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Atypical Cases of Scleroderma en Coup de Sabre

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Abstract

Scleroderma en coup de sabre typically presents with a cutaneous induration, but involvement of the underlying bone, eye, and brain is common. We report on 4 pediatric cases with atypical initial clinical presentations. All cases were seen at the University of California San Francisco. Patients 1 and 2 presented to the Pediatric Rheumatology Clinic with uveitis and orbital pseudotumor in December 2009 and March 2010, respectively. Patients 3 and 4 were mimicking acquired demyelinating disorders of the brain, acute demyelinating encephalomyelitis and multiple sclerosis, and were referred to the Pediatric Multiple Sclerosis center in 2008.

Keywords

scleroderma, acquired demyelinating disease, multiple sclerosis, epilepsy, children

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Localized scleroderma has an incidence of 0.4 to 2.7 per 100 000.[1] Linear scleroderma is a subgroup of localized scleroderma, with two-thirds of patients being diagnosed before 18 years of age.[2,3] If the skin lesion occurs on the head, it resembles the stroke of a saber, thus the term "en coup de sabre."[4] Ninety percent of children affected with scleroderma en coupe de sabre present between 2 and 14 years of age.[5] Patients typically present with a red to violaceous patch on the skin of the forehead, which evolves to an ivory-colored fibrotic, hyperpigmented, and hairless plaque. These plaques are clinically and pathologically well characterized and lead to the diagnosis of scleroderma en coupe de sabre.

Children are more likely than adults to develop extracutaneous involvement of scleroderma en coup de sabre (22%), though the majority present with cutaneous findings initially.[6] The lesion can affect the underlying bone, the eye, and the brain parenchyma, but generally will not cross the midline.[7,8] Four percent of affected children exhibit neurologic symptoms, with seizures, headaches, or peripheral nerve involvement[3]; 3% of children have ocular involvement, so routine ophthalmologic follow-up is mandatory. Children with eye involvement are also more likely to develop brain lesions.[9] Rarely, the extracutaneous manifestations of scleroderma en coup de sabre develop prior to the appearance of typical cutaneous lesions, making diagnosis challenging and at times mimicking other diseases. We describe 4 cases of atypical clinical presentations of scleroderma en coup de sabre, each with neurologic or ophthalmic abnormalities. These symptoms preceded the diagnosis of the characteristic skin lesions and so were initially mistaken for other diseases.

Case Summary

Patient 1

A previously healthy 6-year-old boy presented with a red and swollen left eye. At this time, no skin changes were noted by the parents or the treating physician. Allergic conjunctivitis was suspected; however, he did not respond to treatment with

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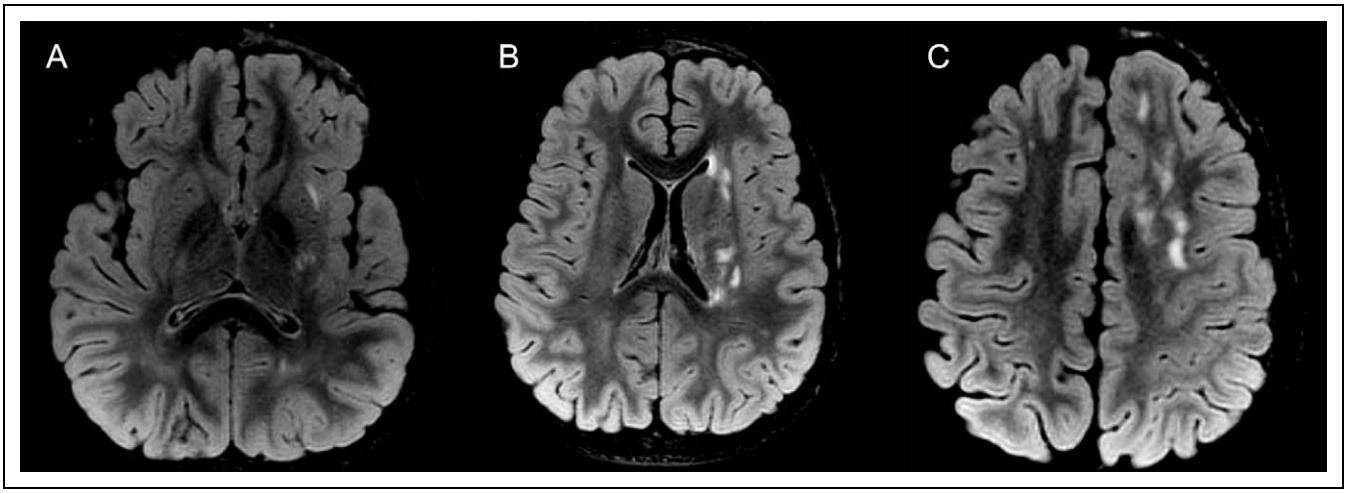

Figure 1. Patient 1: Axial magnetic resonance imaging (MRI) of the brain T2: Edema of the left orbital and periorbital soft tissues including left frontal scalp and left frontal bone (A) White matter lesions in the left cerebral hemisphere accompanied by cortical thickening and sulcal effacement in the left frontal and occipital regions (B and C).

topical antihistamines. Three months later, he developed left-sided headaches, as well as hyperpigmentation of his left eyelid and forehead with a bound-down appearance.

Brain magnetic resonance imaging (MRI) showed left frontal and orbital foci on T2/fluid-attenuated inversion recovery (Figure 1). Antinuclear antibodies were positive with a titer of 1:40. Further serologic workup for rheumatologic or infectious diseases was negative. Six months after the initial development of skin changes, he presented to pediatric dermatology and rheumatology, where he was diagnosed with en coupe de sabre based on the appearance of his facial lesions (Figure 2).

Two months later, he experienced secondary generalized seizures, which were subsequently controlled with levetiracetam. Electroencephalography at that time was normal and MRI was stable.

He received a 6-month course of intravenous methylprednisolone 30 mg/kg/d for 3 days, and continues on oral methotrexate at a dose of 20 mg weekly. An atrophic, hyperpigmented plaque surrounds his left eye and extends onto the cheek and the hairline. The lesion remained stable during the subsequent 6 months after completion of steroid therapy.

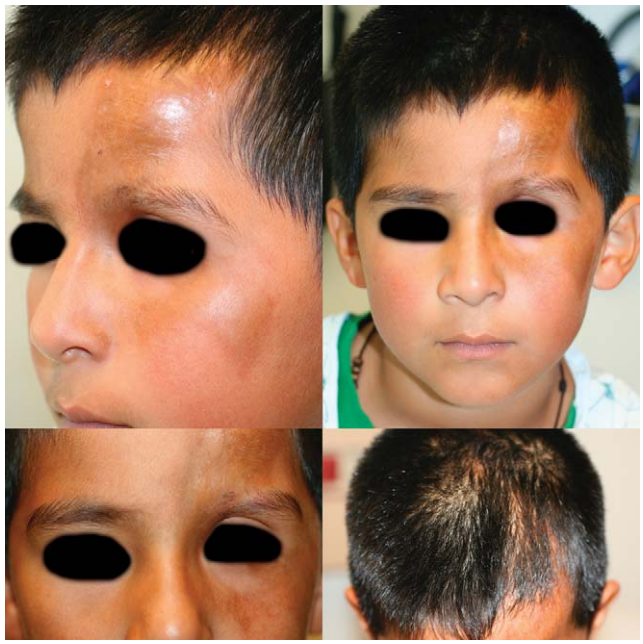

Figure 2. Patient 1: Clinical presentation: induration and hyperpigmentation of the left forehead rising from the hairline to the left cheek resulting in asymmetry of the left eye and atrophy of the eyebrow and eyelashes. The lesion has a shiny and ivory-colored appearance.

Patient 2

A previously healthy 4-year-old girl presented with left-sided ptosis without skin changes. Horner syndrome was suspected. Several months later she developed progressive hypopigmentation of her left forehead including alopecia. One year later, a dermatologist diagnosed scleroderma en coup de sabre based on typical appearance of the skin changes. A comprehensive laboratory workup was negative. MRI revealed an infiltrative, enhancing soft tissue mass in the left orbit, which remained stable 3 and 7 months later (Figure 3). Biopsy was not pursued considering reports of orbital masses in scleroderma en coup de sabre. Nine months later, she developed cranial nerve III/VI palsy.

She received a 6-month course of monthly intravenous methylprednisolone 30 mg/kg/d for 3 days and weekly oral methotrexate 15 mg. She has a 4- by 3-cm hypopigmentation and skin atrophy on her left forehead, as well as thinning of the eyebrow and lashes.

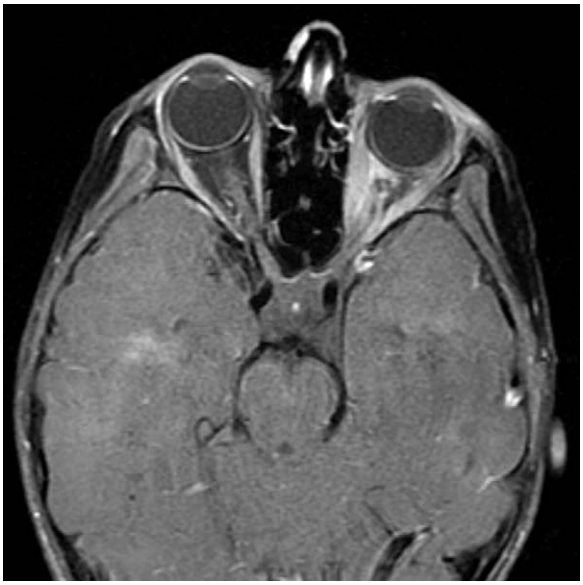

Figure 3. Patient 2: Axial brain magnetic resonance imaging (MRI) after gadolinium injection showing an infiltrative lesion primarily expanding in the left extraocular muscles.

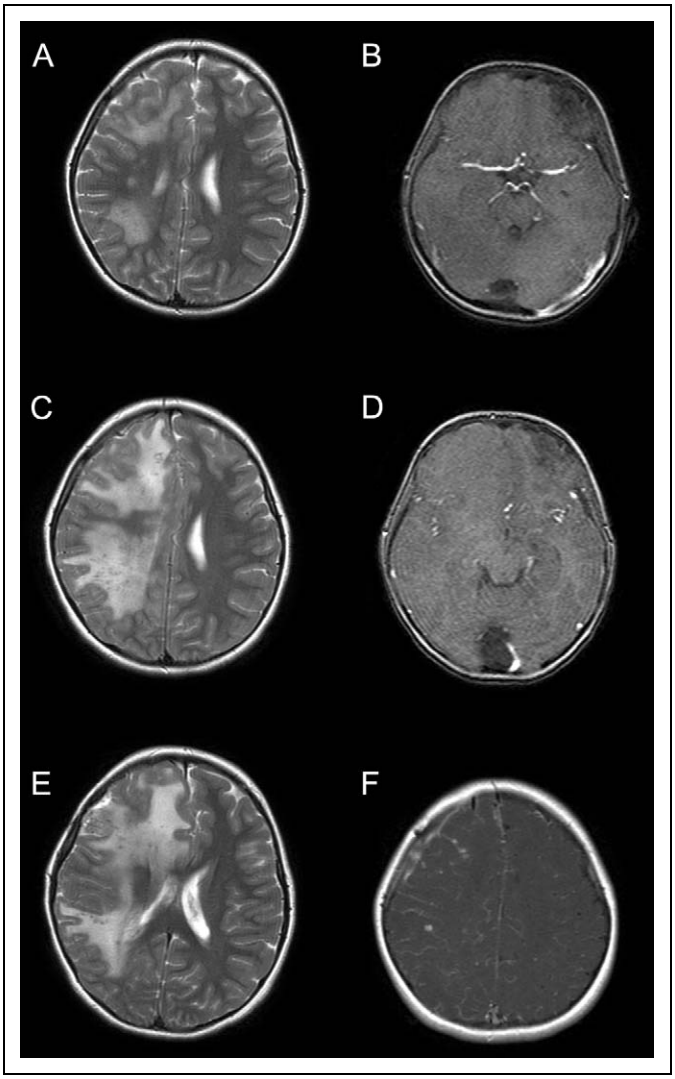

Figure 4. Patient 3: Axial magnetic resonance imaging (MRI) of the brain at the time of diagnosis and on follow-up, T2 (A, C, and E) and post gadolinium (B, D, and F) showing T2-bright areas in the right corona radiata involving the deep white matter and the cortex with effacement of sulci, then enlargement of the lesions to midline shift and on follow-up gadolinium enhancement of the meninges (F).

Patient 3

A 6-year-old previously healthy girl presented with 2 episodes of left-sided pain, weakness, and sensation loss. The first episode was preceded by infectious gastroenteritis. Her family history was remarkable for a cousin with multiple sclerosis. At the time of initial presentation, the parents noted hyperpigmentation on the forehead and an expanding induration of the right scalp. MRI showed enhancement of meninges and T2-bright areas in the right corona radiata (Figure 4) corresponding to calcifications on computed tomographic (CT) scan. Evaluation was negative for infection or rheumatologic autoantibodies. Cerebrospinal fluid showed oligoclonal bands. Acute demyelinating encephalomyelitis was suspected and high-dose glucocorticosteroids were given intravenously. Within a few weeks, she showed full neurologic recovery. Follow-up MRIs revealed enlargement of T2-bright foci and midline-shift (Figure 4). Brain biopsy showed perivascular inflammation, thrombosis, and gliosis in grey and white matter (Figure 5). Seizures were treated with levetiracetam 750 mg daily and lorazepam 2 mg.

She was then referred to University of California San Francisco Pediatric MS Center. At that time, neurologic exam revealed slightly increased deep tendon reflexes of the right arm. A comprehensive infectious, metabolic, coagulation, and rheumatologic evaluation including cerebrospinal fluid was unrevealing. Skin biopsy was consistent with scleroderma.

She was treated with a 6-month course of monthly intravenous methylprednisolone 1 g and weekly oral methotrexate 25 mg and was later switched to cyclophosphamide and oral prednisolone for about 1 year because of progression of her skin lesion. She was then transitioned to weekly oral methotrexate 25 mg. During the following 4 years, she remained seizure-free, and her skin lesion did not progress. Repeat brain MRI showed improvement. However, after 4 years she became noncompliant with her medications and experienced a flare of neurologic disease with tremor and progression of central nervous system lesions on CT scan (images not shown). After refusing additional treatment with cyclophosphamide, she was lost to follow-up.

Patient 4

A 16-year-old girl presented with partial and secondarily generalized seizures. The parents reported spreading of a sclerotic plaque from the left frontal hair line with onset of neurologic symptoms, but this was not considered to be part of the diagnosis

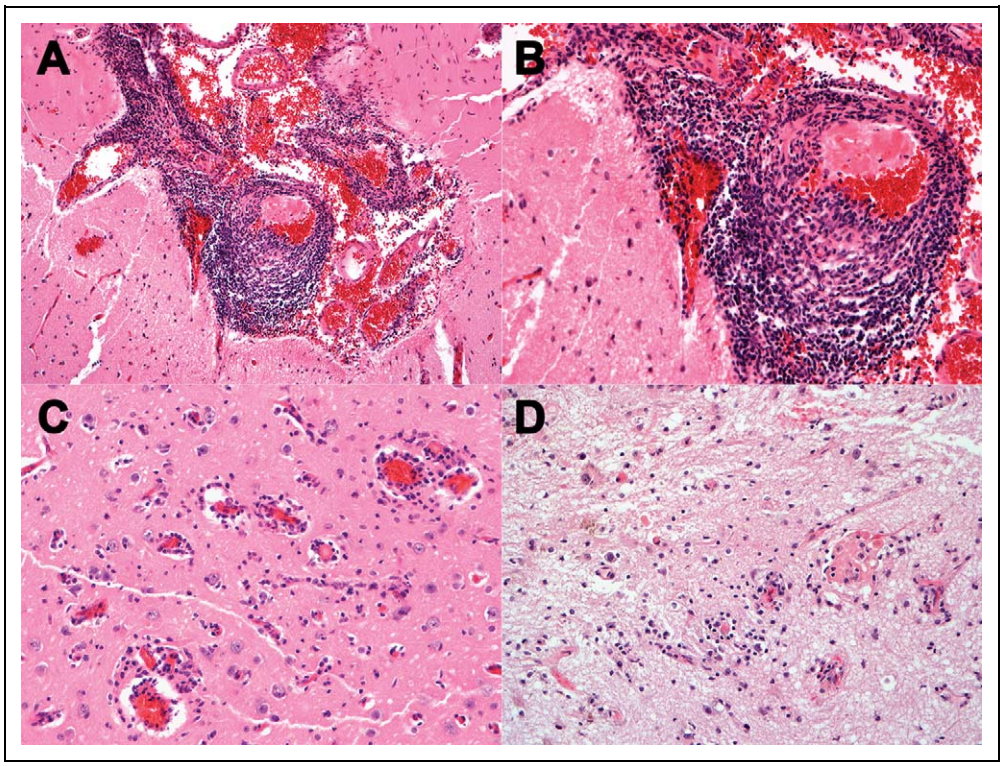

Figure 5. Patient 3: Brain biopsy: histological features from the brain biopsy using hematoxylin-eosin images: (A) Low-power magnification demonstrating brisk perivascular lymphoplasmacytic inflammatory infiltrates involving small-size arteries and arterioles. In this image, the inflammation is predominantly centered around the leptomeningeal vessels (original magnification × 100). (B) Medium-power magnification of the leptomeningeal perivascular inflammation predominantly composed of mature lymphoid cells. Note the associated gliosis within the adjacent cortex (original magnification × 200). (C) Inflammatory infiltrates and gliosis within the neuropil. The inflammation around the small vessels involves the Virchow-Robin spaces but also percolates into the brain parenchyma. There is associated astrogliosis (original magnification × 200). (D) Medium-power magnification of an infarcted region with hemosiderin-laden macrophages suggestive of a hemorrhagic microinfarct. There is tissue rarefaction along with macrophage infiltrates, hemosiderin deposition, and gliosis. These are typically considered nonspecific alterations associated with a hemorrhagic infarction (original magnification × 200).

at first presentation by the treating physician. MRI showed T2-bright lesions in the left frontal white matter. Workup for infection was negative. Cerebrospinal fluid showed elevated white blood cells (8 per mm^3) and oligoclonal bands. She was diagnosed with multiple sclerosis. Glatiramer acetate 20 mg and levetiracetam 1000 mg were initiated. Follow-up MRIs showed enlargement of central nervous system lesions.

Four years later, she was referred to the University of California San Francisco Pediatric MS Center, where she reported headaches, fatigue, clumsiness, bladder/bowel dysfunction, and joint pain. On examination, she showed right-sided spasticity and a linear whitish-blue sclerotic plaque from the left frontal hair line to the eyebrow and erythematous plaques on the elbows. Rheumatologic workup revealed antinuclear antibodies 1:80, positive SSA antibodies (2.5), positive anti-Scl70 antibodies (1.6), and positive anti–smooth muscle antibodies (>1:80). Workup for systemic sclerosis was unremarkable. Skin biopsy showed hyperpigmentation, fibrosis, and perivascular eosinophilic inflammation, consistent with the inflammatory stage of scleroderma.

She was started on a 6-month course of monthly intravenous methylprednisolone 1 g/d for 3 days, oral methotrexate 15 mg weekly, and folic acid 1 mg daily. After 4 months she was seizure-free, but central nervous system lesions had increased on MRI. Methotrexate was changed to 25 mg weekly by subcutaneous injection and levetiracetam was discontinued. Eighteen months later, she was off steroids and seizure-free. Her headaches and fatigue had decreased and MRI showed improvement.

Discussion

Scleroderma en coup de sabre typically manifests as a linear, sclerotic depression and dyspigmentation affecting the face and scalp.[5,8] Concerning focal scleroderma, 13% of children have a preceding mechanical skin trauma, including injections for vaccinations. The subtle lesions then progress to the typical clinical picture most likely due to healing anomalies.[5] The role of skin trauma especially for scleroderma en coup de sabre is uncertain.

Laboratory investigations are nonspecific.[7] Skin findings confirm the diagnosis, and biopsy reveals the depth of involvement.[1] Up to 16% of patients present with neurologic symptoms.[10] Partial seizures are more common than headaches

and paresis.[8,11] Ocular involvement occurs in 14% of cases, includes uveitis and conjunctivitis, and is often associated with brain abnormalities.[8]

In addition, 25% of brain lesions do not border skin changes and can be silent.[7] MRI can show white matter lesions, calcifications, and meningeal or parenchymal enhancement.[10] Occasionally, brain biopsy is required to rule out tumor.[2]

In our cases, no patient was noted to have skin changes before the onset of extracutaneous symptoms. Their findings mimicked allergic conjunctivitis, tumor, or acquired demyelinating diseases. Potential diagnostic pitfalls included the finding of oligoclonal bands and the partial resolution of T2-bright lesions after steroids. Persistent contrast enhancement and calcifications should challenge the diagnosis of acute demyelinating encephalomyelitis/multiple sclerosis.[10,12] In all cases, subtle skin findings were not initially considered to be a part of the neurologic disease presentation.

In summary, laboratory and radiologic findings in scleroderma en coup de sabre are nonspecific. The diagnosis is clinical and dependent on the appearance of characteristic skin findings. A full skin and scalp exam in children presenting with undiagnosed or atypical neurologic or ophthalmologic symptomatology should therefore be pursued. When abnormalities are present, a skin biopsy will confirm the diagnosis and should be obtained early to avoid costly, invasive, and high-risk workups. MRI is helpful to rule out alternative diagnoses or to find intracranial manifestations.[13]

Treatment of scleroderma en coup de sabre is mainly based on expert opinion. Immunotherapy treats cutaneous and extracutaneous changes and stops disease progression. It should be continued and repeated in disease progression. In localized scleroderma, stable remission after methotrexate treatment course was achieved.[1,3,14,15,16] Larger treatment trials are under way to evaluate long-term efficacy. A 6-month course of pulse high-dose corticosteroids and long-term weekly methotrexate controlled disease in all patients of our small case series.[17]

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Author Contributions

VK completed the first draft. EW designed the study and along with VK interpreted the data. VK, EFL, EvS, TT, JG, RGN, and KMC contributed to data collection. All authors revised the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

This study was approved by the Committee on Human Subjects Research at UCSF (IRB 10-04782). Individual HIPAA was required and informed consent was obtained. The study risk was assigned minimal.

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