

Headaches as a Presenting Symptom of Linear Morphea en Coup de Sabre

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ABBREVIATIONS

ECDS—en coup de sabre

ICHD—International Classification of Headache Disorders

MRA—magnetic resonance angiography

Dr. Polcari acquired patient data, drafted the initial manuscript, and made several revisions; Dr Moon acquired patient data and made substantial additions to the initial manuscript; Dr Mathes acquired patient data and photographs and critically reviewed the manuscript; Dr Gilmore acquired patient data and photographs and critically reviewed the manuscript; Dr Paller conceptualized and designed the study, acquired patient data and photographs, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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abstract

Linear morphea en coup de sabre (ECDS) is a form of localized scleroderma that predominantly affects the pediatric population, with a median age of 10 years at presentation. The existence of neurologic findings in association with ECDS has been well described in the literature. Here we describe 4 patients with ECDS who presented with headaches, which were typical migraines in 3 of the patients. The headaches preceded the onset of cutaneous findings by at least 6 months. Our patients' cases emphasize both the importance of recognizing headaches as a harbinger of ECDS and the necessity of performing thorough cutaneous examination in patients with unexplained headaches or other neurologic disease. *Pediatrics* 2014;134:e1715–e1719

Localized scleroderma, or morphea, is an atrophic connective tissue disease in which collagen deposition and inflammatory vascular changes lead to dermal thickening and the development of atrophic cutaneous plaques. Linear morphea en coup de sabre (ECDS) is a clinical variant that occurs predominantly in children and is characterized by a typically unilateral linear or curvilinear plaque on the forehead and frontal scalp. The name ECDS refers to the resemblance of the plaque to the cut from a saber. The relationship between linear morphea of the ECDS type and neurologic findings is well described in the literature. However, there are few reports regarding headaches specifically as the harbinger of ECDS morphea. We describe 4 patients with ECDS that initially manifested as severe headaches, often localized to the site at which the ECDS later appeared.

PATIENT 1

A 15-year-old white girl experienced a 1-day episode of left-sided weakness at 9 years of age her mother reported as a “stroke.” At 10 years of age, she had a seizure, reportedly unresponsive to courses of divalproex sodium, topiramate, carbamazepine, and levetiracetam. As a result, she discontinued her medication and experienced only an occasional seizure after exposure to flashing lights during the subsequent almost 5 years. At 12 years of age, she developed right frontal headaches that met International Classification of Headache Disorders (ICHD) criteria for migraines. These headaches were localized, pounding, and associated with vomiting, photophobia, and sometimes dizziness. They occurred approximately once per month, were preceded by visual hallucinations and numbness/tingling of the hands and feet, most often occurred before lunchtime (after skipping breakfast), and persisted for the entire day. At 13 years of age, she developed hair loss and discoloration, first noted

on the scalp with subsequent extension to the contiguous right side of the forehead (Fig 2A). With time, the discoloration extended to involve the right medial canthus and side of the nose, and she developed enophthalmos and decreased vision of the right eye. Examination revealed a linear hyperpigmented patch with underlying atrophy and induration, consistent with ECDS. MRI revealed irregular areas of signal hyperintensity, predominantly on the right side (Figs 1 A and B). It also demonstrated a defect in the scalp tissues at the site of her morphea. The imaging abnormalities were nonspecific and consistent with a previous insult such as inflammation or ischemia. The relationship to the episode of weakness years before is unclear. She responded to methotrexate 20 mg weekly and a 2-month course of tapering prednisone. When the methotrexate was tapered, both the discoloration and induration of her ECDS and the frequency and severity of her migraine headaches increased (Table 1).

PATIENT 2

An 11-year-old white girl reported a 3-year history of right-sided headaches

that met ICHD criteria for migraines. They were described as “feeling like intense throbbing pressure,” and were associated with nausea and photophobia. The headaches occurred weekly to 3 times per week, were precipitated by stress and decreased sleep, and lasted throughout the entire day. MRI shortly after the presentation of the headaches was normal. One year later, she first developed focal forehead discoloration, and later, induration precisely at the site of her headaches. Physical examination revealed pink discoloration and atrophy involving the right side of the forehead (Fig 2B) and chin. Repeat imaging with MRI/magnetic resonance angiography (MRA) was performed after the onset of forehead discoloration, but before atrophy development, and both the brain and soft tissues were normal. Treatment with prednisone and methotrexate 15 mg/week halted the progression of her ECDS. The frequency and severity of her migraine headaches also decreased after the methotrexate was started, but she had also recently initiated topiramate 25 mg twice daily. She continues to be well controlled with this combination of methotrexate and topiramate (Table 1).

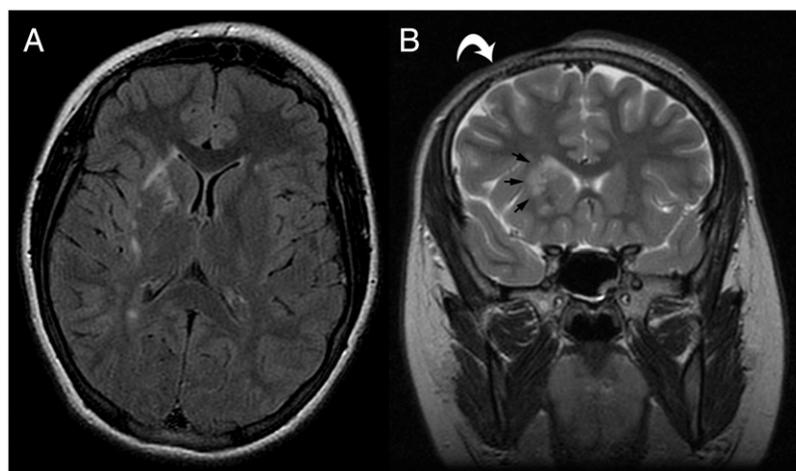


FIGURE 1

A, Axial T2 fluid attenuation inversion recovery (FLAIR) image reveals abnormal high signal in the anterior internal capsule, right corona radiata, and periventricular white matter, predominantly on the right side. B, Coronal T2 image reveals high signal in the corona radiata and deep white matter (black arrows), as well as the defect in the scalp tissues corresponding to her morphea (white arrow).

TABLE 1 Patient Characteristics

| Patient Gender; Age at Presentation to Dermatology | Neurologic Symptoms (Age of Symptom Onset) | Neuroimaging Findings | Cutaneous Findings (Age of Onset) | Treatment | Outcome |
|--|--|---|--|--|--|
| F; 15 y | Transient unilateral weakness (9 y); seizures (10 y); monthly unilateral migraine HA with vomiting, photophobia (12 y) | MRI: abnormal signal intensity at several foci, mostly ipsilateral to skin findings | Unilateral hair loss, linear atrophic plaque, hyperpigmentation (13 y) | Methotrexate, prednisone | Worsening of HA and ECDS after tapering of medications |
| F; 11 y | Unilateral migraine HA (8 y) | MRI, MRA: normal | Unilateral linear atrophic plaque, hyperpigmentation (9 y) | Methotrexate, prednisone, topiramate | Improvement of HA and ECDS |
| F; 13 y | Diffuse migraine HA (6 y) | MRI, MRA: normal | Unilateral linear atrophic plaque, hyperpigmentation (10 y) | Methotrexate, solumedrol, naproxen, greater occipital nerve injections | Improvement of HA and ECDS |
| F; 14 y | Frontotemporal HA (13 y) | MRI, MRA: normal | Bilateral hair loss, linear atrophic plaque, hyperpigmentation after onset of the HAs (13 y) | Methotrexate, prednisolone | No improvement of HA, halted progression of ECDS |

F, female; HA, headache.

PATIENT 3

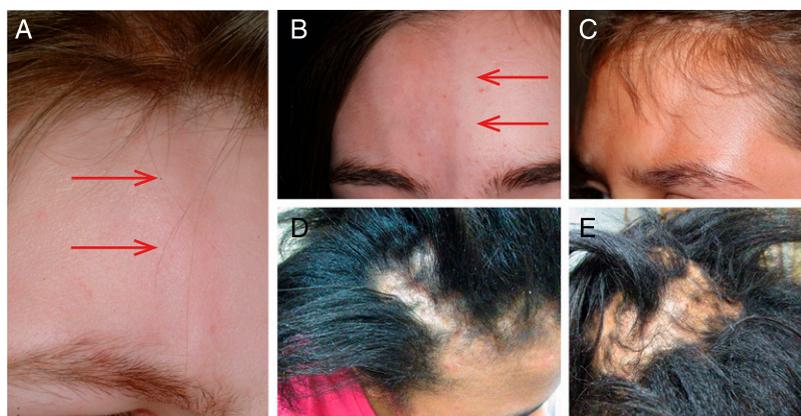
A 13-year-old Latina girl presented with a history of recurrent diffuse migraine headaches since 6 years of age. At 9 years, she developed left upper gingival recession, which reportedly revealed no abnormality in biopsy sections. One year later, examination demonstrated a faint hyperpigmented linear streak on the left paramedian forehead, which became darker and more atrophic during the subsequent 3 years (Fig 2C). The plaque extended linearly from the left eyebrow to several centimeters beyond the left

frontal hairline and was associated with atrophy of the left nasal ala, the left cheek, and the left upper lip and gum. She also complained of severe almost daily headaches accompanied by phonophobia, photophobia, intermittent blurred vision, tearing, flushing of the face, and left-sided retro-orbital pain. Skin biopsy of the scalp was consistent with the inflammatory stage of morphea. MRI revealed soft tissue atrophy and fibrosis of the left scalp, with no intracranial extension and a normal-appearing brain. MRA revealed normal intracranial vasculature. At the time of

diagnosis, she was evaluated by neurology and diagnosed with chronic migraine with aura. She was evaluated by ophthalmology and found to have enophthalmos but no significant ocular sequelae. Four pulses of intravenous solumedrol (1 g per day for 3 days, monthly) and methotrexate 25 mg weekly decreased the progression of the facial plaques and their induration. She has had improvement, but not resolution, of her headaches with naproxen and greater occipital nerve injections of 2% lidocaine and depo-medrol (Table 1).

PATIENT 4

A 14-year-old African-American girl complained of a 1-year history of severe frontotemporal headaches, accompanied by nausea and dizziness, but no other prodromal symptoms. She reported ~4 to 5 episodes of headache daily, each lasting ~45 minutes and associated with irritability and poor sleep. The headaches did not meet ICHD criteria for migraine. Approximately 6 months after the onset of headaches, she developed a hyperpigmented, indurated linear plaque on the right anterior scalp. This progressed into atrophic, hyperpigmented linear plaques involving 70% to 80% of her bilateral scalp with

**FIGURE 2**

Clinical appearance of ECDS morphea. A, Patient 1: Pink mildly indurated plaque with sharp delineation (arrows). B, Patient 2: Sharply defined, pink atrophic patch (arrows). C, Patient 3: Depressed hyperpigmented plaque. D and E, Patient 4: Cicatricial alopecia in linear configurations at several sites on the scalp.

a scarring alopecia (Figs 2 D and E). There was minimal extension onto the right forehead. Biopsy of the scalp revealed dermal sclerosis with eccrine trapping, loss of adnexae, atrophy, and a sparse lymphocytic infiltrate consistent with morphea. Workup for intracranial involvement included MRA and MRI, which revealed no abnormalities other than multiple areas of soft tissue thinning that correlated with her skin findings. Treatment was initiated with oral prednisolone 60 mg daily and methotrexate 15 mg weekly with folic acid. Since starting treatment, there has been no progression of her cutaneous lesions. Her headaches have not improved, and in fact she plans to be home-schooled because her headaches have become incapacitating (Table 1).

DISCUSSION

ECDS is a variant of linear morphea that typically presents as a unilateral, sclerotic plaque with variable associated localized atrophy on the paramedian forehead and frontal scalp.^{1–3} It can coexist with Parry-Romberg syndrome, a form of progressive hemifacial atrophy that is considered a deeper variant of morphea and typically involves the soft tissues of the mid- to lower face as well. ECDS is classically a pediatric disease, presenting in children with a median age of 10 years⁴ and has a slight female predominance.⁵ The relationship between linear morphea ECDS and neurologic findings is well established, with neurologic symptoms described in 18% to 47% of reported cases.^{1,6} Neurologic involvement most commonly manifests as complex partial seizures,^{7–9} but also as hemiparesis, muscle weakness, personality changes, intellectual deterioration, and headaches.^{10–14} Head-

aches associated with ECDS have been poorly characterized in the literature, and only a minority have been classified as migraine headache.^{1,12} Neurologic involvement typically develops several years after the cutaneous findings, although less commonly it can occur first or synchronously with the cutaneous findings.^{12,15–17} We describe 4 pediatric patients whose headaches preceded the onset of ECDS by at least 6 months. In 3 of our 4 patients, the headaches met ICHD criteria for migraine headaches, and in 2 of the 3 patients with unilateral ECDS, the cephalalgia was also unilateral and coincided with the site of the morphea.

Of previously described patients with ECDS and associated neurologic symptoms, 85% to 90% have had abnormal MRI or computed tomography findings, such as intraparenchymal calcifications, cerebral hemiatrophy, gray and white matter hyperintensities, intracranial aneurysms, nonspecific alterations in cerebral vasculature, and brain cavernomas.^{6,12,18–22} In 3 of our 4 patients, no alterations were detected, suggesting a bias toward description in the literature of patients with more severe neurologic abnormalities. Nevertheless, MRI abnormalities have been noted in the absence of clinical neurologic symptoms,^{12,18,23} suggesting that patients with ECDS may deserve brain imaging as a component of evaluation.

The pathogenesis for localized morphea is not well understood, but immune-mediated alterations or injury in local vasculature may play a key role.^{24,25} Indeed, microvascular alterations with vasculitis and fibrosis have been noted in both the affected skin and cerebral tissue.^{6,10,16} The pathogenesis of migraine headache is a topic of debate;

however, recent studies suggest that vascular alterations contribute,²⁶ particularly in the subset of patients with genetic cerebral small vessel disease. Although the onset of migraine headaches typically occurs in the age group of our patients and thus could be coincidental, the precise localization of the headaches to the site of the morphea in 2 of our 3 patients with more localized morphea suggests a shared mechanism. Further suggesting a shared underlying pathogenesis of ECDS and migraine headaches is the improvement of both conditions to methotrexate in 3 of 4 of our patients. Methotrexate has been well-documented as treatment of various forms of vasculitis, including giant cell arteritis,²⁷ antineutrophil cytoplasmic antibody-associated vasculitis,²⁸ and Wegener's granulomatosis,²⁹ although the exact mechanism of action is unclear. Perhaps methotrexate works to intervene in a vascular inflammatory state that contributes to both the ECDS and headache.

CONCLUSIONS

Headaches, including migraine headaches, can be a presenting feature of ECDS. Clinicians should be aware of this association and perform a thorough cutaneous examination in patients presenting with headache. Abnormal skin findings should prompt consideration of ECDS and referral for initiation of aggressive management.

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