Actas Dermosifiliogr. 2008;99:313-22

LETTERS TO THE EDITOR

Sturge-Weber Syndrome and Type 1 Neurofibromatosis: A Chance Association?

A. L. Rodríguez-Bujaldón, C. Vázquez-Bayo, R. J. Jiménez-Puya, and J. C. Moreno-Giménez
Servicio de Dermatología Médico-Quirúrgica y Venereología, Hospital Universitario Reina Sofía, Córdoba, Spain

To the Editor:

We report the case of a 40-year-old man with a history that included epileptic seizures since childhood and paralysis of the external rectus muscle. He had a port-wine stain on the right side of the face (Figure 1) that affected the first and third divisions of the trigeminal nerve. Magnetic resonance imaging revealed venous malformation in the thalamus and contrast enhancement of the right choroid plexus. The patient also had café-au-lait spots and numerous cutaneous and subcutaneous neurofibromas on the trunk and limbs (Figure 2). Axillary freckles were also observed and Lisch nodules were visible upon ocular examination with a slit lamp.

No skin, eye, or brain abnormalities were found in the rest of the family and there was no parental consanguinity.

Neurofibromatosis type 1 is a fairly common finding in dermatology patients, while Sturge-Weber syndrome is seen somewhat less often. However, it is exceptional for the 2 conditions to occur simultaneously in the same individual, whereby we consider this case worthy of comment. Could they be related, or is this a mere coincidence?

In 1923, van der Hoeve proposed the term *phakomatosis* to cover neurofibromatosis and tuberous sclerosis, on the basis that both conditions affect the nerves and skin and have sufficient relevant characteristics to constitute a subgroup in their own right. Various other syndromes, including von Hippel-Lindau and Sturge-Weber syndromes, were gradually added to the group as they showed similar features.

Yakolev and Guthrie were the first to refer to these entities as *neurocutaneous syndromes*. Rudolf Happle defined neurocutaneous disease as a genetic disorder associated with cutaneous and neurologic manifestations, and allowed some to be classified as phakomatoses on the basis of clinical morphology, although he never clearly established which diseases should belong to this subgroup. We therefore consider it more appropriate to describe these as neurocutaneous diseases rather than phakomatoses and to classify them according to formal genetic factors.

Since the 1950s, there have been many references to the possible association of phakomatoses such as neurofibromatosis with tuberous sclerosis[1] or tuberous sclerosis with Sturge-Weber syndrome.

These are uncommon—apart from the association between neurofibromatosis and tuberous sclerosis—but the presentation of neurofibromatosis type 1 and Sturge-Weber syndrome in the same patient is an extraordinary phenomenon.[2] Only 1 article from 1979 actually reported an association between the 2 syndromes,[2] and when the possibility of an association is mentioned elsewhere in the literature, no underlying genetic factor is given. Sturge-Weber syndrome is characterized by the presence of vascular malformation[3] along the trigeminal nerve, and depending on which division of the nerve is affected, there is a greater or lesser risk of internal lesions in the form of leptomeningeal angiomatosis, focal motor epilepsy, or hemianopsia.[4] Only involvement of the first division of the trigeminal nerve has been shown to be associated with port-wine stain and intracranial lesions.

In this syndrome, port-wine stain is accompanied by leptomeningeal or ocular vascular malformations and calcifications on the surface of the brain. Other possible associations are contralateral hemiparesis, hemiatrophy, epilepsy, ocular paralysis, mental retardation, or glaucoma.[4]

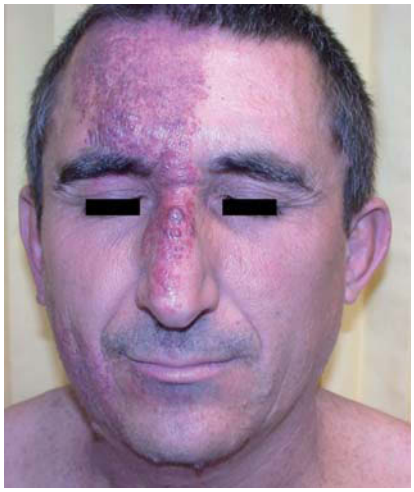

Figure 1. Port-wine stain affecting the entire first division of the trigeminal nerve and part of the third.

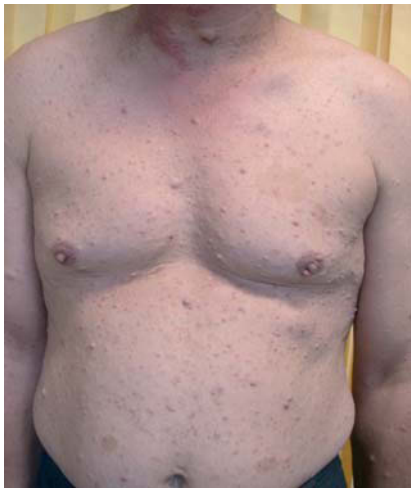

Figure 2. Cutaneous and subcutaneous neurofibromas and café-au-lait spots on the chest and abdomen.

Neurofibromatosis type 1 is defined by well-established clinical criteria.[5] The abnormality is located on chromosome 17 and exhibits autosomal dominant inheritance.

Most cases of Sturge-Weber syndrome are sporadic, but a familial distribution has been reported. As a result, the syndrome is believed to follow paradominant inheritance, such that the individual is heterozygotic for this inherited characteristic and phenotypically normal, and will only suffer from the disease should further mutation occur during the early phases of embryonic development.[6]

In neurofibromatosis type 1 the underlying alteration encodes a protein, neurofibromin, that is responsible for the pathogenesis of the condition. Sturge-Weber syndrome is explained by increased expression of fibronectin, which regulates angiogenesis and constitutes the cerebral response to chronic ischemic damage.

Therefore, there does not appear to be a relationship between the 2 neurocutaneous syndromes in either pathogenesis, transmission, or the underlying genetic defect. We raise the question of whether this case could be the result of the simultaneous occurrence of both process—an extraordinarily rare occurrence. Another explanation could lie in the pathogenesis of neurofibromatosis itself, since numerous articles link this condition with angioma and other vascular abnormalities.[7] Thirdly, it is possible that this could correspond to the most common neurocutaneous syndrome of all, Pascual Castroviejo type II syndrome, which encompasses neurologic abnormalities and various vascular abnormalities, including angioma. Reports of Pascual Castroviejo II syndrome include a description of a patient with neurofibromatosis type 1 and cutaneous and hepatic hemangioma.[8]

References

1. Borgberg A. Clinical and genetic investigations into tuberous sclerosis and Recklinghausen's neurofibromatosis; contribution to elucidation of interrelationship and eugenics of the syndromes. Acta Psychiatr Neurol Scand Suppl. 1951; 71:1-239.
2. Riley FC, Campbell RJ. Double Phakomatosis. Arch Ophthalmol. 1979;97: 518-20.
3. Redondo P. Malformaciones vasculares (I). Concepto, clasificación, fisiopatogenia y manifestaciones clínicas. Actas Dermosifiliogr. 2007;98:141-58.
4. Celebi S, Alagöz G, Aykan U. Ocular findings in Sturge-Weber syndrome. Eur J Opthalmol. 2000;10:239-43.
5. Martínez S, Vera A, Sanz A, Crespo V. Neurofibromatosis segmentaria verdadera. Actas Dermosifiliogr. 2004;95: 175-7.
6. Happle R. Klippel-Trenaunay syndrome: It is a paradominant trait? Br J Dermatol. 1993;128:465-6.
7. Wertelecki W, Superneau DW, Forehand LW, Hoff CJ. Angiomas and von Recklinghausen neurofibromatosis. Neurofibromatosis. 1988;1:137-45.
8. Pascual-Castroviejo I, Cortés P, Fernández-Cuadrado J, de la Flor-Crespo M, Pascual Pascual SI. Cutaneous haemangioma associated with a hepatic haemangioma and neurofibromatosis type 1 (NF1). Rev Neurol. 2002; 34:652-4.

Essential Progressive Telangiectasia

M. Cabanillas, I. Rodríguez-Blanco, M. Ginarte, and J. Toribio

Servicio de Dermatología, Complejo Hospitalario Universitario, Facultad de Medicina, Santiago de Compostela, La Coruña, Spain

To the Editor:

Essential progressive telangiectasia is a rare disorder that affects mainly middle-aged women. It is characterized by the insidious but progressive development of dilated blood vessels and telangiectases. These commonly begin on the lower limbs and gradually extend upwards, potentially extending to cover most of the body surface including the mucous membranes.

We report a 61-year-old woman with no relevant history who presented with the progressive appearance of erythematous lesions on both legs with onset 10 years previously. The lesions were occasionally pruritic and began to appear on both ankles before extending upwards. She reported that her sister and mother suffered from a milder form of a similar disorder. There was no personal or family history of repeated diarrhea, melena, mucosal bleeding, or neurologic abnormalities. Skin examination revealed a large number of enlarged blood vessels that blanched when pressed under glass, against a background of multiple violaceous erythematous punctate lesions from the ankle to the knee and in the distal portion of the thighs on both legs (Figure 1). There were no signs of atrophy, ulceration, tumors, or mucosal abnormalities, and the only outstanding feature was the presence of slight erythema on the face, with some associated papulopustular lesions. Laboratory tests including complete blood count, biochemistry for thyroid