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CASE REPORT

Encephalocraniocutaneous lipomatosis, a rare neurocutaneous disorder: report of additional three cases

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Abstract
Purpose Encephalocraniocutaneous lipomatosis (ECCL) is a rare congenital neurocutaneous disorder. It was described by Haberland in 1970 and is also called Haberland syndrome. It is characterized by unilateral skin lesions such as lipomas, connective tissue nevi, and alopecia with ipsilateral ophthalmological and cerebral malformations with or without psychomotor and mental retardation and early-onset seizure.
Methods We present three pediatric cases (two boys, one girl) with ECCL. All the patients' sociodemographic, clinical, and neuroradiological data was collected.
Results We describe two male (5 and 1.3 years old) and one female (15 years old) cases. All patients have unilateral left-sided alopecia with ipsilateral ocular lesion and the cerebral lesion. All patients were born at term; their past history and family histories were unremarkable. Their electroencephalograms showed hemispheric asymmetry. All of the cases had right-sided mild to moderate hemiparesis. In addition, our second case is having optic glioma and this case is the fifth case with glioma associated with ECCL.
Conclusions We describe three additional cases with ECCL which is an extremely rare neurocutaneous syndrome. Also, case 2 has optic glioma and according to the literature this is the fifth case of low-grade gliomas with ECCL. We suggest that patients who have ocular lesion and ipsilateral skin lesion must be examined for ECCL, and the patients must be followed up with cerebral MRI once a year for low-grade gliomas.

Keywords Encephalocraniocutaneous lipomatosis · Haberland syndrome · Optic glioma · Choristoma

Introduction

Encephalocraniocutaneous lipomatosis (ECCL) is an extremely rare sporadic congenital neurocutaneous disorder. It was described by Haberland in 1970 and is also called Haberland syndrome or Fishman's syndrome [1]. Since 1970, roughly 60 cases have been described. Etiology of ECCL is still unknown; in addition, it is supposed that ECCL may be caused by an autosomal mutation that survives only in a mosaic state [2]. ECCL affects mainly tissues of ectodermal and mesodermal origin unilaterally, although bilateral involvement has been sporadically described [3]. The common phenotypic features of ECCL are the unilateral skin lesions, ocular anomalies, and ipsilateral central nervous system (CNS) anomalies. Nevus psiloliparus (hairless fatty tissue nevus of the scalp) is the most common skin anomaly. The most common ocular lesions are epibulbar choristomas and connective tissue nevi on the eyelids [4]. In literature, varied CNS anomalies have been described including cranial and spinal lipomas, asymmetric cerebral atrophy, cysts, early-onset seizure, severe intellectual disability, or behavioral changes or normal development can be seen [5]. There have been four cases of low-grade gliomas reported in children with ECCL [6–9].

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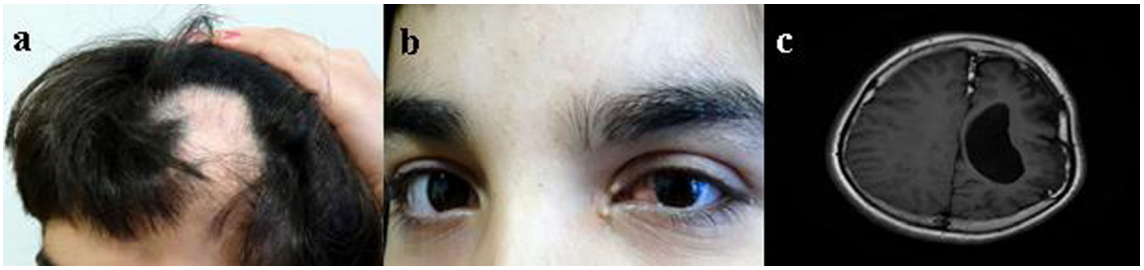

Fig. 1 **a** Nevus psiloliparus of the scalp. **b** Choristoma and skin tag. **c** MRI of the brain—T1-weighed axial images at the level of the ventricles showing dilatation of the left lateral ventricle and atrophy and calcifications in the left frontal, parietal, and temporal lobes

We present three new patients with ECCL, a 15-year-old female, 1.3-year-old male, and 5-year-old male who developed optic glioma.

Case 1

A 15-year-old girl was born to a G2P2 mother at term weeks of gestation via normal spontaneous delivery with vacuum extraction. Her parents are second-degree cousins. There were no abnormalities during pregnancy, and the child's prenatal history was unremarkable. Since birth, she has alopecia area at the left frontal region and there was an epibulbar lipodermoid on the ipsilateral eye. In history, her seizure was generalized tonic-clonic and started while 5 months old, and it continued until 12 years of age. Also, her parents noticed lower muscle strength on the right extremities compared to left side while she was 6 months of age. She has severe psychomotor retardation: she was walking at 5 years old and speaking at 4 years old.

On physical examination, she showed focal area of alopecia on the left frontal region and ipsilateral epibulbar choristomas and two skin tags around the eyelids, while the right eye was normal (Fig. 1a, b). There is no visual acuity defect on the left eye. The muscle strength was 4/5 on the right upper and lower extremities. Deep tendon reflexes were aggregated on the right upper and lower extremity, the left sides were normal, and planter responses were positive on the right side. Cerebellar functions were normal. Brain MRI showed atrophy of the left cerebral hemisphere, dilatation of the left lateral ventricle cerebral calcifications, and tortuous vessels (Fig. 1c).

Case 2

A 5-year-old male was referred for seizures to our clinic. He was born to a G2P1 mother at term weeks of gestation via normal spontaneous delivery. Arachnoid cyst and hydrocephaly were detected with antenatal ultrasonography. After birth, he has respiratory failure and the APGAR score at the first second was 4 and he needs to PBV. After resuscitation 5 s, APGAR score was 9 and he was admitted to the neonatal intensive care unit. Her physical examination revealed focal alopecia area on the left frontoparietal region and ipsilateral conjunctival lesion which is consistent with choristomas (Fig. 2a, b). The first cerebral MRI was performed while he was 1 year old, and it showed dilatation of the left lateral ventricle and cystic lesion on the left temporal lobe which is consistent with arachnoid cyst. His seizures developed at the first day of life and became refractory epilepsy. Ventriculoperitoneal shunt operation was made for hydrocephaly while he was 7 months of age. Control MRI when he was 3 years old showed atrophy on the left cerebral hemisphere, cystic lesion near the brain stem which is making mass effect, and tumoral lesion on trace of the left optic nerve (Fig. 2c). Biopsy of the lesion was consistent with optic glioma, and chemotherapy was started. He could not walk and is unable to make a sentence.

Fig. 2 **a** A large patch of alopecia on the left frontoparietal scalp. **b** Choristoma on the left eye and hypoplastic skin lesion. **c**. MRI of the brain; T2-weighed axial images showed atrophy on the left cerebral hemisphere, cystic lesion on the posterior fossa which is making mass effect, and tumoral lesion on trace of the left optic nerve

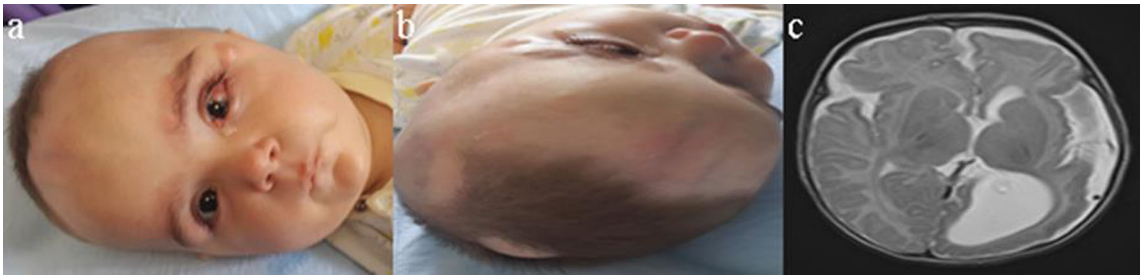

Fig. 3 **a** Choristoma on the left eye and nodular lesion. **b** A large patch of alopecia on the left frontoparietal scalp. **c** MRI of the brain—T2-weighed axial images at the level of ventricles showing dilatation of the left lateral ventricle and atrophy on the left cerebral hemisphere

Case 3

A 1.3-year-old boy was born to a G1P1 mother at term weeks of gestation via cesarean section. There was no consanguineous marriage between parents. There were no abnormalities during pregnancy, prenatal, and neonatal history. On physical examination, he showed focal area of alopecia on the left parietal and frontal region and ipsilateral epibulbar choristomas and nodular lesion around the eye, while the right eye was normal (Fig. 3a, b). He developed seizure at the age of 9 months, and his seizure is secondarily generalized. He could not walk, but he is crawling. Cerebral MRI showed atrophy on the left hemisphere (Fig. 3c).

All of the patients' physical examination findings and neuroimaging results and diagnostic criteria are listed in Table 1.

Discussion

We present three new cases with ECCL which is the extremely rare neurocutaneous disorder. In addition, our second case is having optic glioma and this case is the fifth case with glioma associated with ECCL.

The pathogenesis of the ECCL is still unclear. It has no preferential gender, ethnic, and geographical predisposition. Genetic transmission or chromosomal anomalies could not be identified. Somatic mosaicism is thought to be the underlying pathophysiology in ECCL. On the other hand, dysgenesis of the cephalic neural crest and the anterior neural tube is another theory of the pathogenesis of ECCL. Dysgenesis of the cephalic neural crest and the anterior neural tube is the most widely accepted explanation of this syndrome's pathogenesis [1, 10].

Encephalocraniocutaneous lipomatosis has a very wide multisystemic involvement and primarily affects the skin, eyes, and CNS. Odontogenic, cardiac, and bone findings have also been described. While skin lesions are evident since birth and they are not progressive, central nervous system lesions tend to stay silent with progressive growth, leading to different neurologic symptoms depending on their location. ECCL diagnostic criteria was defined by Hunter in 2006 [4], with the recent stringent criteria revision performed by Moog in 2009 [11].

Non-scarring alopecia, with or without underlying fatty tissue, and subcutaneous fatty masses are the most important skin anomalies [11]. Nevus psiloliparus is a hairless lesion over excess adipose tissue located on the head in the frontotemporal or zygomatic region, often unilateral, rarely crossing the midline. Firstly, NP was thought to be pathognomonic; however, Happle [12] reported that it can be isolated lesion. Subcutaneous fatty masses and small nodular skin tags have also been reported. All our patients have non-scaring alopecia area at the frontoparietal region.

Table 1 Patient findings of physical examinations and neuroimaging studies

	Patient 1	Patient 2	Patient 3
Age (year)	15	5	1.3
Sex	F	M	M
Skin lesion	Nevus psiloliparus[a], skin tag[b]	Nevus psiloliparus[a]	Nevus psiloliparus[a]
Ocular lesion	Epibulbar choristomas[a]	Epibulbar choristomas[a]	Epibulbar choristomas[a]
CNS manifestation	Moderate IDD, seizure, right hemiplegia, atrophy of the left cerebral hemisphere[b], cerebral calcification[b], dilatation of the left lateral ventricle[b], tortuous vessels[b]	Severe IDD, seizure, hydrocephaly[b], cystic lesion[b], atrophy of the left cerebral hemisphere[b], dysgenesis of CC, spinal lipoma[a], cerebral calcifications[b], hypoplastic skin lesion[b]	Normal development, seizure, atrophy of the left cerebral hemisphere[b], cystic lesion[b]

IDD intellectual disability, *CC* corpus callosum, *F* female, *M* male

[a] Major criteria

[b] Minor criteria

The most common ophthalmologic finding is a choristoma, which is including epibulbar or limbal dermoids (dermolipomas). Other ocular abnormalities may include colobomas, corneal and scleral abnormalities, aniridia, microphthalmia, chorioretinitis, and globe calcification [11, 13]. All our patients have choristoma on the left eye.

Intracranial or spinal lipomas are the most prominent feature of ECCL. Other frequent findings include unilaterally or asymmetrically enlarged ventricles, widening of arachnoid spaces, arachnoid cysts, cortical dysplasia, asymmetric cerebral atrophy, corticopial calcifications, thinning of the corpus callosum, and posterior fossa anomalies [5, 14]. Neurologic features are variable; patients may have normal or delayed development, seizures, normal intelligence, or mental retardation of varying degrees. Congenital heart malformations, lytic bone lesions, and hypospadias can also be present [11]. ECCL can be associated with neuroepithelial tumors rarely. There have been four cases of low-grade gliomas reported in children with ECCL: two cases of grade I pilocytic astrocytoma and one case of papillary glioneuronal tumor and grade II glial neoplasm [6–9]. Our one patient (case 2) has optic glioma. His first MRI was not consistent with optic lesion; however, 2 years later, control MRI showed optic lesion.

Conclusions

We describe three patients with ECCL which is the extremely rare neurocutaneous syndrome. Also, we reported the fifth case of low-grade gliomas with ECCL. We suggest that patients who have ocular lesion and ipsilateral skin lesion must be examined for ECCL, the patients have a risk for low-grade gliomas, and the patients must be followed by cerebral MRI once a year.

Conflict of interest The authors declare no conflicts of interest with respect to the authorship and/or publication of this article.

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