Measurement of sulfatides in the supernatant of amniotic fluid: a potential tool for the prenatal diagnosis of metachromatic leukodystrophy


**Introduction**

Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder caused by the deficiency of arylsulfatase A (ARSA) that leads to sulfatide accumulation. Sulfatides have already been quantified in urine, dried blood spots (DBS), and tissues of patients with MLD. As prenatal diagnosis for MLD is frequently requested, in this report, we examine if the quantitation of sulfatides in amniotic fluid can be a helpful tool.

**Material and methods**

The prenatal study was initiated at 19 weeks of gestation, in a pregnant women who had a previous child with MLD with the same parent. ARSA activity was quantified by fluorimetry in cultured amniocytes. C16:0 sulfatides were quantified by LC/MS/MS in the supernatant of amniotic fluid. Molecular analysis of the ARSA gene was performed in cultured amniocytes.

**Results**

The family pedigree is shown in Figure 1.

![Family pedigree](image1.png)

No activity of ARSA was detected in fetal cells. C16:0 sulfatides were significantly elevated in comparison to age-matched controls (5-fold increase). Molecular analysis of the ARSA gene revealed the variant c.465+1G>A in homozygosity, confirming the diagnosis of MLD (Figure 2).

![NGS of the ARSA gene showing the location of the pathogenic variant c.465+1G>A (IVS2+1G>A).](image2.png)

The baby was born at 39 weeks, when DBS and urine samples were collected. ARSA in DBS was 0 umol/h/L and sulfatides were 0.32 ug/mg of creatinine (reference range < 0.029 ug/mg of creatinine) confirming the prenatal findings.

**Conclusions**

The baby has been referred for hematopoietic stem cell transplantation or ex vivo gene therapy. This study indicates that sulfatides can be quantified in the supernatant of amniotic fluid in pregnancies at-risk for MLD and provide useful results, which could potentially be an early indicator of the diagnosis, while enzyme and molecular analyses are in progress.

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