Letter to the Editor

Neurofibromatosis Associated With Plaque-Type Psoriasis: Coincidental Occurrence or Causal Association?

To the Editor:

Neurofibromatosis type 1 (NF-1) is a hereditary disorder commonly associated with cutaneous, neurologic, and orthopedic manifestations.[1] Psoriasis is a chronic multifactorial skin condition characterized by erythematous scaly plaques that affect the scalp, trunk, extensor surfaces of the limbs, and genital region. The condition affects 2% to 4% of the population in Western countries.[2] The clinical association between neurofibromatosis and psoriasis is rare but could be related to common genetic defects.[3-7]

We report a 52-year-old woman who was referred to our department with erythematous scaly lesions on her elbows, knees, and scalp that had appeared in the last year. She presented with café-au-lait spots that were present since birth and an overgrowing formation of tumors over her trunk since 46 years of age. Her family history revealed that her 13-year-old son also had multiple café-au-lait spots. A family history of psoriasis was not reported. Dermatologic examination revealed multiple cutaneous neurofibromas and café-au-lait spots on her trunk (Figure 1). Lisch nodules were seen on ophthalmologic examination. Standard laboratory tests and endocrinologic examination revealed no abnormalities. Neurologic and cardiologic examinations excluded systemic involvement. Neurofibromatosis type 1 was diagnosed based on established diagnostic criteria (Table).[8] She also was diagnosed with plaque-type psoriasis based on clinical findings (Figure 2). Psoriatic lesions were treated with keratolytic ointments and corticosteroid creams.

Only a few reported cases describe the association between NF-1 and psoriasis,[3-6] with the first case published by Roenigk and Manick[3] in 1985. Neurofibromatosis type 1 is a hereditary neurocutaneous disorder that predisposes patients to various forms of neoplasia.[1] Compared to neurofibromatosis type 2, NF-1 is characterized by a better prognosis and a lower incidence of central nervous system tumors. However, morbidity and mortality rates in NF-1 are not negligible. Some of the most severe complications include vision loss secondary to optic nerve gliomas; tumors of the spinal cord; scoliosis; vascular lesions; and long bone abnormalities, which sometimes necessitate amputation.

The neurofibromin 1 gene, *NF1*, encodes a 250- to 280-kDa tumor suppressor protein.[7] Somatic mutations of the *NF1* gene have been found in malignant tissues and a reduced immunosignal for NF1 protein has been reported in psoriasis.[9,10] Moreover, Endo et al[11] found that defects in the regulation of the Hedgehog signaling pathway due to deficiency of neurofibromin contributed to the hyperproliferation of Schwann cells in plexiform neurofibromas. The same pathway is involved in the hyperproliferation of lesional keratinocytes in psoriasis. Furthermore, psoriatic skin expresses the transcription factor Gli1, which was first isolated as an amplified gene in a glioma and now is expressed in several tumors including basal cell carcinoma, and induces decreased neurofibromin expression.[11]

Neurofibromatosis type 1 and psoriasis share transcription factors and tumor suppressor gene expression defects, which suggests common pathogenetic pathways that should be further and deeply investigated. According to these findings, the association between

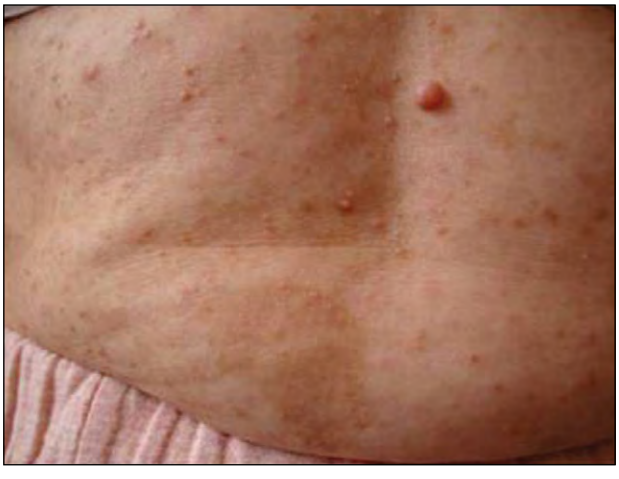

Figure 1. Neurofibromas and café-au-lait spots on the trunk.

Diagnosis of Neurofibromatosis Type 1 (NF-1) According to the National Institutes of Health Consensus Development Conference[8,a]

- ≥6 café-au-lait spots >5 mm in greatest diameter in prepubertal individuals and >15 mm in greatest diameter in postpubertal individuals
- ≥2 neurofibromas of any type or 1 plexiform neurofibroma
- Freckling in the axillary or inguinal region
- Optic glioma
- ≥2 Lisch nodules (iris hamartomas)
- A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis
- A first-degree relative (parent, sibling, or offspring) with NF-1 by the above criteria

[a]The diagnostic criteria for NF-1 are met if an individual presents with ≥2 of the listed features.

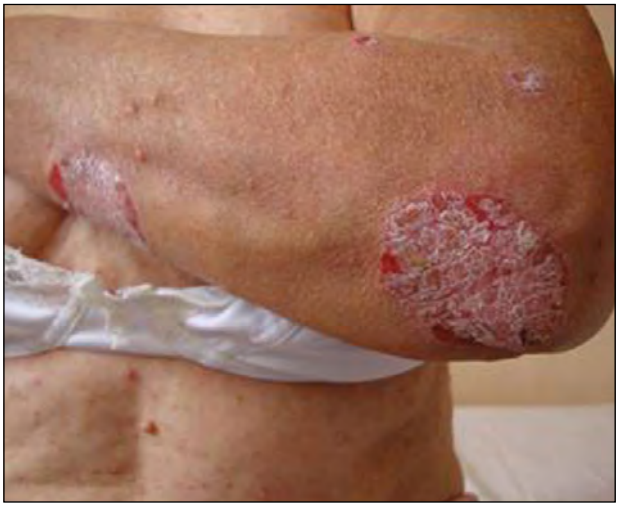

Figure 2. Plaque-type psoriasis with erythematous scaly plaques on the elbows and forearms.

psoriasis and NF-1 could not merely represent a coincidental occurrence.

Sincerely,
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The authors report no conflict of interest.

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