

Radiologic Improvement After Early Medical Intervention in Localised Facial Morphea

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Abstract: We report the case of a young girl who presented with hemiparesis, seizures, and subtle features consistent with a linear form of facial morphea (en coup de sabre). She was treated with pulsed parenteral steroids and oral steroids and started on methotrexate. Magnetic resonance imaging results and neurologic problems improved after 6 months. Switching off inflammation early in the course of disease seemed to reverse some of the central nervous system changes. Assessment of children with unexplained hemiparesis and seizures should include careful examination of the face and scalp, looking for subtle signs of skin change and asymmetry. This is one of the few reported cases of neuroradiologic improvement after immunosuppressive treatment in a child with en coup de sabre.

Scleroderma is a nonhereditary connective tissue disorder that can broadly be divided into systemic disease (with internal organ involvement) and localized disease (limited to the skin). Localized scleroderma (morphea) is further subdivided into linear, generalized, pansclerotic, and mixed types (1). Progression to systemic scleroderma in children is exceedingly rare (2).

CASE REPORT

A previously healthy girl born to a consanguineous couple from Pakistan, presented at the age of 10 years

with acute onset of right-sided weakness, motor dyspraxia, and right facial weakness.

She had no Raynaud's phenomenon, arthritis, dysphagia, sicca symptoms, or weight loss. There was no history of drug exposure, chemicals, tick bite, or trauma. Echocardiography to exclude infective endocarditis or intracardiac thrombus was normal. Cerebral spinal fluid (CSF) protein, lactate, cell count and culture, and oligoclonal bands were normal. CSF virology, including parechovirus, cytomegalovirus, Epstein–Barr virus, enterovirus, herpes simplex virus, human herpes virus 6, and varicella zoster virus according to polymerase chain reaction were unremarkable.

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Further investigations included complete blood count, urea, creatinine, electrolytes, liver function test, thyroid function test (free thyroxine 16.0 pmol/L [range 10.8–19.0 pmol/L], thyroid-stimulating hormone 1.1 mU/L [normal <6.0 mU/L]), serum angiotensin-converting enzyme (30 U/L [range 0–90 U/L]), serum amyloid protein, glucose (3.7 mmol/L [range 3.5–5.5 mmol/L]), lactate (1.0 mmol/L [range 0.7–2.1 mmol/L]), folate (6.3 µg/L [range 1.0–10.2 µg/L]), erythrocyte sedimentation rate, and clotting screen were all within normal reference ranges.

Her immunoglobulin (Ig) levels, including IgG (10.4 g/L [range 5.4–16.1 g/L]), IgA (range 1.17 g/L [range 0.7–2.5 g/L]), and IgM (1.05 g/L [range 0.5–1.8 g/L]), were also within normal limits.

Screening for connective tissue and other auto-antibody diseases, including antinuclear antibodies (ANAs), anti-double-strand DNA (1.0 IU/mL [range 0–9.9 IU/mL]), tissue transglutaminase antibodies (0.20 U/mL [range 0.0–6.9 U/mL]), PR3 (0.30 IU/mL [range 0–1.99 IU/mL]), myeloperoxidase (<0.20 IU/mL [range 0–3.49 IU/mL]), rheumatoid factor (<20.0 IU/mL [range 0–20 IU/mL]), and thyroid peroxidase antibody (<33.4 IU/mL [normal <60 IU/mL]) were all normal as well. Initial computed tomography (CT) (Fig. 1) and magnetic resonance imaging (MRI) (Fig. 2) of the brain showed leptomeningeal, gyral, and basal ganglia calcification with adjacent white matter signal abnormalities in the left hemisphere, along with generalized swelling of the

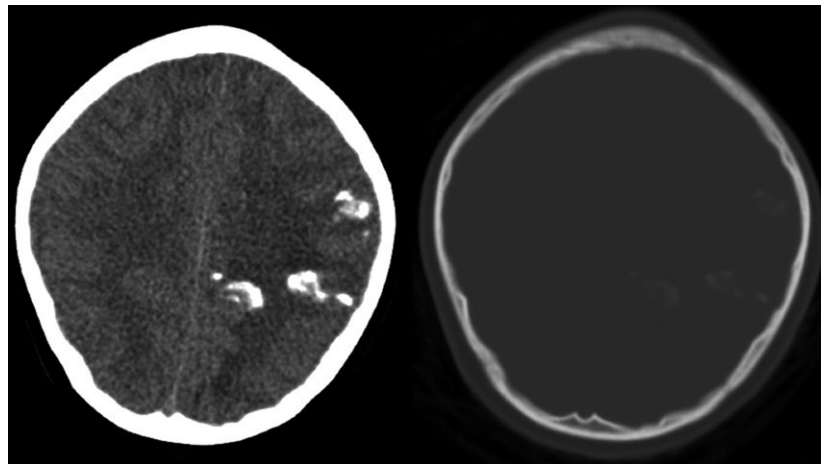


Figure 1. Axial computed tomography scans through the frontal and parietal lobes show leptomeningeal and gyral calcification in the brain underlying the ipsilateral region of thinning of the scalp.

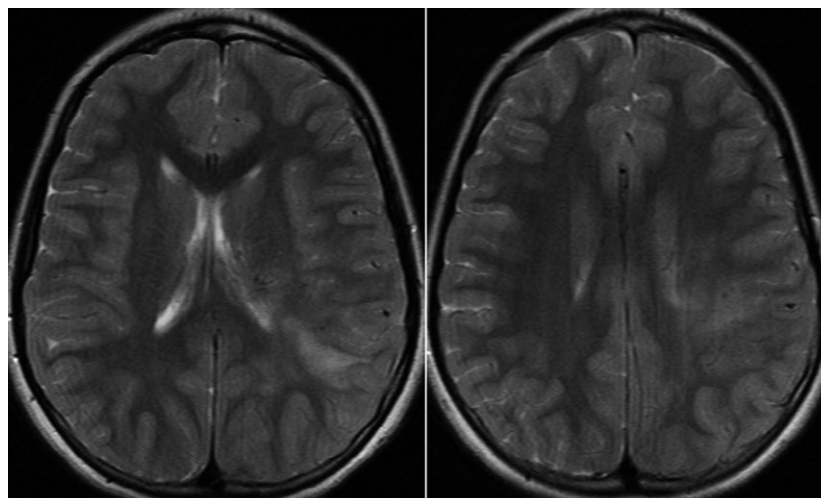


Figure 2. Axial T2-weighted images show patchy white matter abnormality in the left inferior parietal lobe and foci of calcification in the left basal ganglia and adjacent capsular white matter. Subtle generalized swelling of the left hemisphere is also demonstrated.



Figure 3. Scalp shows scarring alopecia.



Figure 4. Left frontal region shows marked thinning and sclerotic changes.

left cerebral hemisphere. Intracranial angiography was normal. Electroencephalography demonstrated nonspecific dysfunction over the left posterior quadrant. She was started on phenytoin because of continued ictal features and the self-resolved episode of right-sided weakness.

Shortly before discharge after first presentation, she was noted to have a depressed hypopigmented band of skin extending from the left brow into the scalp (Figs. 3 and 4). Skin biopsy was examined at several levels, with underlying fatty tissue and skeletal muscle. The overlying epidermis showed mild atrophy and a lack of rete ridges. There were occasional intraepithelial lymphocytes, but there was no obvious hydropic degeneration of the basal keratinocytes. There were pigment-laden macrophages in the superficial dermis, and the reticular dermis was noted to be thick, with an excess of coarse collagen bundles. There was a mild mononuclear, predominantly lymphocytic, inflammatory cell infiltrate between the collagen bundles and around the vessels and the skin appendages. There was no significant fibrosis in the subcu-

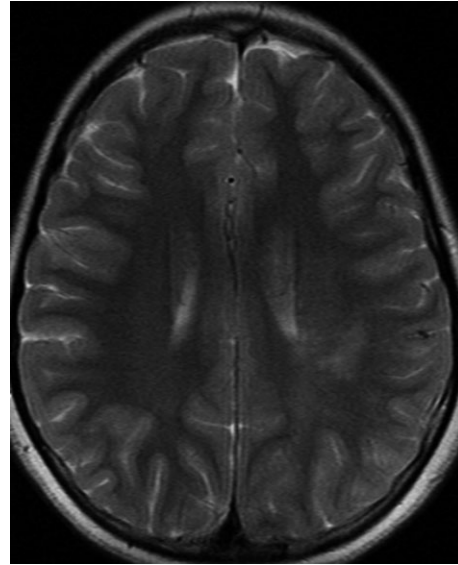


Figure 5. Axial T2-weighted image performed 6 months later shows partial resolution of the parietal white matter abnormality. The calcific foci are unchanged. The hemispheric swelling has resolved.

taneous tissue and no fat entrapping. The changes were consistent with morphea, supporting a diagnosis of en coup de sabre (ECDS) morphea.

She was treated with pulsed methylprednisolone followed by oral steroids and methotrexate (15 mg/m² once a week). Our pulse protocol consists of three doses over three consecutive days, usually repeated on the same days a week later. Each pulse consists of 30 mg/kg of methylprednisolone (maximum 1,000 mg). She had three self-limited 24-hour episodes of right-sided hemiparesis and aphasia over the next 6 months while taking aspirin, oral prednisolone, phenytoin, and methotrexate. Her neurologic episodes declined in frequency and severity over the next 10 months. She was switched to levetiracetam, which helped but did not completely resolve her seizures. Follow-up MRI after 6 months showed partial resolution of the white matter abnormality (Fig. 5).

DISCUSSION

Linear scleroderma is a connective tissue disorder of unknown etiology that may relapse and remit and cause functional impairment and disfigurement. Two-thirds of patients with linear morphea are younger than 18 years (2). The main concern in children is the risk of long-term complications due to musculoskeletal effects of the disease process, which include limb and facial asymmetry. Psychological problems can result from pronounced disfigurement. Neurologic abnormalities have been reported with ECDS on

initial presentation (2). In all of the subclasses of linear scleroderma, the ECDS and Parry–Romberg subtypes are the only ones associated with severe neurologic abnormalities (2).

Her neuroradiologic examinations revealed white matter lesions and intracranial calcification, which are already reported in the medical literature (3). Her calcium deposits were thought to be due to an early primary cerebral inflammatory process, because these have been previously described in the brain in linear scleroderma (4). Epileptic seizures are a known major neurologic complication of ECDS and progressive facial hemiatrophy (3), such as observed in our patient.

Common neuroimaging findings of this syndrome are calcification on CT and high-intensity areas on MRI (5). The localized white matter signal abnormality could have been due to cerebral edema secondary to seizure activity as well, but serial MRIs (three in total) refuted this correlation, because no epileptiform activity was recorded on repeated prolonged electroencephalographic monitoring. This placed an inflammatory process at the top of the differential diagnosis. Her repeated neurologic examinations were unremarkable, but MRI had persistent changes that coincided well clinically with her difficult-to-treat epilepsy. She continued on oral aspirin and antiepileptic treatment to cover the possibility of thrombotic or epileptic episodes.

Several theories about the pathogenesis of linear morphea have been suggested, including chronic inflammation, abnormal perfusion, cortical dysgenesis, autoimmune disease, and sympathetic overexcitation (3). This case points to an inflammatory and potentially reversible process. It is possible that conflicting findings might represent the disease process at different points in its evolution. Facial linear morphea affects the central nervous system in nearly two-thirds of patients, as previously reported (6).

The previous reports of onset in the first or second decade, female predilection, and commonly affecting the left side of face (7) fit well with our patient's demographic characteristics.

Because of its uncommon occurrence, a spectrum of agents has historically been used to treat it, including agents such as D-penicillamine, oral steroids, antimalarial medications, methotrexate with pulse oral steroids, topical calcipotriol, and psoralen with ultraviolet A light (8).

We think that switching off the inflammatory process early by using corticosteroids and disease-modifying antirheumatic agents not only helped

reduce inflammation, but also reversed the initial damage caused by underlying inflammatory processes.

Her ictal features declined after treatment, correlating well with her neuroradiologic follow-up images. We did not see any significant electroencephalographic abnormalities, although she was extensively screened, and electroencephalographic changes have remained nonspecific.

CONCLUSION

This case highlights the underrecognized relationship between neurologic complications and linear scleroderma. Neurologic manifestations were the presenting symptom, before the diagnosis of ECDS, which is unusual. Although our patient still has significant neurologic symptoms despite radiologic improvement on antiinflammatory treatment, this might be secondary to her residual intracerebral calcifications, because these have not responded to treatment and can still be seen on imaging. This calcification may represent older, more refractory changes. We would suggest a baseline MRI in patients with a new diagnosis of ECDS as well as in all patients with ECDS who develop any neurologic symptoms. This is one of the few reported cases of neuroradiologic improvement in a child with ECDS after treatment.

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