Bilateral Segmental Neurofibromatosis

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Sir,
Neurofibromatosis (NF) has a variable expression, clinically characterized by multiple café-au-lait spots, neurofibromata, intertriginous freckles and iris Lisch nodules. A female patient with bilateral segmental NF is described. This disease is extremely rare. To our knowledge, only 19 cases have been reported in the English literature.

CASE REPORT

A 57-year-old Japanese woman was referred to our hospital for a complete medical evaluation after multiple lentiginous lesions were found on her trunk during a health examination for adults conducted by a local medical association. From birth, this woman has had brownish macules on her trunk, right arm, and left leg. At the age of 30, numerous rice-sized pigmentations appeared on her trunk, and she noticed a soft lump on her right flank. The lump gradually increased in size, but she did nothing about it as there was no pain or itching. No other members of her family or close relatives exhibited a similar condition. Her past history was unremakable, except for a duodenal ulcer and cholecystitis. Physical examinations revealed a solitary, soft, reddish, asymptomatic nodule measuring 2 cm in diameter on her right flank. A biopsy of the nodule showed typical features of neurofibroma. Multiple small, brown lentigines were found on the right side of the upper back, chest, abdomen, and gluteal region, and on the left side of the lower back, lower abdomen, and gluteal region. There were 4 café-au-lait spots on the left lower abdomen (Fig. 1*a*), the right upper arm, and the left gluteal region (Fig. 1*b*), and the left post-femoral region. There were no detectable abnormalities such as iris Lisch nodules on ophthalmological examination, and there were no abnormal neurological findings. As mild scoliosis was noticed (11-degree scoliosis at T8-L2), the patient consulted the orthopedic department, but the orthopedist explained that there was no remarkable change and no need for treatment.

Laboratory findings revealed slightly elevated values of norepinephrine (502 pg/ml) and alkaline phosphatase (234 IU/l) (normal range: 90–420 pg/ml and 60–201 IU/l, respectively), but her blood pressure was within normal limits. Results of an electrocardiograph, X-ray of the skull, and CT scans of the brain, chest, and abdomen were normal.

DISCUSSION

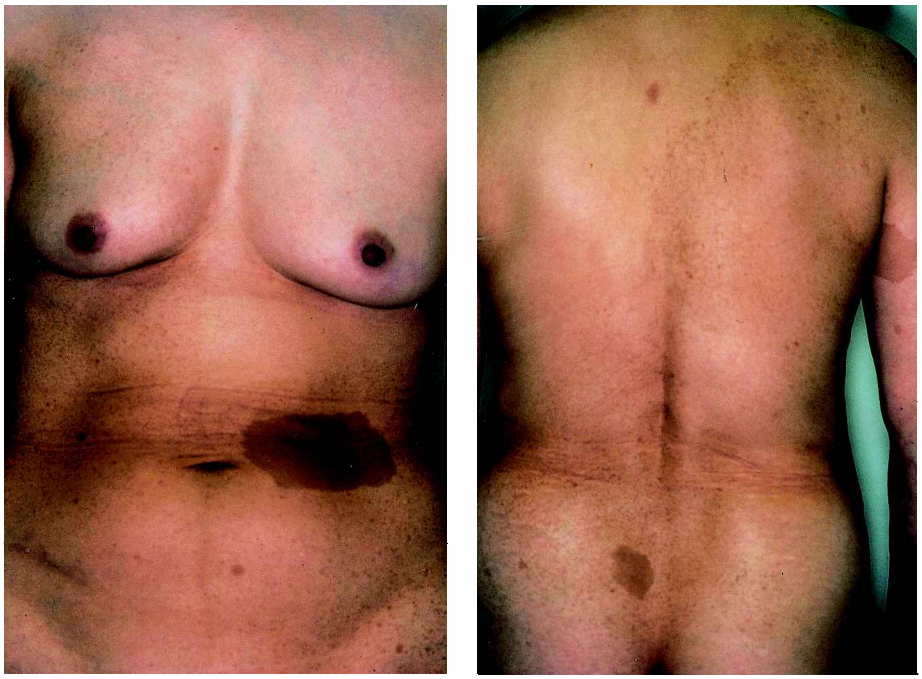
Classical NF was first described as von Recklinghausen's disease in 1882 (1). Because of the great variability of its clinical presentation, Riccadi classified NF into 7 categories. Among them, type V is a segmental NF characterized by café au lait spots or neurofibromata in a unilateral, segmental distribution, with an absence of both inherited and non-cutaneous manifestations (2).

Some years later, Roth *et al.* recognized several cases of segmental NF that did not neatly adhere to any definitions by Riccadi. On this basis, they decided to further divide segmental NF into 4 possible subsets, i.e., type I, true segmental; type II, localized cases with deep involvement; type III, hereditary segmental; and type IV, bilateral segmental (also classified as type VIII NF by Riccadi *et al.*) (3). Many authors have cited Roth's work and generally accept his subsets of segmental NF. Our case showed features consistent with the bilateral segmental NF subset, and this is extremely rare. To our knowledge, only 19 such cases have been reported in the English literature (4–6). Lentigines and café au lait spots have been recognized together in only 4 cases of bilateral segmental NF. Our case is the first report of bilateral segmental NF with café-au-lait spots on both sides of the body.

Non-cutaneous manifestations of the types that occur in generalized NF are uncommon in bilateral segmental NF, although the development of non-cutaneous manifestations (7), hereditarity links (8), and iris Lisch nodules (9) has recently been reported in cases of segmental NF.

In any case, our patient, her family, and relatives need to be followed regularly over the long term, as the development of non-cutaneous manifestations or different forms of NF could occur through time.

In the pathogenesis of bilateral segmental NF, it is generally accepted that somatic mutations simultaneously occur in the different sites of the body (10). Cecchi *et al.* have postulated that this is why bilateral segmental NF is extremely rare (11). While the causative genes of NF-1 (12) and NF-2 (13) have been identified, the roles of these genes in the formation of neurofibromata and café-au-lait spots remain unknown. To clarify whether the causative gene of bilateral segmental NF is



(*a*) (*b*)

Fig. 1. (*a*) Diffuse lentigines and café-au-lait spot on the anterior aspect of the patient's trunk. (*b*) Diffuse lentigines and café-au-lait spot on the posterior aspect of the trunk.

identical to that of NF-1 or NF-2, further genetic investigation and accumulation of cases are needed.

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