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Clinical Observation

Spinal Epidural Lipomatosis: A Rare Complication From Hormonal Therapy for Infantile Spasms

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ABSTRACT

Background: Spinal epidural lipomatosis (SEL) represents pathologic overgrowth of extradural adipose tissue in the spinal canal that can result in spinal cord compression. SEL has been associated with excess corticosteroids, whether from exogenous steroid use or from excess endogenous steroids. Spinal epidural lipomatosis is rarely reported in children and has not been reported in association with hormonal therapy for infantile spasms.
Methods: We performed a detailed retrospective chart and literature review.
Results: We describe two children with symptomatic SEL associated with the use of high-dose hormone treatment for infantile spasms.

Introduction

Spinal epidural lipomatosis (SEL) is a pathologic overgrowth of unencapsulated extradural adipose tissue in the spinal canal; it may compress the spinal cord or nerve roots in the dural sac or the extradural blood vessels causing vascular compromise to the cord.[1,2] SEL is a rare but well-documented complication of chronic exogenous corticosteroid treatment for various conditions, endogenous steroid excess or hypercortisolism, and obesity.[2,3] Idiopathic or primary SEL is also described in the absence of an identified cause.[4] The presentation varies with the level of spinal cord injury. Most patients present with progressive back pain, numbness, weakness, gait abnormalities, incontinence, and rarely, acute paralysis.

Adrenocorticotropic hormone (ACTH) and prednisone are the standard first-line treatments for infantile spasms (IS), the most common infantile epileptic encephalopathy.[5] Here we describe two individuals with SEL caused by ACTH therapy for IS, a previously unreported complication of this therapy.

Patient descriptions

Patient 1

This 20-month-old girl who experienced focal seizures on the day she was born. She had left hemimegalencephaly, right perisylvian polymicrogyria, left facial hemihypertrophy, cortical visual impairment, and global developmental delay. Genetic testing revealed a variant of unknown significance in the mammalian target of rapamycin gene (denoted p. V18851). She developed IS at age three months but was lost to follow-up. Care was re-established after she was placed in foster care at age six months. Electroencephalography confirmed left hemihypsarrhythmia, and she experienced daily clusters of flexor spasms of the right arm and leg.

She began high-dose vigabatrin (VGB) at 150 mg/kg/day. After a month of persistent spasms, prednisone was added at 8 mg/kg/day. Two weeks later, due to failure to respond, prednisone was switched to high-dose ACTH (150 U/m^2). After two weeks at full dose, ACTH was weaned over two weeks. Midway through the ACTH weaning period she presented with decreased leg movements. She cried or appeared uncomfortable with diaper changes. The decreased movements rapidly progressed to flaccid paraplegia of both legs.

Her examination was notable for increased weight with body mass index of 19.25 kg/m^2 (ninety-seventh percentile) with Cushingoid facies. She exhibited diminished sensation to light touch and pain in both legs, with a sensory level at thoracic T6 dermatome

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and an absence of the patellar and ankle reflexes bilaterally. Anal reflex was absent. Magnetic resonance imaging (MRI) of the spine demonstrated extensive SEL extending from the T6 to the S3 levels with moderate to severe thecal sac effacement and compression (Fig 1). The spinal cord was decompressed by resection of pathologically confirmed fatty tissue. Paraplegia gradually improved during the next few weeks.

Patient 2

This eight–month-old boy with trisomy 21 and reflux presented with IS and developmental regression. He was started on high-dose ACTH (150 U/m^2). A few days later levetiracetam was added for new-onset generalized tonic-clonic seizures. After two weeks, due to persistent spasms, VGB was added and titrated to 150 mg/kg/day. ACTH was simultaneously weaned over two weeks. During the time on ACTH, he experienced weight gain (19.4 kg/m^2 [ninety-third percentile]), Cushingoid facies, hypertension, and hematochezia. By week five, his spasms and hypsarrhythmia had resolved. A few days later, he presented with increased somnolence, decreased oral feeding, and decreased movements in both legs. No bowel or bladder dysfunction was reported. He demonstrated frequent jerking movements of upper extremities, which raised concerns for epileptic myoclonus. Also noted were orofacial dyskinesias and repeated head movements downward and to the left, all of which disappeared in sleep. These movements had no electrographic correlate.

On examination, he had hyperactive deep tendon reflexes in both legs. Anal reflex was preserved. Sensation to light touch was slightly diminished in both legs with preserved withdrawal to painful stimulation. No clear sensory level was appreciated. MRI of the spine was obtained because of concerns for lower extremity paraparesis, which revealed diffuse SEL without thecal sac compression (Fig 2).

Brain MRI revealed hyperintensities on diffusion-weighted images in the basal ganglia, thalami, and pons consistent with vigabatrin-associated brain abnormalities on MRI[6] and diffuse cortical atrophy. VGB was quickly weaned with reversal of his encephalopathy and movement disorder. As encephalopathy improved, his leg movements also improved. On follow-up examination one week later, no motor or sensory deficits were appreciated.

Discussion

SEL is characterized by excessive unencapsulated adipose tissue in the spinal epidural space. Most patients have excess endogenous or exogenous steroids.[7] SEL was first reported in 1975 by Lee et al. in a patient who had undergone renal transplantation.[1] It has since been well-characterized in adults.[2] Only a few case reports and small series have been published regarding SEL in the pediatric population.[8,9] SEL is mostly commonly associated with chronic exogenous corticosteroid use. Indications for corticosteroids have included nephrotic syndrome, organ transplantation, juvenile idiopathic arthritis, systemic lupus erythematosus, Crohn disease, Sjögren syndrome, pineoblastoma, relapsing polychondritis, Henoch-Schönlein purpura,[10] non-Hodgkin lymphoma, and leukemia.[3]

A 2011 review of the literature analyzed 20 pediatric patients with SEL.[10] The average age at diagnosis was 11 years, with the youngest at age five years. SEL was diagnosed after a mean of 1.3 years of corticosteroid treatment (median, 0.8 years; range, three weeks to 6.5 years). The dose of corticosteroid at the time of presentation of SEL ranged from 5 mg and 80 mg of prednisone/day. The majority of patients had Cushingoid features, and back pain was the most common presenting symptom. Singh et.al. recently described the youngest known patient with symptomatic SEL, a 15-day-old, term neonate who was presumed to have excessive endogenous steroids from Cushing disease.[11]

To date, there have been no reports of SEL in association with hormonal therapy for IS. In both of our patients, SEL was associated with high-dose corticosteroid treatment with iatrogenic Cushing syndrome. Postcontrast images of the spine did not reveal contrast enhancement. There was no evidence of disk or vertebral column signal changes, ruling out other causes for spinal cord lesion in this age group. Both of our patients presented with decreased leg movements, with subacute progression to paraplegia in one individual. Epidural lipomatosis seems to have developed rapidly

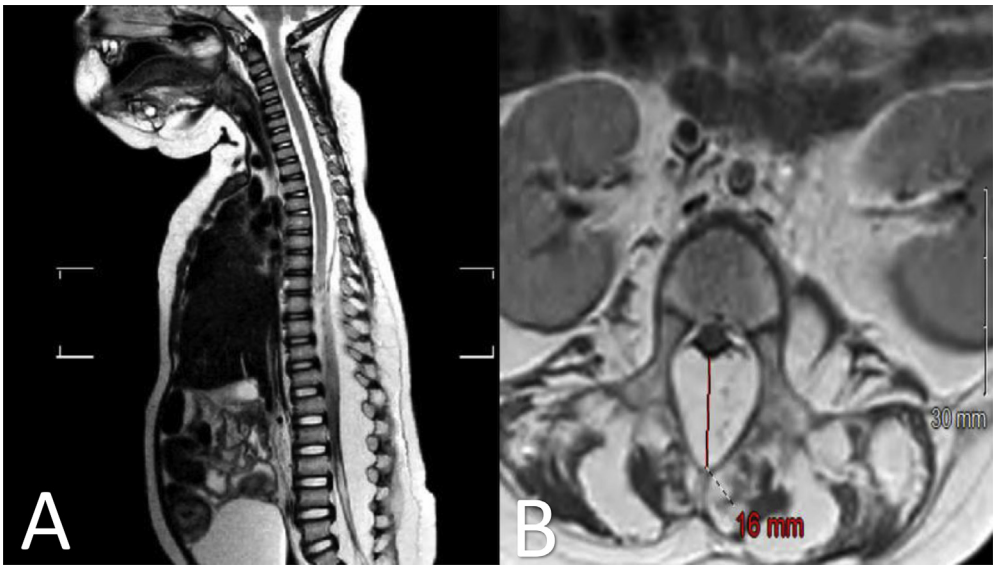

FIGURE 1. T2-weighted sagittal view (A) and T1-weighted axial view (B) of magnetic resonance imaging of the spine demonstrating homogeneously hyperintense fatty tissue in the posterior aspect of the spinal canal of maximum thickness 16 mm, causing thecal sac compression with obliteration of the subarchanoid space from T6 to S3 level, maximal across lumbar spine and sacral spine. The color version of this figure is available in the online edition.

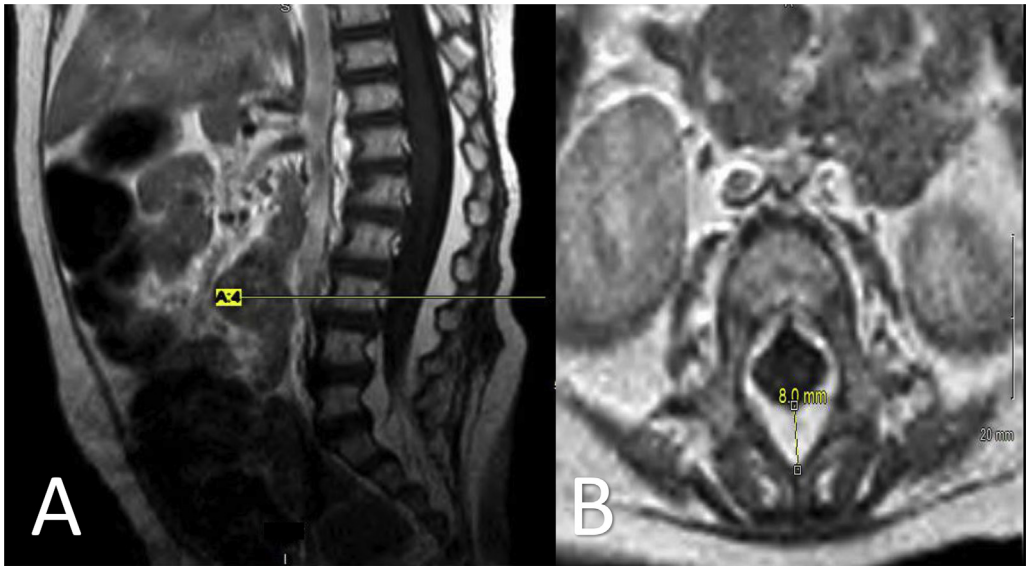

FIGURE 2. Magnetic resonance imaging of the spine. T1-weighted sagittal view (A) and axial view from the level of the horizontal line (B) demonstrating diffuse spinal epidural lipomatosis with maximum thickness 8 mm across the lumbar spine (represented by thr yellow line across corresponding sections of L2 vertebra), without thecal sac compression. The color version of this figure is available in the online edition.

within a few weeks of ACTH therapy. In our first patient, high-dose prednisone therapy before initiation of ACTH may have contributed.

The pathogenesis of corticosteroid-associated SEL remains unclear, it is most commonly associated with exogenous administration of corticosteroids and less commonly with elevated endogenous steroids as seen in ectopic ACTH syndrome or Cushing syndrome.[2] There are a few case reports describing other endocrinopathies such as hypothyroidism or macroprolactinoma[4]; it has also been described with obesity. Certain overgrowth syndromes with a germline mutation in phosphatase and tensin homolog genes such as Bannayan-Riley-Ruvalcaba syndrome have also presented with SEL.[12] Individuals with idiopathic SEL have been described.[13] Corticosteroids are hypothesized to cause SEL via stimulation of glucocorticoid receptors in normal epidural adipose tissue, leading to its hypertrophy.[14] The majority of the fatty epidural tissue is located in the thoracic and lumbar spine. Overgrowth of this tissue effaces the subarachnoid space and displaces the spinal cord anteriorly causing deformation or compression, leading to myelopathy. MRI is the preferred diagnostic test of choice for early recognition.[8] A uniformly high signal intensity on T1-weighted images and an intermediate signal on T2-weighted images are characteristic of adipose tissue. An objective MRI grading system for adults with mild, moderate, and severe SEL has been previously published.[15] Normal adult volunteers had a mean sagittal epidural fat thickness of 4.6 mm (range, 3 to 6 mm). Epidural adipose tissue with thickness greater than 7 mm (ranging 7 to 15 mm with a median of 8 mm) has been reported as diagnostic of SEL.[8] Radiologic criteria for pediatric SEL have not been well described. The thickness of epidural fat tissue was measured at 16 mm for Patient 1 and 8 mm for Patient 2.

The treatment of SEL is often dependent upon the severity of the neurological symptoms. In the setting of obesity, conservative measures including weight loss and tapering of corticosteroid therapy are the mainstays treatment. In cases of acute compressive myelopathy, surgical decompression is the treatment of choice.[16]

In conclusion, SEL is a rare, serious, but potentially reversible complication of hormonal therapy for IS. SEL in infants presents as paraplegia or decreased leg movement and should be included in the differential diagnosis for any infant on exogenous steroids with this finding. Early diagnosis and intervention can lead to complete recovery.[17]

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