3-O-methyldopa in dried blood spot: a quick guide in the diagnostic work-up for AADC deficiency

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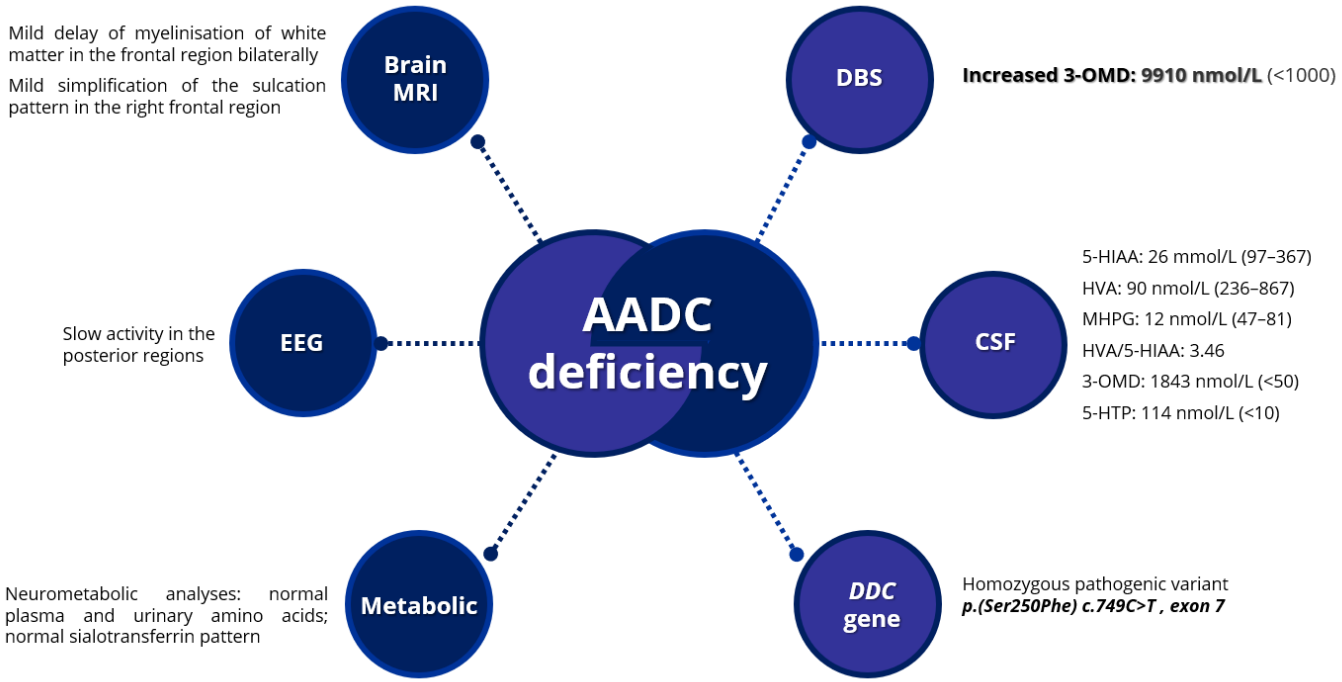
Introduction Aromatic L-amino acid decarboxilase deficiency (AADCD) is a rare and underdiagnosed neurometabolic disorder caused by mutations in dopa decarboxylase gene (*DDC*). The prevalence is currently unknown, and a large spectrum of symptoms is possible. The diagnosis is based on a typical CFS pattern, recessive mutations in the *DDC* gene and a low plasma AADC activity. The use of dried blood spot (DBS) for evaluation of 3-O-methyl-dopa (3-OMD) has been recently considered for AADCD screening. We aim to describe an early diagnosis of AADCD by use of DBS 3-OMD.



Clinical case This is the case of a male patient born at term. The clinical picture, at 12 months of age, was characterized by developmental delay, mild dysmorphisms, axial hypotonia with fluctuating limbs dystonia, bilateral ptosis, and abnormal ocular movements. Irritability and severe GERD were also observed.

Discussion Due to the ocular manifestations, the patient was enrolled in a research project, and he early underwent DBS 3-OMD. Increased 3-OMD levels were found (9910 nmol/L). The DDC gene analysis revealed the homozygous variant c.749C>T (p.Ser250Phe), suggestive for AADCD. Lumbar puncture confirmed a typical AADCD CSF pattern (5HIAA 26 nmol/L, HVA90 nmol/L, 3-OMD 1843 nmol/L, 5-HTP 114 nmol/L, MHPG 12 nmol/L, HVA/5HIAA 3,46). All the other instrumental and neurometabolic analyses were normal. A pharmacological treatment with selegiline and pyridoxine was started with initial clinical improvement. The enrollment of the patient in a gene therapy trial is currently being evaluated.

Conclusion In this case study we showed an early use of DBS 3-OMD in the diagnostic workup for AADCD, a simple and non-invasive test which rapidly help towards the diagnosis. Up to now, only few data is available on the use of this diagnostic test, and our patient is one of first documented cases of AADCD to be diagnosed by DBS 3-OMD. At the moment, our patient is also the youngest candidate for gene therapy in Italy.

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