Title
Encephalocraniocutaneous lipomatosis accompanied by the formation of bone cysts: Harboring clues to pathogenesis?

Journal
American Journal of Medical Genetics Part A, 143A(24)

ISSN
1552-4825

Authors
Moog, Ute
Roelens, Filip
Mortier, Geert R
et al.

Publication Date
2007-12-15

DOI
10.1002/ajmg.a.31957

 American Journal of Medical Genetics Part A 143A:2973–2980 (2007)

Clinical Report

Encephalocraniocutaneous Lipomatosis Accompanied by the Formation of Bone Cysts: Harboring Clues to Pathogenesis?

Ute Moog,[1,2,3]* Filip Roelens,[4] Geert R. Mortier,[5] Han Sijstermans,[6] Mary Kelly,[7] Gerald F. Cox,[8,9] Caroline D. Robson,[9,10] and Virginia E. Kimonis[8,9,11]

[1]Department of Clinical Genetics, University Hospital Maastricht, Maastricht, The Netherlands
[2]Research Institute Growth & Development (GROW), Maastricht University, Maastricht, The Netherlands
[3]Institute of Human Genetics, Heidelberg University, Heidelberg, Germany
[4]Heilig Hart Hospital, Roeselare, Belgium
[5]Department of Medical Genetics, Ghent University Hospital, Ghent, Belgium
[6]Atrium Medical Center, Heerlen, The Netherlands
[7]Coordinated Care Service, Children's Hospital Boston, Boston, Massachusetts
[8]Division of Genetics, Department of Medicine, Children's Hospital Boston, Boston, Massachusetts
[9]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts
[10]Department of Radiology, Children's Hospital Boston, Boston, Massachusetts
[11]University of California, Irvine, California

Received 13 December 2006; Accepted 22 February 2007

Encephalocraniocutaneous lipomatosis (ECCL) is a sporadically occurring neurocutaneous disorder characterized by ocular anomalies, mainly choristomas; by skin lesions consisting of hairless fatty tissue nevi (nevus psiloliparus), focal dermal hypoplasia, alopecia, and periocular skin tags; and by CNS anomalies, including intracranial and spinal lipomas and often mental retardation and seizures. Here, we report on three boys with ECCL with typical abnormalities of the eyes, skin and brain and, in addition, coarctation of the aorta. All three children developed multiple cystic bone lesions, which progressively spread throughout the skeleton in Patient 1 and was shown histologically to be non-ossifying fibromas in Patient 2. We hypothesize that ECCL may be caused by mosaicism for a mutated gene involved in benign mesenchymal tumors and in vasculogenesis.

Key words: hyperpigmentation; lines of Blaschko; alopecia; epibulbar dermoids; periocular skin tags; nevus psiloliparus; non-ossifying fibroma; coarctation of the aorta; mental retardation; benign mesenchymal tumors; vascular dysplasia; oculoectodermal syndrome; oculocerebrocutaneous syndrome; Proteus syndrome; epidermal nevus syndrome; ECCL; *HMG2A*; 12q15; multiple aberration region (MAR); *NF1*

How to cite this article: Moog U, Roelens F, Mortier GR, Sijstermans H, Kelly M, Cox GF, Robson CD, Kimonis VE. 2007. Encephalocraniocutaneous lipomatosis accompanied by the formation of bone cysts: Harboring clues to pathogenesis? Am J Med Genet Part A 143A:2973–2980.

INTRODUCTION

Encephalocraniocutaneous lipomatosis (ECCL) is a sporadically occurring neurocutaneous disorder described in more than 50 cases to date. The disorder affects predominantly the eyes, skin, and brain. The clinical features were reviewed by Hunter [2006], who proposed diagnostic criteria. Ocular anomalies are mainly epibulbar dermoids (also called dermolipomas) or lipodermoids. Skin lesions predominantly affect the craniofacial region and consist of a characteristic hairless fatty tissue nevus termed nevus psiloliparus (NPL) [Happle and Kűster, 1998]; focal dermal hypoplasia and alopecia; and periocular skin tags. CNS anomalies are diverse and include intracranial and, especially spinal lipomas. Patients

*Correspondence to: Ute Moog, M.D., Ph.D., Institute of Human Genetics, Heidelberg University, Im Neuenheimer Feld 366, 69120 Heidelberg, Germany. E-mail: ute.moog@med.uni-heidelberg.de
DOI 10.1002/ajmg.a.31957

with ECCL often have mental retardation (MR) of variable degree. Protuberances of the cranial bones underlying areas of alopecia can be associated, and some patients have jaw tumors [MacLaren et al., 1995; Hauber et al., 2003; Andreadis et al., 2004]. The etiology of ECCL remains unknown to date. Here, we report on three boys with ECCL. In addition to their typical ocular, dermal and CNS anomalies, they had congenital malformations of the aorta; two of them had recurrent chylothoraces; and one also had hyperpigmentation following the lines of Blaschko and leg asymmetry. All three developed multiple bone cysts.

CLINICAL REPORTS

All three patients had abnormalities of the skin, eyes, and brain, which fit the diagnosis of ECCL. Findings are summarized in Table I and illustrated in Figures 1–14.

Patient 1, a dizygotic twin boy, was born at term to unrelated parents as the product of a 2nd pregnancy. His birth weight was 2,800 g and his length was 48 cm. Abnormalities of the skin, eyes, and brain are summarized in Table I and illustrated in Figures 1–3. He was previously published as a case of oculocerebrocutaneous syndrome (OCCS) [Narbay et al.,

TABLE I. Clinical Features of the Three Patients With ECCL

	Patient 1	Patient 2	Patient 3
Sex, age at last examination	Male, 10 y	Male, 4 y	Male, 9 y
Figure(s)	1–6	7–11	12–14
Skin			
Focal scalp defects with alopecia	+	+	+
Alopecia	+	+	+
Focal skin hypoplasia in face	+		+b
Small nodular skin-tags	+a, b	+a	+a
Subcutaneous lipomatous tissue	+c		+c
Linear hyperpigmentation		+	
Eyes			
Microphthalmia	+ODS		+ODS
Epibulbar dermoids	+ODS	+ODS	
Hypertrophic conjunctivae		+ODS	
Sclerocorneae		+ODS	
Small pupils		+ODS	
Iris hypoplasia	+OD		
Anterior chamber anomalies			+ODS
Absent macular reflex	+OS, OD n.i.		
Eyelid coloboma	+ODS	+ODS	
Short/abn. palpebral fissures			+ODS
Irregular eyebrows	+	+	+?
Central nervous system			
Imaging, based on	1, 3, 4, 5	1, 2, 3	1, 2, 3
Intracranial lipoma	−	+Multiple	−
Spinal lipoma	n.i.	+	+
Cortical dysplasia	+PMG	−	−
Enlarged lateral ventricle(s)	+R		−
Hydrocephalus	−	+	−
Megacisterna magna/DWM	+	−	+DWM
Calcification	−	+Orbits	+n. caudatum
Psychomotor retardation	+++	+++	+++
Refractory epilepsy	+	+	+
Heart			
Coarctation	+	+	+
Hypoplasia thoracic aorta	+		
Bicommissural aortic valve		+	
Subvalvular aortic stenosis			+
Peripheral pulmonary stenosis			+
ASDII + open ductus Botalli			+
Skeletal cysts, first seen at age	+, 8 y	+, 3 y	+, 9 y
Further anomalies			
Turricephalic skull	+	+	+
Cryptorchism	+L		
Pelvic kidney	+R		
Hydronephrosis		(+)* L	+L
Leg asymmetry		+	
Ear abnormalities		+	+R

DWM, Dandy–Walker malformation; L, left; n.i., not investigated; PMG, polymicrogyria; R, right; y, year(s); a, periorbital; b, post-auricular; c, temporal; 1, MRI brain; 2, spinal MRI; 3, CT scan; 4, X-ray skull; 5, autopsy.
*Mild dilatation renal pelvis.

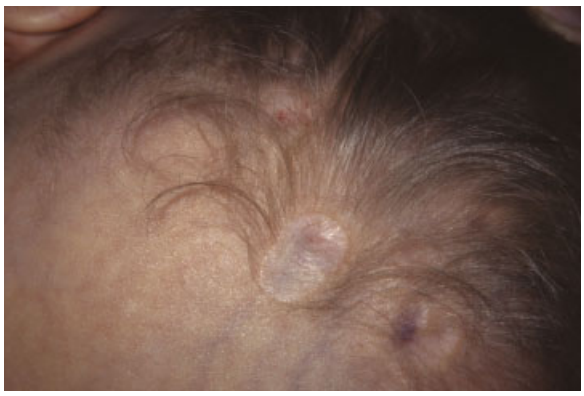


FIG. 1. Patient 1: several small skin defects with alopecia on the scalp. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

1996, Patient 2]. An atrial flutter at age 1 month prompted a cardiac evaluation which demonstrated coarctation of the aortic arch distal to the subclavian artery with prestenotic dilatation and marked hypoplasia of the thoracic aorta (Fig. 4). His development was severely delayed. He never learned to sit unsupported or to walk, and had no speech. From his first month of life, he had severe epilepsy with daily seizures, refractory to treatment with multiple anti-epileptic drugs. The patient also had cerebral blindness. When last seen at the age of 10 years and 9 months (Fig. 5), he was small and lean and had pectus carinatum and contractures of the upper limbs. Cytogenetic analysis on lymphocytes and array-CGH analysis at a resolution of about 1 Mb disclosed normal results.

Multiple cystic bone lesions were first seen at the age of 8 years and initially involved the long bones. They led to increased bone fragility and progressively spread throughout his skeleton (Fig. 6). At 8 years, he had a fracture of his right tibia after physiotherapy.

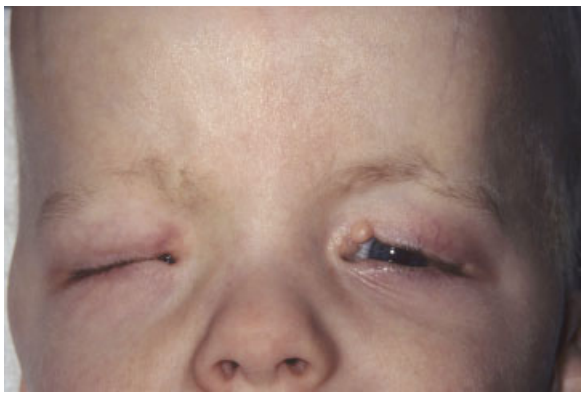


FIG. 2. Patient 1: note small nodular skin tags in the periorbital region, bilateral eyelid coloboma, bilateral microphthalmia, interrupted eyebrows, subcutaneous tissue in the right temporal region. Not depicted are the bilateral epibulbar dermoids. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

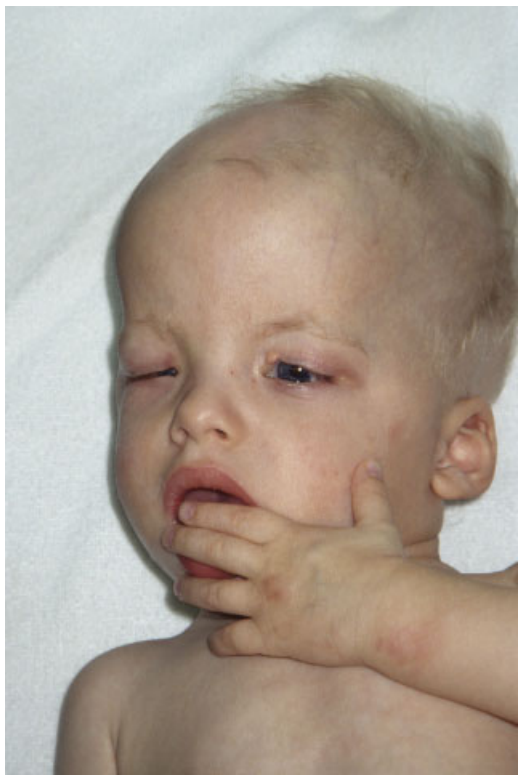


FIG. 3. Patient 1: note hypoplastic skin defects above the left ear which is low-set and has over-folded helices. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

The boy suffered from recurrent chylothoraces with subsequent pneumonia and died at the age of 10 years. Postmortem examination confirmed previous findings. Autopsy of the spine was not performed.

His twin brother had no congenital anomalies and was in good health.

Patient 2 was born at 38 weeks by Cesarean to a 21-year-old primipara. During pregnancy, fetal movements were reduced, and decreased amniotic fluid,

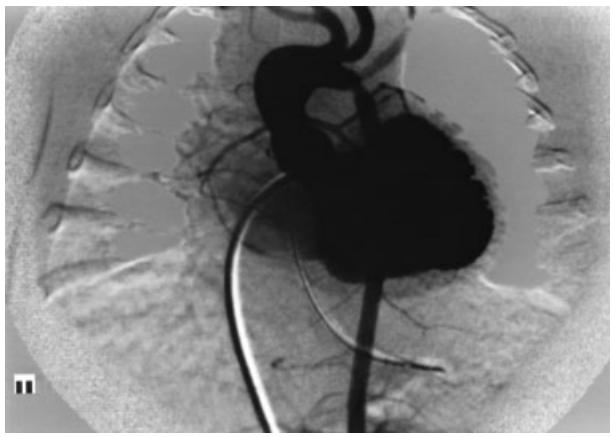


FIG. 4. Patient 1: coarctation of the aortic arch distal to the subclavian artery with prestenotic dilatation, and marked hypoplasia of the thoracic aorta seen on catheterization.

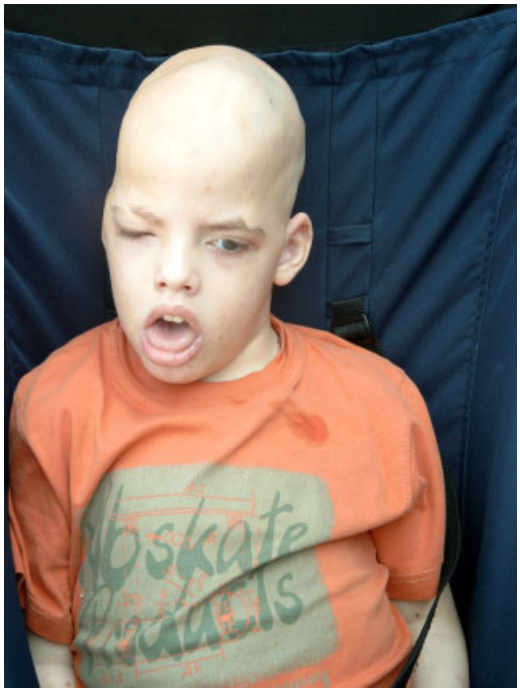


FIG. 5. Patient 1 at 10 years: note total alopecia, irregular eyebrows and turricephalic skull. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

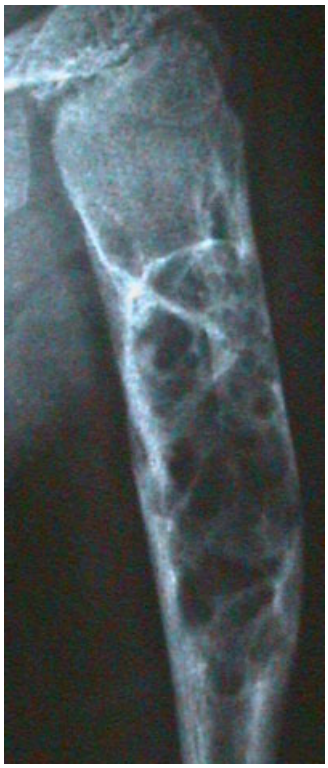


FIG. 6. Patient 1: large multilocular cyst in the right humerus. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

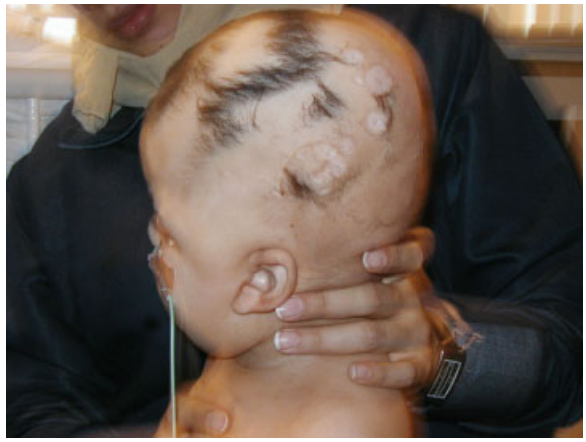
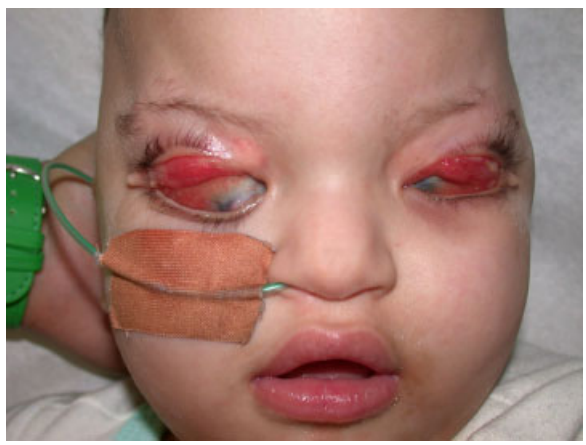


FIG. 7. Patient 2: tall, dolichocephalic skull with linear patches of alopecia and focal aplastic scalp lesions which in the newborn period presented as fluid-filled cysts. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

hydrocephalus, and aortic malformation were seen on ultrasound. Birth weight was 2,700 g. Abnormalities of the skin, eyes, and brain are described in Table I and illustrated in Figures 7–9. He had a repair of his coarctation and also developed intractable seizures at 1 week of life. His hydrocephalus was treated by a ventriculoperitoneal shunt at 1 month. His development was significantly delayed. On examination at 16 months, length and weight were at the 90th centile and head circumference was 44 cm (<2nd centile). Linear hyperpigmentations following the lines of Blaschko were seen on his arms and legs, abdomen, and back (Fig. 9), which became more prominent over time. His right leg was wider and two inches longer than his left leg; his arms were relatively short, and he had deep palmar creases. Cardiac evaluation disclosed a bicommissural aortic valve with no residual coarctation of the aortic arch. A renal ultrasound showed mild dilatation of the left renal pelvis but no other abnormalities. He underwent extensive eye surgery and lid reconstruction with a skin graft, and a Nissen fundoplication



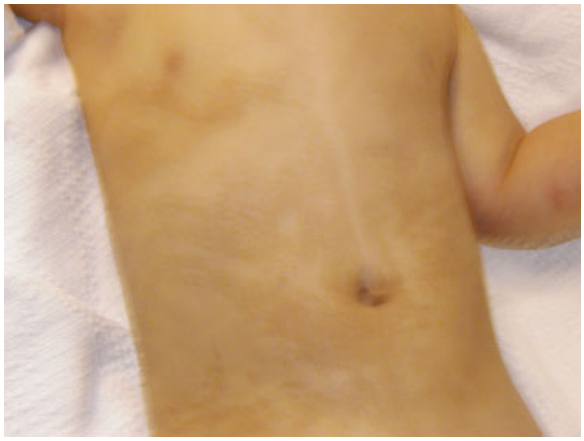


FIG. 9. Patient 2: linear hyperpigmentations following the lines of Blaschko on the abdomen. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

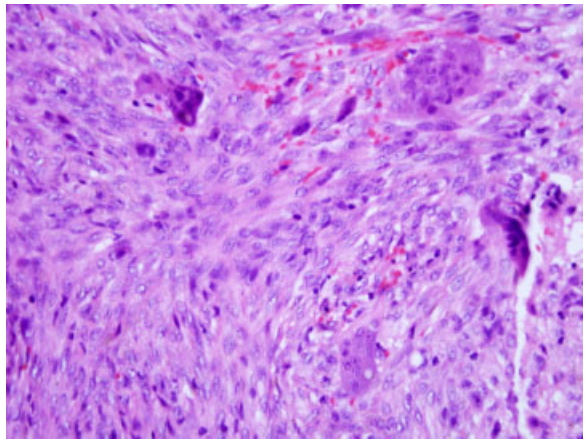


FIG. 11. Patient 2: histology of femoral lesions, showing fibrohistiocytic cells in a storiform pattern admixed with a few multinucleated giant cells and extravasated erythrocytes (H&E 400×). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

because of persistent vomiting. The boy suffered from recurrent chylothoraces. At 5 years, he was making some developmental progress and was able to sit with some support. He was fed with a gastrostomy tube and his seizures had improved with a vagal stimulator. Karyotype of the pigmented area was normal as was CGH analysis and FISH for microphthalmia with linear skin defects (MLS).

Radiographic examination at nearly 3 years for his hemihyperplasia disclosed multiple well-circumscribed, lucent defects bilaterally in the proximal portions of the humerus, ulna, distal left radius, proximal and distal parts of the femora, and proximal tibiae (Fig. 10). Histology of his femoral lesions obtained during a heel cord lengthening procedure showed non-ossifying fibromas (Fig. 11). Radiographs taken at age 4 years and 4 months indicated that the lesions appeared essentially unchanged.

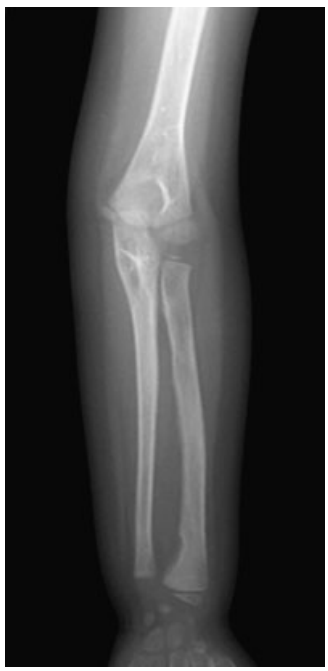


FIG. 10. Patient 2: radiograph of his left arm showing lytic lesions in the metaphysis of proximal ulna and distal radius.

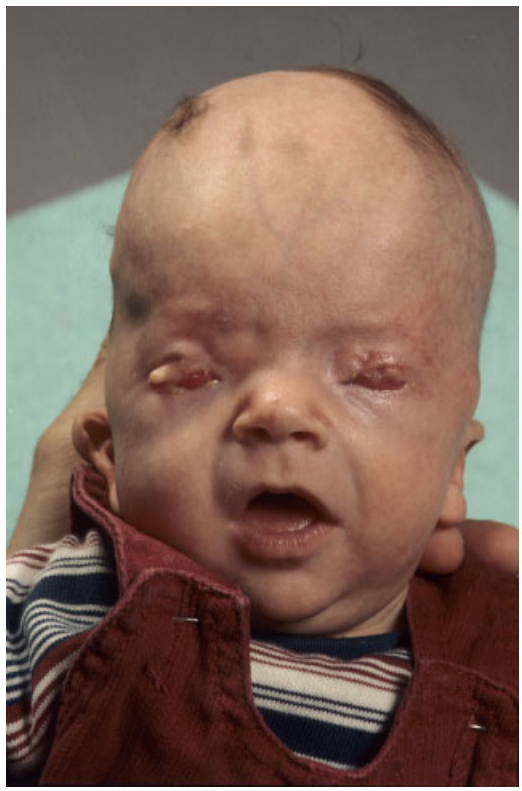


FIG. 12. Patient 3: bilateral microphthalmia, short abnormal palpebral fissures with an incomplete row of eyelashes, small fibromas on the eyelids, eyebrows, subcutaneous lipomatous mass in the temporal region, turricephalic skull, small dysplastic right ear. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

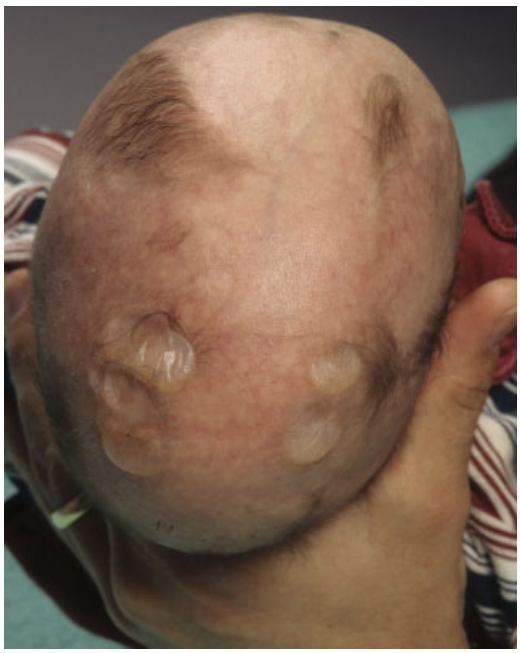


FIG. 13. Patient 3: focal scalp defects in the occipital region which in the beginning presented as fluid-filled cysts, patches of alopecia. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Patient 3 was born at 35 weeks as the first child to a 26-year-old mother and a 31-year-old father. He had congenital abnormalies of the skin, eyes, and brain, which are summarized in Table I and illustrated in Figures 12 and 13. A cardiac evaluation disclosed a patent foramen ovale (ASD II), patent ductus arteriosus, and a small aorta anulare, possibly coarctation, with dilatation of the ascending aorta. At 4 months, the foramen ovale was closed, and subvalvular aortic stenosis and peripheral pulmonary stenosis were diagnosed. With increasing age the aortic stenosis became more severe. His development was severely delayed; he never learned to sit unsupported or to walk and he had no speech. He was blind due to his congenital eye malformation, and from age 1 year, he developed refractory epilepsy. He had severe feeding problems, and a gastrostomy tube was placed when he was $1^1/_2$ years old. In the first years of his life, he had frequent upper airway infections. There were a few urinary tract infections as well, and hypercalciuria and a renal calculus arose in the left renal pelvis. At 4 years, he was severely hypotonic, had about five seizures per day on medication with valproic acid and vigabatrine, still had frequent airway infections, and his G tube was in situ. At 9 years, he still had hardly any development and had irregular epileptic episodes, but appeared less prone to infections and was orally fed. Chromosome analysis showed a normal 46,XY karyotype. No mutation was found on molecular analysis of the total coding sequence of the *NF1* gene.

Radiographs taken at 9 years disclosed cystic lesions in the distal parts of both femorae (Fig. 14).

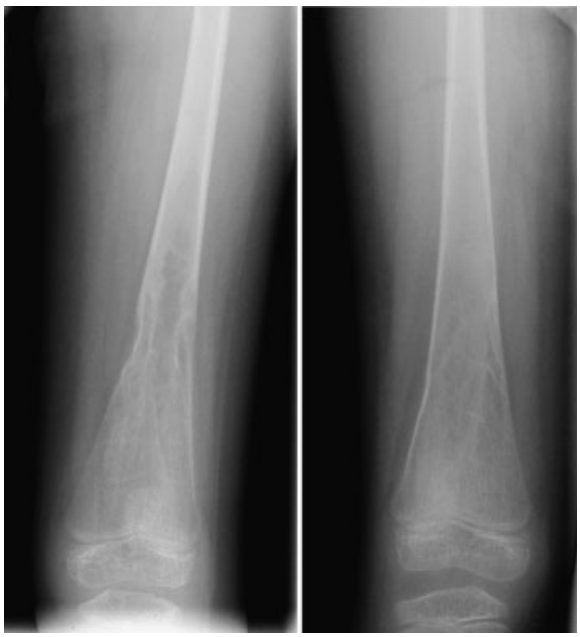


FIG. 14. Patient 3: radiographs show cystic lesions in the distal part of both femurae.

DISCUSSION

We present three patients with ECCL, who in addition to the characteristic skin, eye, and brain features, had a malformed aorta, particularly coarctation, other congenital heart defects as well, and skeletal cysts. The bone lesions started in the submetaphyseal regions of the long tubular bone and appeared to be progressive. Histology in one case showed non-ossifying fibroma. All three children had a severe form of ECCL with significant developmental delay, refractory seizures, and bilateral involvement of the skin and eye lesions.

We excluded an *NF1* mutation in Patient 3. Legius et al. [1995] found an *NF1* mutation in a case of ECCL. However, their patient had, in addition, more than five café-au-lait spots; ECCL and neurofibromatosis occurred in their patient by chance.

ECCL affects females and males equally. Manifestations are highly variable with respect to severity and to the extent of tissue involvement. The patchy skin lesions and alopecia, focal bone alterations, pigmentary abnormalities following the lines of Blaschko, and leg asymmetry (Patient 2) argue in favor of mosaicism. The severe form the disorder also manifests in bone tissue and in the great vessels, particularly the aorta. Ardinger et al. (this issue) discuss the striking similarity of ECCL and oculoectodermal syndrome. In this latter condition, skeletal cysts have been described in several less severely affected patients.

Based on the current knowledge about the overall phenotype of ECCL and OCCS [Hunter, 2006], and taking into account the distinguishing brain malformation in OCCS [Moog et al., 2005], it is evident that both conditions represent separate entities. According to diagnostic criteria, the features of Patient 1 are considered to be consistent with a diagnosis of ECCL. This is corroborated by the fact that he does not have the typical OCCS brain malformation or its cutaneous or ocular hallmarks (post-auricular almond-shaped, hypoplastic, skin defect and cystic microphthalmia, respectively). ECCL seems to be an autosomal mosaic condition in contrast to OCCS, which probably is non-mosaic and may be X-linked [Moog et al., 2005]. ECCL shares several features in common with Proteus syndrome, including lipomas, hyperostosis of the skull, MR, and seizures [Cohen, 2005]. However, lipomas and fatty tissue nevi are non-progressive and present at birth together with ocular and cerebral anomalies. In addition, a cerebriform connective tissue nevus, one of the characteristics of Proteus syndrome, and progressive asymmetric, distorting limb overgrowth are unknown in ECCL. Clearly, the features and course of ECCL do not meet existing diagnostic criteria for Proteus syndrome [Biesecker et al., 1999], and ECCL is considered to be different from Proteus syndrome. ECCL shows considerable overlap with the neurologic variant of epidermal nevus syndrome (ENS), another mosaic condition. In ENS, hemimegalencephaly is the predominant brain anomaly, but gyral malformations occur frequently, and cerebral and spinal lipomas can be seen [Pavone et al., 1991; Mall et al., 2000; Booth and Rollins, 2002]. The eye findings in ENS are comparable to those in ECCL and include choristomas, coloboma, and extension of epidermal nevi to involve the eyelid or conjunctiva [Gorlin et al., 2001]. Skeletal defects are frequently seen and include focal bone lesions [Heike et al., 2005]. The main differential criteria appear to be the skin lesions. In ENS, the skin lesions are complex, include different forms of epidermal nevi and change over time, whereas in ECCL, the cutaneous hallmark is the NPL. After its delineation, NPL was believed to be pathognomonic for ECCL [Happle and Kűster, 1998], but has recently been shown to occur also in a non-syndromic form [Happle and Hörster, 2004]. As ENS is etiologically heterogeneous (ENSs) [Happle, 1991], a pathogenetic intersection with ECCL is speculative.

Strikingly, multiple benign tumors can be found in ECCL, many of which are mesenchymal. Lipomas are the name-giving feature of the condition, and manifest (a) as spinal and intracranial lipomas, resulting from abnormal persistence and maldifferentiation of the meninx primitiva which is a derivative of the neural crest [Truwit and Barkovich, 1990], (b) as cutaneous and subcutaneous lipomas, particularly on the scalp (NPL) and the temporal region of the face, and (c) as rare fatty involvement of the internal organs. Choristomas are the ocular hallmark. Jaw tumors have been described in several cases and include odontomas, osteomas, and ossifying fibromas [MacLaren et al., 1995; Hauber et al., 2003; Andreadis et al., 2004; Zielinska-Kazmierska et al., 2005]. Bone cysts, identified as non-ossifying fibromas in one case, but not investigated histologically in the others, are described in the patients presented here. The small craniofacial papules and nodules seen in ECCL are lipomas, fibrolipomas or angiofibromas [Happle and Kűster, 1998]. All of these facts point to a factor involved in the pathogenesis of multiple benign tumors comparable to the architectural transcription factor HMG2A. Its encoding gene (*HMG2A*) has been mapped to the "multiple aberration region" (MAR) on chromosome 12q15, which frequently shows cytogenetic alterations in a variety of human mesenchymal tumors. Recently, the first constitutional rearrangement of 12q affecting *HMG2A* has been reported in a boy with overgrowth, advanced bone age, cerebellar tumor, and multiple lipomas [Ligon et al., 2005].

Another preliminary clue to the pathogenesis appears to be the various vascular anomalies that may be seen in patients with ECCL. The patients presented here all had aortic malformations, in particular coarctation. Some patients described in the literature showed abnormal intracranial vessels or leptomeningeal angiomatosis [Hunter, 2006]. Some of the brain anomalies known to occur in ECCL as asymmetric atrophy of the brain, porencephalic cysts, and calcifications may be the result of prior ischemia or hemorrhage caused by underlying vascular dysplasia. Thus, a defect in vasculogenesis in ECCL is also probably involved.

In conclusion, mosaicism for a mutation in an autosomal gene encoding a factor involved in vasculogenesis and the development of mesenchymal tumors should be considered in the etiology of ECCL.

ACKNOWLEDGMENTS

We thank the families, physicians, and health care providers involved in the care of the three patients. On behalf of the parents of Patient 1 we wish to thank Dr. E. Devos, Heilig Hart Hospital at Roeselare, Belgium, for his continuous and devoting medical care, and for Patient 2, we thank Dr. J. Kasser for obtaining the biopsy and Dr. H. Kozakewich for his expertise on the pathological evaluation of the fibroma.

REFERENCES

Andreadis DA, Rizos CB, Belazi M, Peneva M, Antoniades DZ. 2004. Encephalocraniocutaneous lipomatosis accompanied by maxillary compound odontoma and juvenile angiofibroma: Report of a case. Birth Defects Res A Clin Mol Teratol 70:889–891.

Biesecker LG, Happle R, Mulliken JB, Weksberg R, Graham JM Jr, Viljoen DL, Cohen MM Jr. 1999. Proteus syndrome: Diagnostic criteria, differential diagnosis, and patient evaluation. Am J Med Genet 84:389–395.

Booth TN, Rollins NK. 2002. MR imaging of the spine in epidermal nevus syndrome. Am J Neuroradiol 23:1607–1610.

Cohen MM Jr. 2005. Proteus syndrome: An update. Am J Med Genet Part C Semin Med Genet 137C:38–52.

Gorlin RJ, Cohen MM Jr, Hennekam RCM. 2001. Syndromes of the Head and the Neck. 4th edition. New York: Oxford University Press. p 480–484.

Hauber K, Warmuth-Metz M, Rose C, Brőcker EB, Hamm H. 2003. Encephalocraniocutaneous lipomatosis: A case with unilateral odontom as and review of the literature. Eur J Pediatr 162:589–593.

Happle R. 1991. How many epidermal nevus syndromes exist? J Am Acad Dermatol 25:550–556.

Happle R, Hörster S. 2004. Nevus psiloliparus: Report of two nonsyndromic cases. Eur J Dermatol 14:314–316.

Happle R, Kűster W. 1998. Nevus psiloliparus: A distinct fatty tissue nevus. Dermatology 197:6–10.

Heike CL, Cunningham ML, Steiner RD, Wenkert D, Hornung RL, Gruss JS, Gannon FH, McAlister WH, Mumm S, Whyte MP. 2005. Skeletal changes in epidermal nevus syndrome: Does focal bone disease harbor clues concerning pathogenesis? Am J Med Genet Part A 139A:67–77.

Hunter AG. 2006. Oculocerebrocutaneous and encephalocraniocutaneous lipomatosis syndromes: Blind men and an elephant or separate syndromes? Am J Med Genet Part A 140A:709–726.

Legius E, Wu R, Eyssen M, Marynen P, Fryns J-P, Cassiman JJ. 1995. Encephalocraniocutaneous lipomatosis with a mutation in the *NF1* gene. J Med Genet 32:316–319.

Ligon AH, Moore SD, Parisi MA, Mealiffe ME, Harris DJ, Ferguson L, Quade BJ, Morton CC. 2005. Constitutional rearrangement of the architectural factor HMG A2: A novel human phenotype including overgrowth and lipomas. Am J Hum Genet 76:340–348.

MacLaren MJ, Kluijt I, Koole FD. 1995. Ophthalmologic abnormalities in encephalocraniocutaneous lipomatosis. Doc Ophthalmol 90:87–98.

Mall V, Heinen F, Uhl M, Wellens E, Korinthenberg R. 2000. CNS lipoma in patients with epidermal nevus syndrome. Neuropediatr 31:175–179.

Moog U, Jones MC, Bird L, Dobyns WB. 2005. Oculocerebrocutaneous syndrome: The brain malformation defines a core phenotype. J Med Genet 42:913–921.

Narbay G, Meire F, Verloes A, Catseels I, Devos E. 1996. Ocular manifestations in Delleman syndrome (oculocerebrocutaneous syndrome, OCC-syndrome) and encephalocraniocutaneous lipomatosis (ECCL). Bull Soc Belge Ophthalmol 261:65–70.

Pavone L, Curatolo P, Rizzo R, Micali G, Incorpora G, Garg BP, Dunn DW, Dobyns WB. 1991. Epidermal nevus syndrome: A neurologic variant with hemimegalencephaly, gyral malformation, mental retardation, seizures, and facial hemihypertrophy. Neurology 41:266–271.

Truwit CL, Barkovich AJ. 1990. Pathogenesis of intracranial lipoma: An MR study in 42 patients. AJR 155:855–864.

Zielinska-Kazmierska B, Grodecka J, Jablonska-Polakowska L, Arkuszewski P. 2005. Mandibular osteoma in the encephalocraniocutaneous lipomatosis. J Craniomaxillofac Surg 33: 286–289.