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Encephalocraniocutaneous Lipomatosis: A Rare Association With Tethered Spinal Cord Syndrome With Review of Literature

Amal Naous, MD[1], Abdel Rahman Shatila, MD[1], Zeina Naja, MD[1], Ahmad Salaheddine Naja, MD[1], and Mariam Rajab, MD[1]

Abstract

Encephalocraniocutaneous lipomatosis or Haberland syndrome is a rare, congenital neurocutaneous syndrome. It is characterized by unilateral lipomatous hamartomata of the scalp, eyelid, and outer globe of the eye and ipsilateral neurologic malformations. We describe the first case from Lebanon, an infant with classical encephalocraniocutaneous lipomatosis characterized by nevus psiloliparus, unilateral right facial and frontal–temporal subcutaneous lipomas, alopecia, ocular coloboma, aniridia and eyelid nodular tags, ventriculomegaly with intracranial and intraspinal lipomas, and tethered spinal cord. We report this case of rare association between encephalocraniocutaneous lipomatosis and tethered spinal cord syndrome and stress on the importance of spinal cord evaluation in encephalocraniocutaneous lipomatosis.

Keywords

encephalocraniocutaneous lipomatosis, tethered spinal cord syndrome, hydrocephalus

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Encephalocraniocutaneous lipomatosis, sometimes referred to as Haberland syndrome, is a rare neurocutaneous syndrome first described by Haberland and Perou in 1970.[1,2] Its characterization occurred following an autopsy examination of a severely retarded 5-year-old boy who had unilateral lipomas of the cranium, face, and neck; lipodermoids of the eye; and ipsilateral brain anomalies. Since that initial report, roughly 54 cases have been described and diagnostic criteria have been developed.[3-5] The genetics of the disease are unknown, but because of its sporadic occurrence and phenotypically characteristic skin and bone lesions, encephalocraniocutaneous lipomatosis is thought be a genetically mosaic condition. It affects males and females equally, the patients' IQ can range from severely retarded to normal, seizure disorders are common, and no familial recurrences have been reported. This is a mesenchymal disorder affecting mostly neural crest derivatives, and all central nervous system anomalies are caused by mesenchymal defects affecting the tissues surrounding the brain or involving the cerebral vasculature, without a primary abnormality of the nervous tissue. The hallmark lesions of encephalocraniocutaneous lipomatosis are benign central nervous system lipomas. The lipomas of this syndrome are generally stable throughout the patient's life, but the progression or late development of porencephalic cysts, cerebrovascular aneurysms, and cystic bone lesions has been reported.[2,4,6,7] Previous case reports and reviews regarding this neurocutaneous syndrome have focused on diagnostic criteria, clinical examination findings, and possible pathogenesis.[4-6] We present, to the best of our knowledge, the first case from Lebanon with definite diagnosis of encephalocraniocutaneous lipomatosis and a rare case of encephalocraniocutaneous lipomatosis associated with tethered spinal cord syndrome. Our patient first presented to us at day 1 of life, and the results of our neuroradiological evaluation, treatment of the patient's hydrocephalus, and the diagnosis of tethered cord syndrome over the course of approximately 2 years are also presented in this study.

[1] Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon

Corresponding Author:
Amal Naous, MD, Department of Pediatrics, Makassed General Hospital, Lebanon, Beirut, Beirut, 11-6301, Lebanon.
Email: amalnaous@hotmail.com

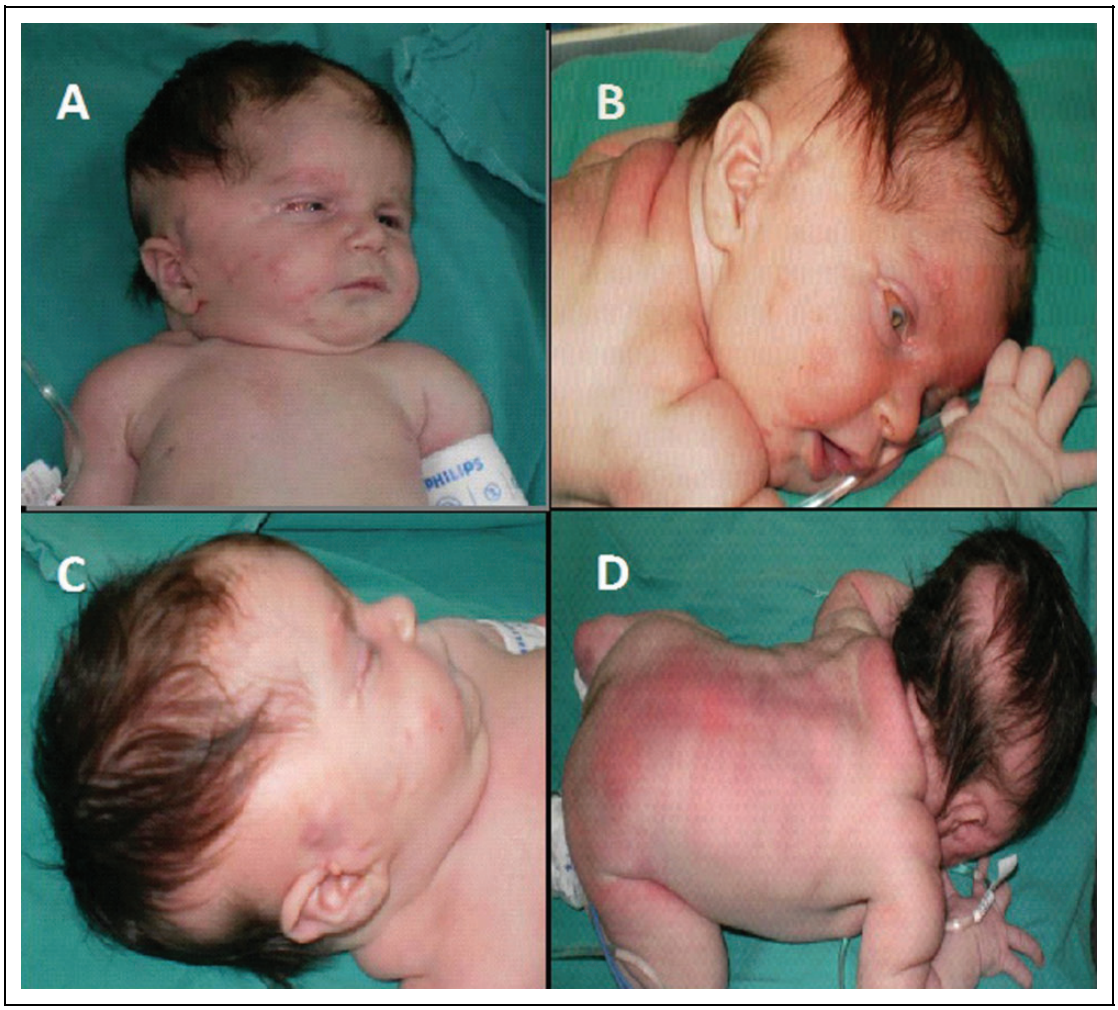

Figure 1. A and C, Clinical photograph showing flat areas of alopecia on the scalp and multiple small elevated nodules on the right side of the face and low-set ears. B, Nodular lesion at the outer canthus of right eye suggestive of dermoid and reddish lesion on the bulbar conjunctiva suggestive of epibulbar dermoid and aniridia of the right eye. D, Multiple soft subcutaneous masses over the back.

Case Report

History and Examination

This girl was born at 39 weeks of gestation to a gravida I para I, 25-year-old healthy mother and 28-year-old healthy father, with no history of consanguinity and no remarkable family history. The mother was followed regularly during her pregnancy and had prenatal diagnosis of fetal hydrocephalus at 30 weeks of gestation. The female baby was delivered by cesarean delivery due to fetal distress and was born with Apgar scores 8 and 9 at 1 and 5 minutes, respectively. At birth, the baby was noticed to have skin lesion and so she was transferred, at day 1 of life, to the Pediatric Department at Makassed General Hospital for further management.

Physical Examination

Upon presentation, the baby had a weight of 3690 g, length of 49 cm, and macrocephaly with head circumference of 37.5 cm (above the 95th percentile for her age). She had flat areas of alopecia on the scalp and multiple small elevated nodules on the right side of the face. Nodular lesion at the outer canthus of right eye suggestive of dermoid and reddish lesion on the bulbar conjunctiva suggestive of epibulbar dermoid and aniridia of the right eye were also noted (Figure 1A-C). She also had low-set ears with multiple soft subcutaneous masses over the back (Figure 1D). Fundus examination showed bilateral optic disc coloboma. Cardiovascular and respiratory system examinations were normal. There was full passive and active range of motion of the extremities on nervous system examination. Her reflexes and muscle tone were normal. Results of a radiography study of the chest and skeleton were unremarkable. A head computed tomography (CT) scan was performed, which demonstrated homogeneous low-density lesions in the cistern magna and right cerebellopontine angle indenting smoothly the brachium pontis. There was severe right lateral ventricular dilation. The patient underwent magnetic resonance imaging (MRI) of the head, which showed a lipomatus mass, measured at 25 $\times$ 12 mm, seen at the right cerebellopontine angle cistern, indenting smoothly the brachium pontis with no alteration of its

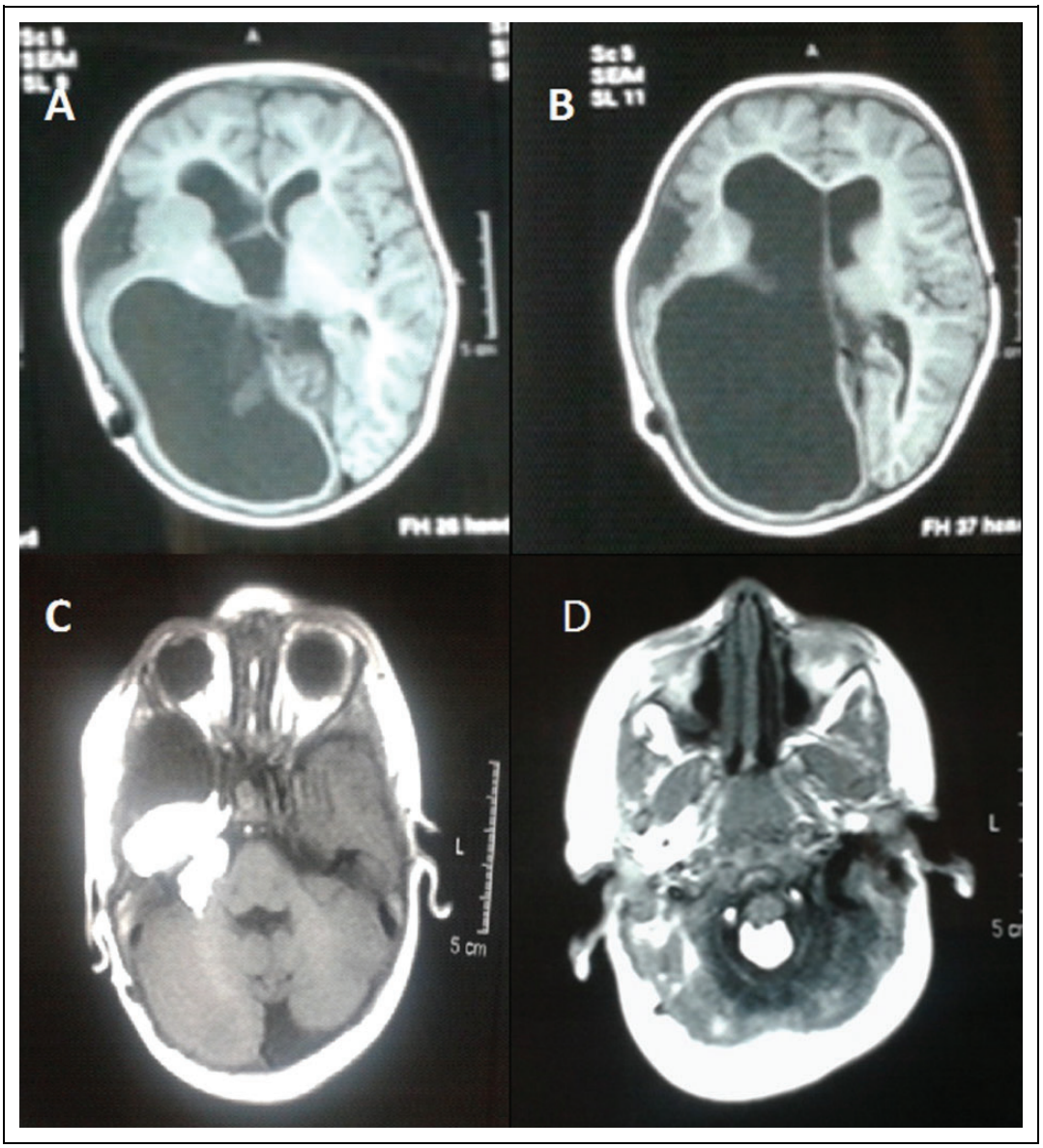

Figure 2. Axial T1-weighted magnetic resonance imaging of the brain with intravenous contrast showing (A and B) the lateral ventricle is dilated and the right cerebral hemisphere is atrophic with prominence of the overlying subarachnoid spaces. Imaging studies (C) showing a fat containing mass, measured at 25 × 12 mm, is seen at the right cerebellopontine cistern angle, indenting smoothly the brachium pontis with no alteration of its signal, and (D) similar lesions are also noted in the posterior aspect of magnum foramen and cervical canal.

signal, also with similar lesions noted in the posterior aspect of foramen magnum; cervical canal with no bleed, intact brain stem, with atrophic right cerebral hemisphere; and dilated lateral ventricle and prominent overlying subarachnoid spaces (Figure 2A-D). The right periauricular cutaneous lesion was submitted to histopathological examination and showed that the dermis has rudimentary hair follicles surrounded by fibrous connective tissue interpreted by mature fat lobules. The patient was neurologically normal for her age, and no deficiency of the right upper extremity was appreciated during the course of the hospital admission. It was decided to follow the infant closely to observe for increase in her hydrocephalus and for development of any neurological deficit.

Follow-Up Findings and Treatment

The patient began to show increase in her head circumference, and neuroimaging showed an increase in the size of her ventricles. At 9 months of age, the patient underwent ventriculoperitoneal shunt and had a significant improvement in motor skills over the following months. The size of her head circumference stabilized. The patient could stand independently and was beginning to formulate words at approximately 1 year of age. However, at the age of 1 year 10 months, the patient was admitted with staring, unresponsiveness, and tonic–clonic movements associated with weakness in her lower extremities. Her neurological examination

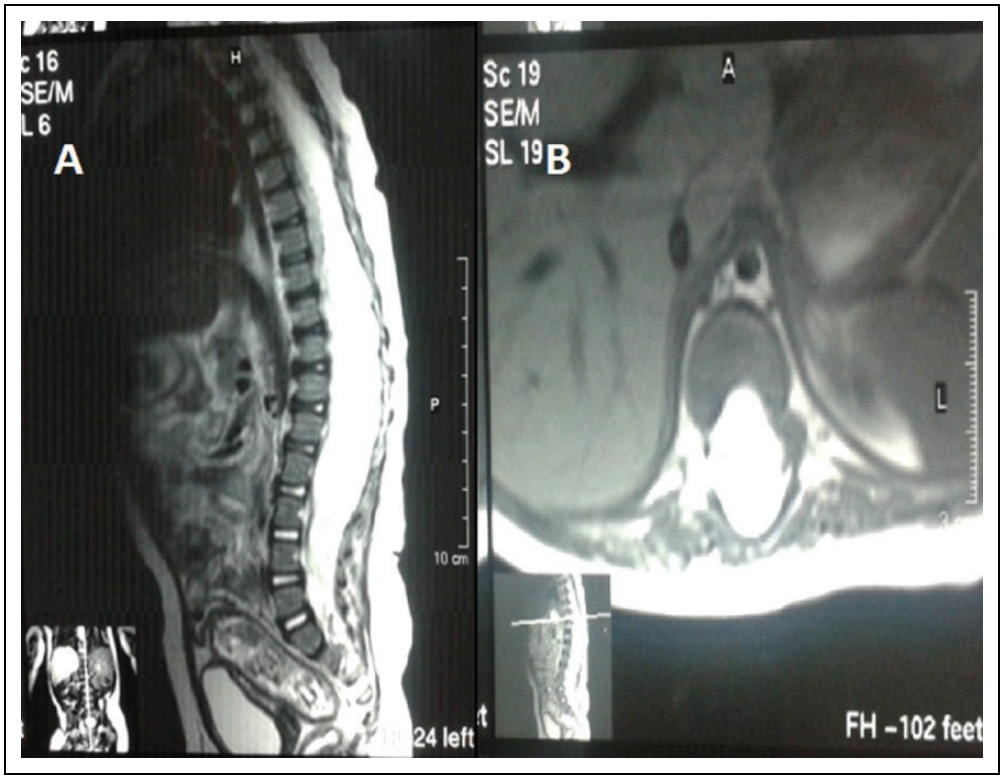

Figure 3. Magnetic resonance imaging of the spine. A, Saggital T2-weighted image showing a large subpial juxtamedullary lipoma filling the entire spinal canal engulfing the spinal cord that is tethered. B, Axial T2-weighted image showing the spinal cord remarkably compressed at the thoracic level displaced to the left and protruding into the left lateral foramina at the level of dorsolumbar junction.

revealed spasticity in her lower extremities and sustained left ankle clonus.

Deep tendon reflexes were hyperactive without clonus (3+) in both the upper extremities and hyperactive with clonus (4+) in both the lower extremities, mainly in the left lower limb. No scoliosis of the back was observed.

Electroencephalography (EEG) was done, which showed the presence of diffuse slow delta activity related to brain damage (encephalopathy). The patient was started on both phenobarbital and phenytoin, and her seizures were controlled. Ultrasound of both kidneys revealed 2 cm cortical cyst in the upper pole of the right kidney.

Repeat MRI of the brain demonstrated no change. Magnetic resonance imaging angiography of the brain was normal. The MRI of the spine showed large subpialjuxtamedullary lipoma filling the entire spinal canal, which is widened, and engulfing the spinal cord. The spinal cord is tethered and is remarkably compressed at the thoracic level, displaced to the left and protruding into the left lateral foramina at the level of dorsolumbar junction. The vertebrae are of normal heights and signal, and normally aligned and the discs are unremarkable (Figure 3A and B).

Discussion

Encephalocraniocutaneous lipomatosis is a rare, congenital neurocutaneous syndrome, not inherited in a mendelian fashion. The tissues and organs primarily affected are of ectoderm and mesoderm origin, namely skin, eye, adipose tissue, and brain. Encephalocraniocutaneous lipomatosis is limited to one side of the cranium, the face, and brain. The most typical lesions, which occur almost exclusively in this syndrome, are subcutaneous soft tumors, consistent with lipomas, and areas of alopecia; other common findings are ocular lesions, such as defects of the eyelids and epibulbar dermoids.[8] Our patient presented with many of the classic features of encephalocraniocutaneous lipomatosis, such as nevus psiloliparus, ocular lipodermoid, aniridia, bilateral optic disc coloboma, and intracranial and spinal lipomas (Figures 1-3). These clinical findings are considered major diagnostic criteria by Hunter and surpass the requirement of two or more major criteria to make a definitive diagnosis of encephalocraniocutaneous lipomatosis.[1,3] Histopathological examinations of the skin colored papules/nodular tags represent lipomas, fibromas, fibrolipomas, and connective tissue nevi or hamartomatous tissue consisting of cartilage, fat, and connective tissue. The alopecic area of the scalp usually shows focal dermal fibrosis associated with increased amounts of subcutaneous fat extending into the reticular dermis.[4] Similar changes were appreciated on the histopathological examination of skin lesions in our case.

The first neurological problem that our patient presented with was hydrocephalus, which could be seen on her earliest brain imaging studies (Figure 2). However, the patient had no

symptoms of hydrocephalus at initial presentation and was therefore treated with observation. Symptoms did not manifest until several months later, and the patient successfully underwent ventriculoperitoneal shunt insertion. Hydrocephalus is not an uncommon problem in encephalocraniocutaneous lipomatosis, and several patients with this syndrome have undergone successful placement of ventriculoperitoneal shunts.[3,8,9] Ventriculomegaly, porencephalic cysts, and macrocephaly are common findings in patients with encephalocraniocutaneous lipomatosis, but not all patients with these findings develop hydrocephalus.[9] Hydrocephalus was diagnosed in approximately one-third of patients with encephalocraniocutaneous lipomatosis and ventriculomegaly, making longitudinal observation of these patients necessary to determine who will need shunt placement.

Our patient had a lipomatus mass at the right cerebellopontine angle with similar lesions noted in the posterior aspect of the forum magnum and cervical canal as shown by her MRI of the brain. Lipomas were the most prominent feature and were found on neuroimaging in 33 of the 54 patients. Intracranial lipomas (31 of 54) were often located in the cerebellopontine angle (19 of 31), which is exceptional because, in general, lipomas are more often found between the hemispheres.[4] At the age of 1 year 10 months, when our patient presented with weakness of her lower extremities, she also had multiple subcutaneous nodules over her back, which were present since birth. The MRI of the spine showed large subpialjuxtamedullary lipoma filling the entire spinal canal with tethered spinal cord. Spinal lipomas were found in most of the patients when looked for (12 of 14), which can extend over the whole length of the spinal cord. Both intra- and extramedullary lipomas have been described, most of which are asymptomatic. It is therefore recommended that a spinal MRI is performed when encephalocraniocutaneous lipomatosis is suspected. Subcutaneous fatty masses can overly be the spinal lipomas or are found next to the spinal cord.[4] Surprisingly, tethered cord has not been previously described in encephalocraniocutaneous lipomatosis except in a 3-month-old boy described by Ayer et al, who was diagnosed with encephalocraniocutaneous lipomatosis having intraspinal lipoma associated with tethered spinal cord. He presented at the 19 months of age with progressive lower limb weakness and severe scoliosis. He underwent posterior fossa craniectomy, C1-C6 laminectomies, and debulking of the cervicomedullary junction lipoma, and he was treated for his scoliosis with a brace.[1] This indicates a rare association between encephalocraniocutaneous lipomatosis and tethered spinal cord syndrome, making our case the second one with this rare association to be described in the literature.

Our patient developed seizures at the age of 1 year 10 months, which was controlled by antiepileptic medications. Upon reviewing the literature, it was found that 27 patients with encephalocraniocutaneous lipomatosis had a history of epileptic seizures and 3 did not; in 24 patients, no information was given on whether or not seizures occurred. In 9 of the 27 patients with seizures, seizure onset was during the first month of life, in 7 it was during the first year, in 6 after the age of 1 year, and no documentation was given for 5 patients. Of the 27 patients, 8 had refractory epilepsy, and, in a further 6, the seizures were at least difficult to treat. In 13 patients, seizures responded well to antiepileptic treatment.[4]

Currently, our patient shows normal intellectual development. Developmental data were available for 45 patients with encephalocraniocutaneous lipomatosis. Of these, 13 developed normally up to a reported age ranging from 3 months to 24 years (mean 7 years), 16 cases showed mild retardation, and 16 moderate to severe or unspecified retardation.[4]

Although serial MRI studies of the brain obtained with and without contrast demonstrated no vascular abnormalities, progressive aneurysmal dilation of cerebral vessels has been described in this syndrome, with 1 patient developing subarachnoid hemorrhage.[7] Cerebrovascular dysplasia and leptomeningeal angiomas have been described in 9 patients with encephalocraniocutaneous lipomatosis, and vascular anomalies are believed to be responsible for the development of cerebral atrophy, thin white matter, porencephaly, and calcifications that are often seen in the syndrome.[4,5]

Our patient has not demonstrated any of these characteristics, but the prevalence of developing these abnormalities over the life span of a patient with encephalocraniocutaneous lipomatosis is unknown. It is something that has to be considered, should there be any changes in neurological status, and may warrant performance of routine surveillance imaging.

Conclusion

This case report and review of relevant literature is to describe the first pediatric case from Lebanon, presenting with encephalocraniocutaneous lipomatosis. Based on the review of the literature, this is the second case with encephalocraniocutaneous lipomatosis associated with tethered spinal cord syndrome. Although the incidence of tethered cord syndrome in patients with encephalocraniocutaneous lipomatosis is unknown, it is probably significant. Besides, serial observation of patients with ventricular abnormalities is recommended, given that approximately one-third of these patients can develop hydrocephalus. Additionally, baseline neuroimaging is part of the initial assessment, but routine serial imaging of lipomas is probably not warranted, given the benign nature of the masses and their documented lack of growth. Currently, the incidence of symptomatic versus asymptomatic central nervous system lipomas is unknown. The monitoring of these patients for signs of myelopathy is probably required for those with imaging findings that are a cause for concern. Changes in the neurological examination should prompt a reevaluation of the patient. Patients should be monitored for the development of these conditions, and their families should be educated on the signs and symptoms of their development. However, the limited information

provided by the literature does not supply enough evidence to support any specific recommendations.

Author Contribution

This work was carried out in collaboration between all authors. All authors were responsible for the coordination of the overall work, including: manuscript preparation and literature review.

Declaration of Conflicting Interests

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Ethical Approval

After the approval of the Institutional Review Board, written informed consent was obtained from the parents of the child.

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