Case Report

# Linear Scleroderma *en Coup de Sabre* and Brain Calcification: Is There a Pathogenic Relationship?

DIANA ELSA FLORES-ALVARADO, JORGE A. ESQUIVEL-VALERIO, MARIO GARZA-ELIZONDO, and LUIS R. ESPINOZA

***ABSTRACT***. Extracutaneous calcifications are rare in scleroderma and related conditions. We describe a female patient with linear scleroderma *en coup de sabre* and a longstanding clinical history of tonic and clonic convulsions. Radiographic study showed extensive cerebral calcifications in the right occipital hemisphere, homolateral to the involved side of her face. This report further suggests a relationship between localized scleroderma and neurological manifestations. Brain imaging studies should be routinely performed in scleroderma patients exhibiting neurological manifestations, especially seizure disorder. (J Rheumatol 2003;30:193–5)

*Key Indexing Terms:*
LINEAR SCLERODERMA PARRY-ROMBERG SYNDROME
MORPHEA STURGE-WEBER SYNDROME CALCIFICATION

Localized scleroderma describes a variety of conditions of clinical and histopathological similarity to the skin manifestations of systemic sclerosis, but in which systemic internal organ involvement and vascular features are lacking. Three major variants of localized scleroderma have been recognized, including morphea, linear scleroderma, and generalized morphea[1].

Linear scleroderma represents an unusual, non-hereditary disorder more often observed in the pediatric age group, with 67% of patients diagnosed prior to 18 years of age[2]. The legs are usually involved; less commonly it affects the frontoparietal area and the anterior scalp. Characteristically, this form of scleroderma is restricted to one half of the face and has a slow but progressive clinical course, which may be associated with autoantibodies, peripheral eosinophilia, and increased levels of IgG.

We describe a patient with linear scleroderma associated with significant neurologic involvement characterized by tonic and clonic seizures associated with extensive brain calcification.

## CASE REPORT

In February 2000 a 33-year-old woman was admitted to the University Hospital due to severe and recurrent tonic and clonic seizures. She had a longstanding history of recurrent tonic and clonic convulsions which first began in 1980. She had been treated with phenobarbital and diphenylhydantoin with a fair initial clinical response. Over the first 10–15 years, she used to have one or 2 attacks; however, they intensified over the past several years, necessitating hospitalization and increased dose of anticonvulsive therapy. In addition and concomitant to the onset of seizures in 1980, she noticed an indolent skin lesion localized in her right frontal area. This lesion progressed slowly over the years in a linear fashion and eventually produced both dermal and muscle atrophy, accompanied by alopecia and deformity, with a depressed area involving both the frontal and parietal scalp. More recently, in 1998 she noticed a second indurate lesion in the posterior aspect of her neck. There was no history of systemic involvement including Raynaud's phenomenon, arthritis, dysphagia, sicca symptoms, cough, weakness, diarrhea, and/or weight loss. She denied exposure to drugs, radiation, tick bite, trauma, or chemicals such as vinyl chloride and tryptophan. Family history was noncontributory.

Physical examination disclosed characteristic clinical findings consistent with linear scleroderma involving the right frontal and parietal areas (it did not extend below the forehead) (Figure 1), and morphea on the posterior aspect of her neck.

Routine laboratory tests including complete blood count with differential, chemistry profile, and urinalysis were normal. Rheumatoid factor, antinuclear antibodies, anti-ds-DNA, anti-Scl-70, and anticentromere antibodies were absent. Complement C3 and C4 were normal.

An electroencephalogram revealed spikes of a beta rhythm and theta waves in the right temporo-occipital area. A cerebral computerized tomographic (CT) scan showed extensive cerebral calcifications in the right occipital hemisphere (Figure 2). Her seizures were controlled with intravenous phenobarbital and diphenylhydantoin. She has remained under fair control while receiving this therapy.

## DISCUSSION

Neurological involvement is relatively rare in systemic sclerosis, although a variety of manifestations such as cranial nerve abnormalities, central nervous system (CNS) vasculitis, peripheral neuropathy, autonomic peripheral neuropathy, epilepsy, transient ischemic attacks with focal neurological defects or transient global amnesia, and psychological disorders are increasingly recognized in as much as 10–20% of patients. By far, however, the most frequent neurologic abnor-

*From the Departments of Medicine, Sections of Rheumatology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA; and Universidad Autonoma de Nuevo Leon, Leon, Mexico.*

*D.E. Flores-Alvarado, MD, Research Fellow in Rheumatology, Louisiana State University Health Sciences Center (LSU-HSC); J.A. Esquivel-Valerio, MD, Staff Physician; M.A. Garza-Elizondo, MD, Professor, Department of Medicine, Section of Rheumatology, Universidad Autonoma de Nuevo Leon; L.R. Espinoza, MD, Professor and Chief, Section of Rheumatology, LSU-HSC.*

*Address reprint requests to Dr. D.E. Flores-Alvarado, Section of Rheumatology, Louisiana State University Health Sciences Center, 1542 Tulane Avenue, New Orleans, LA 70112-2822.*

*Submitted January 22, 2002; revision accepted June 24, 2002.*

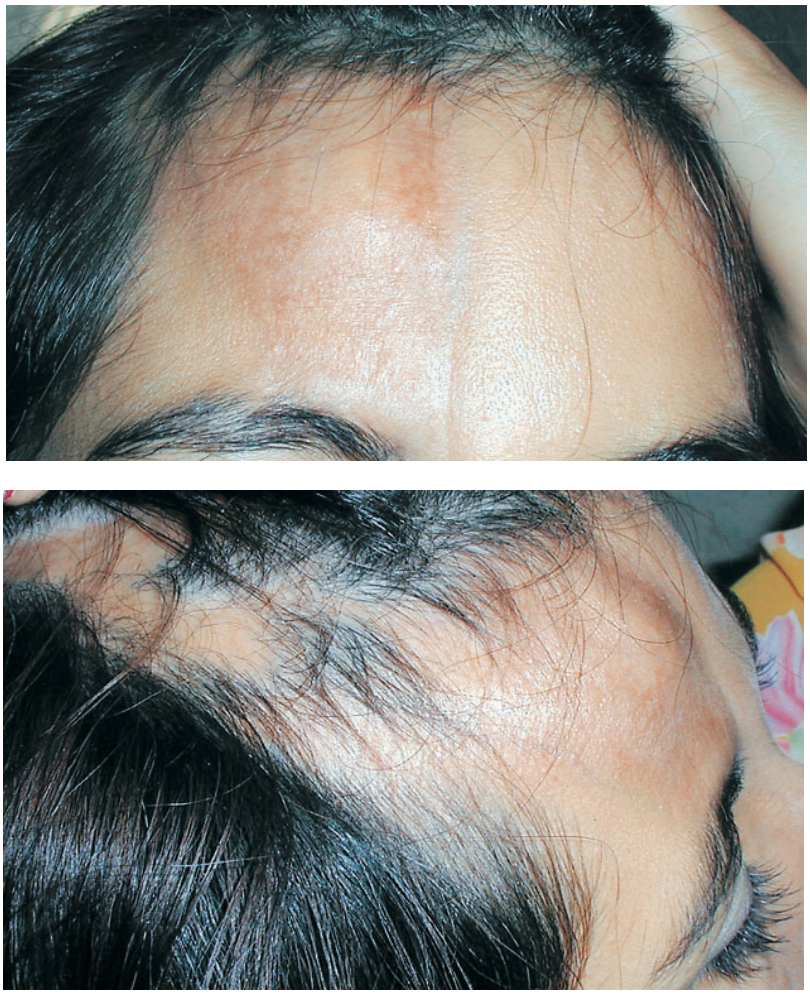


*Figure 1*. Linear scleroderma involving the right frontal (A) and parietal (B) areas. Skin involvement did not extend below the forehead.

mality in limited scleroderma is seizure disorder, usually of complex partial type[3-5].

As with other forms of scleroderma, the etiopathogenesis of linear scleroderma remains unknown, although various causative factors including trauma, infections, and surgery may precede its development[6,7]. Endothelial cell damage leading to generalized vascular involvement is an important event in the pathogenesis of scleroderma and related conditions. It has been proposed that there is an early cerebral inflammation stage in localized scleroderma leading to intraparenchymal calcification, ectatic vessels with gliosis without inflammation, which may play an important role in the pathogenesis of the neurological manifestations seen in some patients[8]. Heron, *et al*[9] recently studied 37 consecutive scleroderma patients with cerebral CT. Sixteen patients (43%) had diffuse scleroderma and 21 (57%) had the limited form of systemic sclerosis. Intracerebral calcification was found in 12 patients (32.4%) and 7 controls (9.5%) ($p = 0.006$), and was only found in patients with Raynaud's phenomenon ($p = 0.005$). Calcifications were small and localized in the basal ganglia in 11 patients, and only one patient exhibited calcifications in the temporal lobe. No association with calcinosis cutis was found. None of the patients or controls had a seizure disorder. Similar type and localization of calcifications have been described in Parry-Romberg syndrome, the elderly, CNS infections including HIV, cerebral lupus, hypoparathyroidism, Down's syndrome, mitochondrial myopathy, and other conditions[9].

Parry-Romberg syndrome deserves special consideration, since differentiation with scleroderma *en coup de sabre* is extremely difficult to accomplish[10,11]. Both occur during childhood and can be associated with neurologic and autoimmune serological manifestations. Parry-Romberg syndrome is characterized by extensive and progressive self-limited shrinking and deformation of one side of the lower face without significant induration of the skin and usually does not cross the midline. Linear scleroderma *en coup de sabre* is

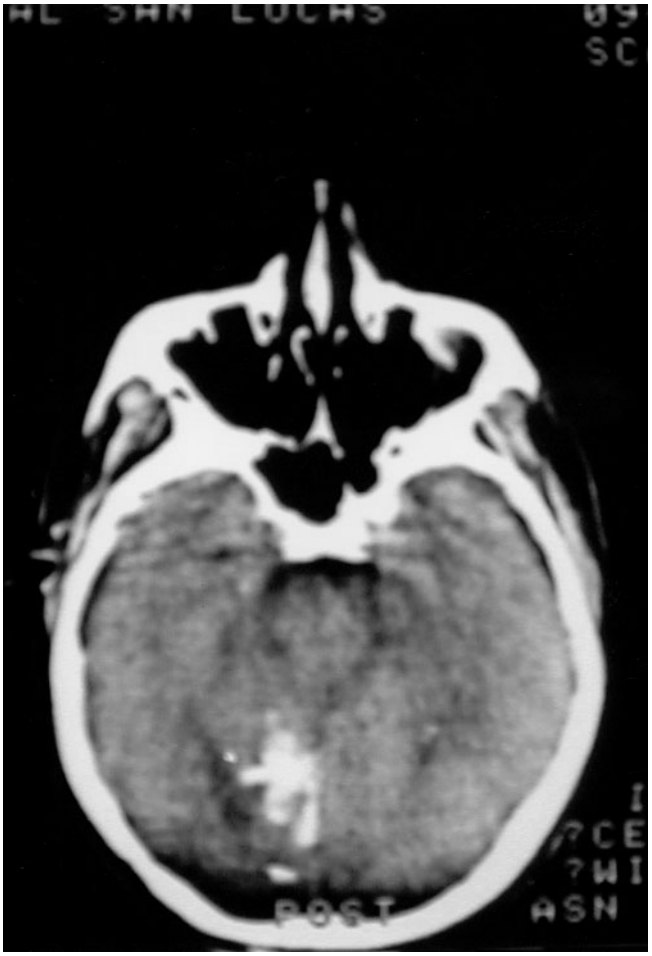


*Figure 2*. Brain CT demonstrating extensive brain calcifications in the right occipital hemisphere homolateral to the linear scleroderma area.

associated with induration of the skin in the area of the scalp lesion and usually does not extend below the forehead[12,13]. We favor a diagnosis of linear scleroderma over Parry-Romberg syndrome in our patient due to the presence of skin involvement as initial clinical manifestation, which did not extend below the forehead and preceded muscle atrophy by years, and also to the development in recent years of morphea at the back of her neck.

While the Parry-Romberg syndrome of progressive facial hemiatrophy is of unknown origin and no specific therapy is available, linear scleroderma is considered a rheumatologic disease for which D-penicillamine therapy may be useful, but both may have a good clinical response with the use of steroids and other second-line agents[11,14]. It is likely, however, that both disorders share similar pathogenesis and represent overlapping syndromes.

Soft tissue calcium deposits are a common occurrence in scleroderma and related conditions. More rarely, calcium deposits have been described in other areas such as the spine, pericardium, and brain. Its pathogenesis remains poorly understood, although it has been postulated that the brain calcification process may be related to an early primary cerebral inflammatory process[8]. At variance with this hypothesis, however, is the suggestion by Chung, *et al*[15] that limited scleroderma may represent a mucocutaneous syndrome of vascular dysplasia similar to the Sturge-Weber syndrome, rather than a localized form of collagen vascular disease. These authors reported a young woman 27 years of age who exhibited identical clinical and radiological manifestations to those of our patient.

There are no longterm reports of limited scleroderma with neurological manifestations, and the potential therapeutic role of calcium-channel blockers and/or other agents used in patients with extensive soft tissue calcifications have not been explored.

In summary, we describe the unusual occurrence of linear scleroderma *en coup de sabre* and seizure disorder with cerebral calcifications. The origin and exact relationship of the limited scleroderma and brain calcifications remain to be established; moreover, whether they are secondary to the cerebrovascular damage of scleroderma or represent a separate mucocutaneous syndrome of vascular dysplasia awaits further elucidation.

## REFERENCES

1. Hawk A, English JC III. Localized and systemic scleroderma. Semin Cutaneous Med Surg 2001;20:27-37.
2. Itin PH, Schiller P. Double-lined frontoparietal scleroderma en "en coup de sabre". Dermatology 1999;199:185-6.
3. Falanga V, Medsger TA Jr, Reichlin M, Rodnan GP. Linear scleroderma: clinical spectrum, prognosis, and laboratory abnormalities. Ann Intern Med 1986;104:849-57.
4. Stava Z, Stein J. Electroencephalography in scleroderma: A study of 57 cases of diffuse and 30 cases of circumscribed scleroderma. Dermatologica 1961;123:375-90.
5. Blanco P, Viallard JF, Ellie E, et al. Extensive brain calcifications in systemic sclerosis. J Neurol Neurosurg Psychiatr 1999;67:697-8.
6. David J, Wilson J, Woo P. Scleroderma "en coup de sabre". Ann Rheum Dis 1991;50:260-2.
7. Patrizi A, Marzaduri S, Marini R. A familial case of scleroderma "en coup de sabre" [letter]. Acta Derm Venereol 2000;80:237.
8. Stone J, Franks AJ, Guthrie JA, Johnson MH. Scleroderma "en coup de sabre": pathological evidence of intracerebral inflammation. J Neurol Neurosurg Psychiatr 2001;70:382-5.
9. Heron E, Hernigou A, Chatellier G, Fornes P, Emmerich J, Fiessinger JN. Intracerebral calcification in systemic sclerosis. Stroke 1999;30:2183-5.
10. Jablonska S, Rodnan GP. Localized forms of scleroderma. Clin Rheum Dis 1979;5:215-41.
11. Lehman TJA. The Parry-Romberg syndrome of progressive facial hemiatrophy and linear scleroderma "en coup de sabre". Mistaken diagnosis or overlapping conditions? J Rheumatol 1992;19:884-5.
12. Fry JA, Alvarellos A, Fink CW, Blaw ME, Roach ES. Intracranial findings in progressive facial hemiatrophy. J Rheumatol 1992;19:956-8.
13. Terstegge K, Kunath B, Felber S, Speciali JG, Henkes H, Hosten N. MR of brain involvement in progressive facial hemiatrophy (Romberg disease): reconsideration of a syndrome. Am J Neuroradiol 1994;15:145-50.
14. Goldberg-Stern H, deGrauw T, Passo M, Ball WS Jr. Parry-Romberg syndrome: follow-up imaging during suppressive therapy. Neuroradiol 1997;39:873-6.
15. Chung MH, Sum J, Morrell MJ, Horoupian DS. Intracerebral involvement in scleroderma "en coup de sabre": report of a case with neuropathologic findings. Ann Neurol 1995;37:679-81.