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Case Report

ALDH18A1-related cutis laxa syndrome with cyclic vomiting

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Abstract

Cutis laxa (CL) syndromes are connective tissue disorders characterized by redundant, sagging, inelastic and wrinkled skin, with organ involvement. Here, we describe a patient with *ALDH18A1*-related CL who developed cyclic vomiting. The patient was a 12-year-old boy who presented with poor postnatal growth, hypotonia, short stature, joint hyperlaxity, microcephaly, strabismus, bilateral cataracts, facial dysmorphism and severe mental retardation. Bone radiographs showed osteopenia and osteoporosis, and magnetic resonance angiography showed marked kinking and tortuosity of the brain vessels. These findings were clinically compatible with *ALDH18A1*-related CL. Molecular analysis revealed a *de novo* heterozygous mutation (p.R138Q) in *ALDH18A1*. No mutations were found in *PYCR1* gene. The patient developed cyclic vomiting with decreased blood levels of ornithine, citrulline, arginine and proline without hyperammonemia and other hypoaminoacidemias were also found. *ALDH18A1* encodes Δ^1-pyrroline-5-carboxylate synthase, which is related to the biosynthesis of ornithine, citrulline, arginine, and proline. Cyclic vomiting has never been reported in other *ALDH18A1*-related CL patients. This is the first case report of *ALDH18A1*-related CL with cyclic vomiting associated with amino acid abnormalities.

Keywords: Cutis laxa syndrome; *ALDH18A1*; R138; P5CS; Cyclic vomiting

1. Introduction

Cutis laxa (CL) syndromes are connective tissue disorders characterized by redundant, sagging, inelastic and wrinkled skin with clinical features, including psychomotor retardation, seizures, hypotonia, athetoid movements, dysmorphic features, growth delay, joint hyperlaxity, bone fracture, hernias, and cataracts [1]. The CL syndromes can be inherited in X-linked recessive, autosomal recessive (AR) and autosomal dominant (AD) manner [1]. The recessive forms can be subdivided into three distinct groups as ARCL type 1, ARCL type 2 and ARCL type 3 (ARCL3) which refers to De Barsy syndrome (DBS) [2,3]. The autosomal dominant forms can be subdivided into three distinct groups as ADCL1, ADCL2 and ADCL3 [4]. Mutations have been reported in several genes, such as *FBLN5*, *EFEMP2* and *LTBP4*

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in ARCL type 1, *ATP6V0A2* and *GORAB* in ARCL type 2, *PYCR1* and *ALDH18A1* in ARCL3, *ELN* in ADCL1, *FBLN5* in ADCL2, and *ALDH18A1* in ADCL3 [1,3–7]. Recently, *ALDH18A1*-related CL is divided to ARCL3A and ADCL3 [4]. So far, only 23 affected patients with *ALDH18A1*-related CL were reported [3–6,8–12]. Here, we described the first patient who was diagnosed as *ALDH18A1*-related CL with cyclic vomiting.

2. Case report

The patient was a 12-year-old boy who was born at 39 weeks of gestation after an unremarkable pregnancy. His birth weight was 1800 g (−3.0 SD), height was 40 cm (−4.3 SD), and head circumference was 30 cm (−2 SD), with a large anterior fontanel. He presented poor postnatal growth, hypotonia, short stature, joint hyperlaxity, microcephaly, strabismus, and severe

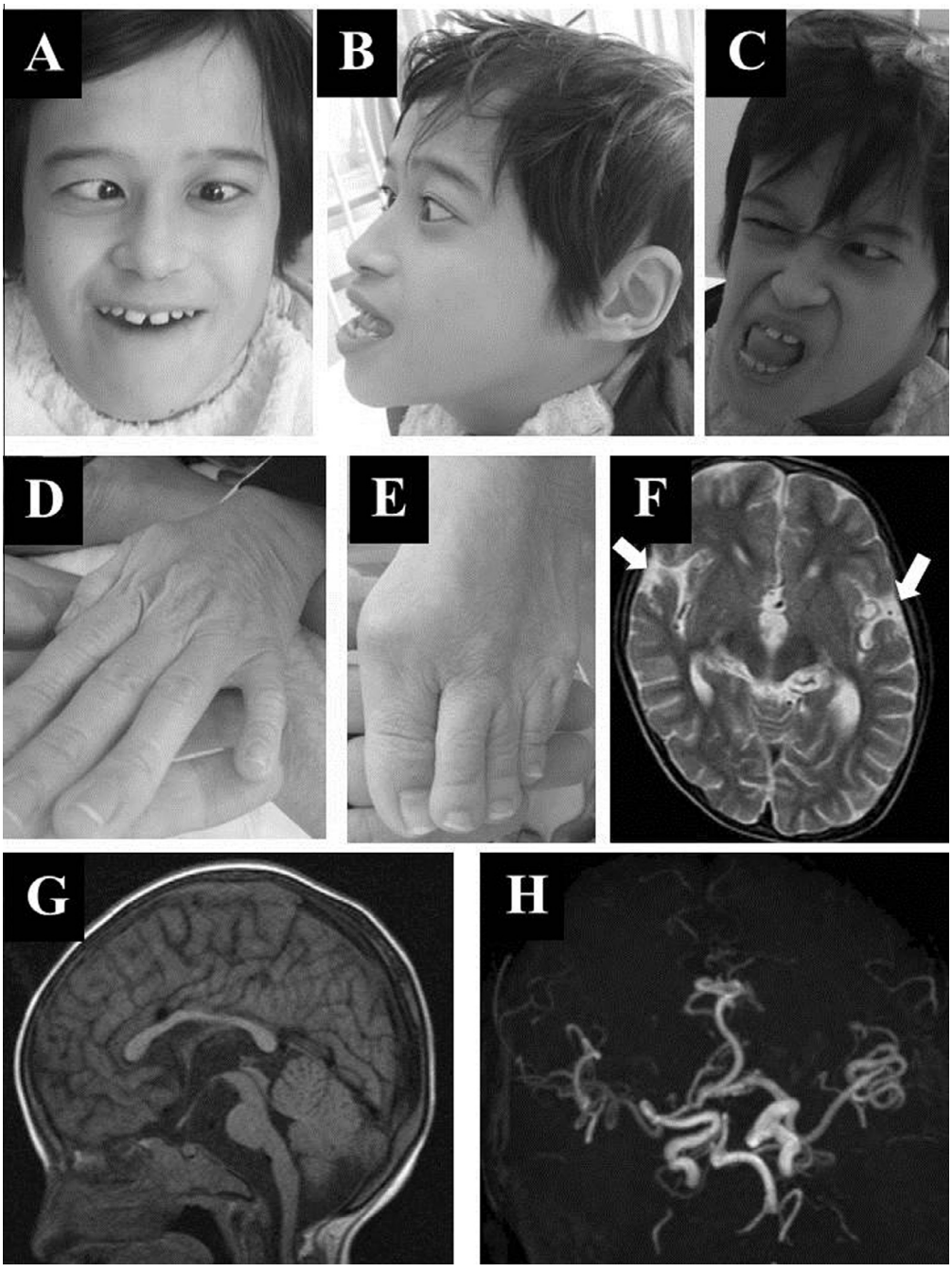

Fig. 1. (A) and (B) Frontal and lateral views of the patient's facial dysmorphism. (C) Grimacing. (D) The patient's left hand and (E) foot show cutis laxa. (F) Axial T2-weighted brain MRI showing mild cortical atrophy (solid arrows). (G) Sagittal T1-weighted brain MRI showing the thin corpus callosum, and (H) magnetic resonance angiography showing marked kinking and tortuosity of the brain vessels. (We got written consent form for usage of pictures of the patient from parents).