic proliferation identified. These findings were consistent with a neurofibroma.

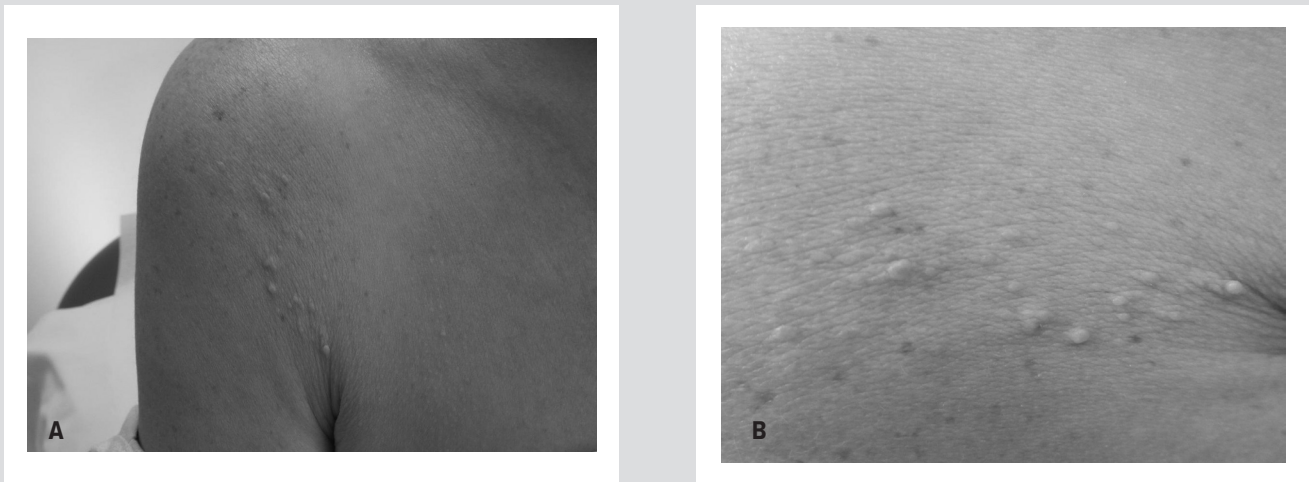
DISCUSSION

Segmental neurofibromatosis most commonly presents as isolated and unilateral neurofibromas occurring in a cervical distribution, although there are other rare variants.^{2,4} It is considered a non-inherited form of NF caused by a post-zygotic mutation resulting in mosaicism. If mosaicism is present within gonadal cells, it is possible that a person with NF5 can have offspring with generalized NF.^{4,5}

This disease is interesting in that the clinical picture can provide insight into which particular somatic cell lines harbor the mutation. For example, patients with manifestations limited to only neurofibromas are thought to have the mutation in Schwann cells, explaining why neurofibromas occur in a dermatomal distribution. Patients with only pigmentary manifestations are thought to have the mutation in fibroblasts, explaining the blaschkoid distribution of café au lait macules in NF5.⁶

In contrast to NF, systemic complications including ophthal-

Figure. Dermatomal Distribution



Lesions on right shoulder (A); close-up examination of segmental neurofibromas (B).

mologic involvement and neurological complications are rare in NF5.^{1,4,7,8} Recently there has been speculation that the incidence of malignancy in patients with NF5 may be comparable to those with NF1, and therefore, age-appropriate malignancy screening is indicated.⁷⁻⁹

CONCLUSION

Segmental neurofibromas or café au lait macules should prompt further evaluation with complete history and physical examination and dermatology consultation to ensure that patients do not have more generalized disease consistent with NF1. Genetic counseling and evaluation of offspring for NF skin lesions or cognitive impairment is also advisable given the small risk of transmission to offspring. Patients should be followed-up to monitor for disease progression and to screen for systemic complications seen in NF1.

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Table. Clinical Differential Diagnosis of Dermatologically Distributed Nodules^a

Infection
Syphilis
Neoplasm
Benign: Syringocystadenoma papilliferum, Trichoepithelioma
Malignant: Basal cell carcinoma, squamous cell carcinoma, lymphoma, plasmacytoma, cutaneous metastases
Other
Granuloma annulare, neurofibromatosis type I, pseudolymphoma, rheumatoid nodules, sarcoidosis, xanthomas

^aAdapted from Hager et al.²

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