Linearity and cerebral scleroderma with associated neurologic abnormalities

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ABSTRACT

Linear scleroderma en coup de sabre represents a unique form of localized scleroderma that primarily affects the pediatric population, with 67% of patients diagnosed before 18 years of age. When linear scleroderma occurs on the head, it is referred to as linear scleroderma en coup de sabre, given the resemblance of the skin lesions to the stroke of a sabre. Here, we describe 3 pediatric patients with linear scleroderma en coup de sabre who presented with neurologic abnormalities before or concurrent with the diagnosis of their skin disease. Our patients’ cases highlight the underrecognized relationship between neurologic complications and linear scleroderma en coup de sabre and illustrate the importance of a thorough skin examination in patients with unexplained neurologic disease.

CASE REPORTS

CASE 1. A 5-year-old girl presented with new-onset partial complex seizures and skin lesions. An epileptiform pattern in the left posterotemporal area was detected by electroencephalogram (EEG), and she was started on anticonvulsants. Imaging by computed tomography (CT) and MRI was normal. Enlargement of the skin lesions prompted a referral to dermatology, and examination revealed a linear, indurated plaque with alopecia extending from her left eyebrow into the hair-bearing scalp. Gray-brown atrophic plaques were also present on the midline of her scalp and extending from her left mandible to the anterior shoulder. A diagnosis of linear scleroderma en coup de sabre was made based on the characteristic skin changes observed. Her anti-single-stranded DNA level was slightly elevated at 159 μ/ml; her antinuclear antibodies (ANA), rheumatoid factor, complete blood count, anti-extractable nuclear antigens, and anti-double-stranded DNA levels were all within normal limits.

Key Words: pediatric, scleroderma, en coup de sabre, neurologic, children

Abbreviations: EEG, electroencephalogram; CT, computed tomography; ANA, antinuclear antibodies


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indurated plaque over her left malar eminence. The cutaneous disease eventually stabilized, and topical treatment was discontinued after a total of 18 months. Over the next 4 years, serial EEGs showed improvement in wave form, and the patient was tapered off anticonvulsants successfully. At age 14, 5 years after anticonvulsants were stopped, she had another generalized seizure (after 8 seizure-free years). A repeat brain MRI was again normal. She has been restarted on anticonvulsants and has been seizure free for the last year. At the last follow-up visit, all her lesions were soft, but she had persistent hyperpigmentation and linear depressed plaques most notable over the forehead. No facial asymmetry was present.

CASE 2. A 6-year-old previously healthy boy was first noted to have decreased movement of the right side of his mouth at the age of 5. Several months later, it was noted that the palsy had progressed to include his right cheek. The patient was also experiencing mild headaches 2 to 3 times per week and intermittent abdominal pain with poor weight gain. The patient was evaluated by a neurologist and was found to have palsy of the mandibular branch of the right facial nerve. An MRI was normal, and the etiology of his neurologic changes was unexplained. No cause was found for the abdominal symptoms.

Several months after his neurologic symptoms began, his parents noted a small annular, erythematous area of alopecia on his right parietal scalp. The lesion expanded slowly over the next several months and extended anteriorly toward the forehead and posteriorly toward his occiput. Linear scleroderma was diagnosed; however, his parents were told that his skin changes were not related to his neurologic abnormalities. Treatment with monthly intramuscular triamcinolone acetonide injections was started after a trial of oral steroids was not tolerated.

At the time of presentation to our clinic, the patient’s parents reported rapid expansion of the cutaneous lesion. On examination, there was a 12-cm indurated, linear plaque on the right parietal scalp that extended from just behind the ear to the frontal hairline (Fig 1). This lesion was mostly yellow in color, but the advancing edge was violaceous. On the right upper arm the patient also had four 2- to 3-cm, dull pink-brown, atrophic patches. An atrophic, smooth, elliptical patch orientated longitudinal was also noted on the right side of the patient’s tongue (Fig 2). A detailed neurologic examination revealed decreased retraction and depression of the right angle of the mouth, which affected his smile. Elevation of the right angle of the mouth was slightly diminished compared with the left with nasolabial fold sparing. Taste was decreased on the right side of his tongue compared with his left. All other cranial nerves were intact. Follow-up MRIs have been normal.

The patient was treated with intravenous methylprednisolone and subcutaneous methotrexate. The protocol included receiving 3 consecutive days of intravenous methylprednisolone at 30 mg/kg per day followed by monthly infusions of methylprednisolone at 30 mg/kg for 3 months. Weekly subcutaneous methotrexate 7.5 mg was started in combination with the methylprednisolone. The patient’s cutaneous and neurologic disease has stabilized on this regimen.

CASE 3. A 5½-year-old girl presented with a white patch on the midline of her forehead extending onto the nasal bridge and was diagnosed initially with vitiligo. Two
Localized scleroderma or morphea may be subdivided into 5 main types: bullous morphea, plaque morphea, generalized morphea, deep morphea, and linear scleroderma. Unlike most forms of localized scleroderma, which lack cutaneous manifestations, a subset of linear scleroderma referred to as en coup de sabre has been associated with several neurologic abnormalities. Many of the epidemiologic studies of scleroderma have come from dermatology and rheumatology centers, where referral bias influences estimates of the incidence, prevalence, and severity of this disease. Systemic scleroderma is rare in the pediatric population, and localized scleroderma has been estimated to be at least 10 times more common than systemic disease. A population-based retrospective study of Olmsted County in Rochester, Minnesota, over a 33-year period has provided some epidemiologic information regarding localized scleroderma. Of the subtypes of localized scleroderma, the predilection of linear scleroderma for childhood is well recognized. In the Minnesota study, 67% of the patients with linear scleroderma were diagnosed before the age of 18. All forms of localized scleroderma have a 3:1 female predominance except for linear scleroderma, in which males and females are affected equally.

Linear scleroderma en coup de sabre is a rare subset of linear scleroderma defined by its characteristic location on the forehead and scalp. Clinically, it is manifested by ivory-colored, sclerotic plaques with violaceous borders distributed in a band-like fashion on the frontotemporal scalp and forehead. Alopecia of the affected scalp is common and often the presenting complaint. Lesions may extend to the nose, cheek, chin, and neck. Facial hemiatrophy may develop as a result of hypoplasia of the underlying bone and soft tissues. Progressive hemifacial atrophy (Parry-Romberg syndrome) is a related disorder characterized by progressive hemifacial atrophy without cutaneous sclerosis. Debate continues as to whether Parry-Romberg syndrome is a distinct disease entity or a variant of linear scleroderma, but many would agree that they are closely related forms of craniofacial scleroderma. The diagnosis is a clinical one that relies on the characteristic cutaneous and soft tissue findings because there are currently no diagnostic laboratory tests. ANA with homogeneous and speckled patterns may be positive in 37% to 50% of patients with linear scleroderma, and anti–single-stranded-DNA antibodies may be present. More specific autoantibodies such as Scl-70, anticentromere, Ro/La, and U1RNP may precede development of systemic disease, and patients with these markers should be followed closely for several years.

Patients with localized scleroderma, by definition, have sclerosis limited to their skin and soft tissue. However, linear scleroderma, mainly the en coup de sabre subtype, often has extracutaneous associations. When linear scleroderma occurs on the extremities, local ab-
neuralgias such as limb-length discrepancy or joint contrac-
tures may occur secondary to sclerosis of the skin. In 
contrast, the en coup de sabre subtype of linear sclero-
derma is notorious for multisystem morbidity. Marzano 
et al reported the presence of ocular, oral, and neuro-
logic abnormalities in almost half of the 17 patients 
identified with craniofacial involvement (including en 
coup de sabre, Parry-Romberg, and mixed types). Spe-
cific associations with craniofacial scleroderma reported 
in the literature are listed in Table 1. Development of 
cutaneous disease typically precedes the onset of extra-
cutaneous manifestations. The time line for the de-
velopment of systemic findings is typically on the order 
of months, but reports of delayed onset of neurologic di-
sease several years later exist.4,17 Systemic signs and 
symptoms may not parallel cutaneous disease activity.1,7 

Neurologic complications are the most common sys-
temic association with linear scleroderma en coup de 
sabre. Complex partial seizures have been reported most 
frequently.5 Abnormalities on MRI and CT studies may 
be seen in patients with linear scleroderma en coup de 
sabre even in the absence of neurologic disease.6,7 Radi-
ologic abnormalities are predominately ipsilateral to 
the skin disease but may be contralateral.4,8 Neuroradio-
logic abnormalities including cerebral atrophy, white-
matter lesions, intraparenchymal calcification, mening-
geocortical alterations, and skull atrophy have all been 
described in the literature.4,6,7,9,18 Resolution and recur-
rence of radiologic lesions may correlate clinically with 
neurologic disease activity.4,9 Just as imaging may be 
avnormal in patients without neurologic symptoms, 
normal imaging can be seen despite the presence of 
neurologic disease as demonstrated by 2 of our patients 
as well as the case of a patient with facial and oculomo-
tor nerve palsy and grand mal seizures described by 
Gambichler et al.19 The lack of specific and/or sensitive 
 radiologic findings for the associated neurologic disease 
contributes to the difficulty in counseling these patients 
regarding prognosis. Certainly the presence of radiologic 
abnormalities warrants close clinical follow-up.

As in our third patient, brain biopsies have been 
performed when concerns for neoplasm arise.4,8 The re-
ported histologic findings are variable: most cases report 
a perivascular infiltrate or vasculitis. Sclerosis, fibrosis, 
and gliosis involving brain parenchyma, meninges, and 
vasculation have also been reported.8,20 As in our patient 
and in keeping with the neuroimaging results often de-
scribed in these patients, scattered calcifications can be 
seen, often in association with blood vessels.20

The pathogenesis of localized scleroderma is not com-
pletely understood. Most of the proposed pathogenic 
mechanisms relate to systemic scleroderma. Similar to 
 systemic sclerosis, endothelial cell damage leading to 
increased fibroblast activity and ischemia through lumi-
nal narrowing with subsequent modification of collagen 
production has been proposed as the pathogenic mecha-
nism.15,21,22 The inciting event for such microvascular 
damage remains unknown. Borrelia burgdorferi infection, 
although implicated in Europe and Japan, has not 
proven to be a major factor in the United States.12 Ge-
netic factors also are thought to play a role, with higher 
incidence of connective tissue disease in family mem-
ers. An association with preceding trauma has been 
found, particularly in the pediatric population.23

Linear scleroderma is usually a self-limited disease. 
Regression or softening of skin lesions often occurs, 
but complete resolution is unusual and reactivation 
can occur.3 Adequate resolution of extracutaneous 
changes may occur, but unfortunately pediatric patients 
are at an increased risk of long-term morbidity because 
they may have decreased growth of underlying bones 
and may develop limb and facial asymmetry.12,16,17 If 
residual disfigurement develops, psychological disability 
may be pronounced.12 Additional orthopedic sequelae 
such as flexion contractures may occur when the skin 
overlying joints is involved.18 Reports of progression to 
 systemic scleroderma in the pediatric population are 
exceedingly rare.3,12,21

Adequate treatment for linear scleroderma remains 
elusive. The self-limited nature of the disease coupled 
with mixed results obtained from small, uncontrolled 
trials with most therapeutic regimens makes decisions 
regarding treatment difficult. Topical, intralesional, and 
 systemic corticosteroids reduce the inflammation of skin

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**TABLE 1** Extracutaneous Changes Associated With Linear Scleroderma en Coup de Sabre and Parry-Romberg Syndrome

<table>
<thead>
<tr>
<th>Neurologic</th>
<th>Ophthalmologic</th>
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<tbody>
<tr>
<td>Seizure disorder, typically complex partial</td>
<td>Ptosis</td>
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<tr>
<td>Hemiparesis/muscle weakness</td>
<td>Exophthalmos</td>
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<tr>
<td>Trigeminal neuralgia</td>
<td>Uveitis</td>
</tr>
<tr>
<td>Intracranial aneurysm</td>
<td>Motility disorder/atrophy of eye muscles</td>
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<td>Rasmussen encephalitis</td>
<td>Heterochromia of iris</td>
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<td>Mental deterioraton</td>
<td>Papillitis</td>
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<tr>
<td>Subdural hygroma</td>
<td>Retrolubular pain</td>
</tr>
<tr>
<td>Peripheral facial nerve palsy</td>
<td>Enophthalmus</td>
</tr>
<tr>
<td>Oculomotor nerve palsy</td>
<td>Displacement of outer canthus from resorption of orbital bone</td>
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<tr>
<td>Migraine headaches</td>
<td>Iridocyclitis</td>
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<tr>
<td>Oral</td>
<td></td>
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<tr>
<td>Altered dentition</td>
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<tr>
<td>Malocclusion</td>
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<td>Tongue atrophy</td>
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* Changes reported in pediatric patients.
lesions. In an open-label study, use of topical calcipotriene in 12 patients with localized scleroderma (including linear scleroderma) led to improvement in the cutaneous lesions for all of them. Systemic agents used when more aggressive therapy is warranted include vitamin E, vitamin D₃ (oral calcitriol), amino-benzoate potassium, penicillin, retinoids, diphenylhydantoin, interferon-γ, immunosuppressive agents, and UV-A therapy. Immunosuppressive agents that have been used with reported efficacy include hydroxychloroquine, D-penicillamine, methotrexate, cyclosporine, and cyclophosphamide. Immunosuppressive agents that have been used with reported efficacy include hydroxychloroquine, D-penicillamine, methotrexate, cyclosporine, and cyclophosphamide. For patients with disfiguring facial atrophy, reconstructive surgery may be beneficial.

In our patients, neurologic manifestations occurred before or concurrent with the diagnosis of linear scleroderma en coup de sabre. Their neurologic symptoms were previously unexplained when they presented to dermatology for evaluation of their skin lesions. These cases illustrate the need for placing craniofacial linear scleroderma on the differential of any patient with neurologic abnormalities such as partial seizures. A thorough examination of the skin should be performed in these patients, with particular attention to the face and scalp. Long and careful follow-up of these patients is prudent based on evidence that neurologic abnormalities may develop at any time during the course of the disease.

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## Linear Scleroderma en coup de sabre With Associated Neurologic Abnormalities

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