Towards a suggestive facial dysmorphism in adenylosuccinate lyase deficiency?

M Holder-Espinasse, S Marie, G Bourrouillou, I Ceballos-Picot, M-C Nassogne, L Faivre, J Amiel, A Munnich, M-F Vincent, V Cormier-Daire

The association of severe developmental delay with seizures was suggestive of a metabolic disorder. The modified Bratton-Marshall urinary test was positive, suggesting ADSL deficiency. This diagnosis was confirmed by measurement of urine and cerebrospinal fluid (CSF) SAICAr and S-Ado by HPLC. Urinary SAICAr and S-Ado concentrations were 4.18 and 3.86 µmol/mg creatinine, respectively, and CSF SAICAr and S-Ado concentrations were 376 and 367 µmol/l, respectively. The SAICAr/S-Ado ratio was 0.92 in urine and 0.97 in CSF. Finally, molecular analyses of the ADSL gene showed compound heterozygosity for ADSL mutations (M1L and R374W). The mother was found to be heterozygous for the M1L and the father for the R374W mutations.

DISCUSSION

Dysmorphic features have not previously been mentioned in ADSL deficiency. We have had the opportunity to analyse pictures of another case of an ADSL deficient child previously reported by Nassogne et al 19 (fig 3). This girl had similar dysmorphic features to our patient, namely brachycephaly, prominent metopic sutures, small nose with anteverted nostrils, long, smooth philtrum, and thin upper lip. All of these features, characteristic of metabolic disorders, have been described in mitochondrial disorders (respiratory chain deficiencies), peroxysomal disorders, and fetal alcohol syndrome, and could be the result of either toxicity of the abnormal metabolite accumulation or the direct effect of the primary enzyme deficiency. The simplicity of the urinary screening test should allow consideration of this diagnosis when dealing with the association of developmental delay, dysmorphic features, and seizures.

Authors’ affiliations
M Holder-Espinasse, L Faivre, J Amiel, A Munnich, V Cormier-Daire, Department of Genetics, Necker-Enfants Malades Hospital, Paris, France
S Marie, M-F Vincent, Laboratory of Physiological Chemistry, Christian de Duve Institute of Cellular Pathology, and Université Catholique de Louvain, B-1200 Louvain, Belgium
G Bourrouillou, Department of Genetics, Purpan Hospital, Toulouse, France
I Ceballos-Picot, Department of Biochemistry, Necker-Enfants Malades Hospital, Paris, France
M-C Nassogne, Department of Paediatrics, Necker Enfants Malades Hospital, Paris, France

Correspondence to: Dr V Cormier-Daire, Département de Génétique

Abbreviations: ADSL, adenylosuccinate lyase deficiency; SAICAr, succinylaminoimidazole carboxamide ribotide; AICAR, aminoimidazole carboxamide ribotide; SAMP, adenylosuccinate; AMP, adenosine monophosphate; S-Ado, succinyladenosine; SAICAr, succinylaminoimidazole carboxamide riboside; HPLC, high performance liquid chromatography
REFERENCES


Figure 1  Pathways of purine metabolism.

Figure 2  Facial dysmorphism in our case. Note the brachycephaly, prominent metopic sutures, small nose with anteverted nostrils, the long and smooth philtrum, and poorly modelled and low set ears.

---

**Key points**

- Adenylosuccinate lyase deficiency (MIM 103050, ADSL) is a rare autosomal recessive disease causing mental retardation, seizures, and autistic features. The diagnosis is based on the detection of the dephosphorylated SAICAR and S-AMP products and the modified Bratton-Marshall test is a simple urinary screening test.
- Here, we report on a new case of adenylosuccinate lyase deficiency presenting with mental retardation, seizures, and facial dysmorphism and having brachycephaly, prominent metopic suture, a small nose with anteverted nostrils, long and smooth philtrum, thin upper lip, and low set ears.
- The analysis of another previously reported child with ADSL shows the same dysmorphic features, which could be the result of toxicity of the abnormal metabolite accumulation.
- We conclude therefore that the diagnosis of ADSL should be considered when dealing with the association of developmental delay, dysmorphic features, and seizures.

---