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From Childhood to Adulthood: A Descriptive Analysis of Clinical Features in Patients with Acid Sphingomyelinase Deficiency (ASMD)

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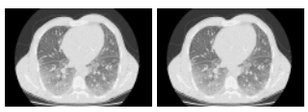

From Childhood to Adulthood: A Descriptive Analysis of Clinical Features in Patients with Acid Sphingomyelinase Deficiency (ASMD)

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Introduction

ASMD is an ultra-rare lysosomal storage disorder caused by mutations in the SMPD1 gene, leading to multisystemic substrate accumulation. The clinical spectrum ranges from a rapidly progressive infantile neurovisceral disease to slower visceral chronic forms. Olipudase alpha, an enzyme replacement therapy, has been approved for non-central nervous system manifestations

Objective/Methods:

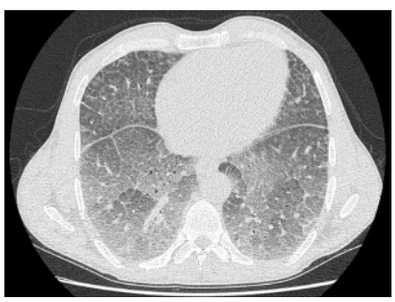
To characterize the clinical, genetic, biochemical and radiological aspects of patients with ASMD disease. This retrospective cohort study analyzed nine ASMD patients at a referral hospital.

Results

ID	Sex	Age of Dx	Type	Consanguinity	Primary symptom	Variant SMPD1	ASM Activity nmol/mg (%)	LysoSM nmol/L	LysoSM509 nmol/L
1	F	13 months	ASMD A	No	Neurological regression + hepatoespmenomegaly	c.421_517del (p.E141Sfs*84) c.1420_1421del(p.L474Efs*20)	3.7 (6%)	988	
2	F	20 months	ASMD A/B	Yes	Hepatosplenomegaly	homozygous c.1493G>A, (p.Arg498His)	0.9 (3%)	590	30484
3	M	10	ASMD B	Yes	Hepatosplenomegaly	homozygous.1829_1831del,(p.Arg610del)	2 (7%)	108	6.164
4	F	7	ASMD B	Yes	Hepatosplenomegaly	homozygous.1829_1831del,(p.Arg610del)	1.4 (5%)	285	8771
5	F	11	ASMD B	Yes	Hepatosplenomegaly	homozygous.1829_1831del,(p.Arg610del)	9 (15%)		
6	M	51	ASMD B	No	Hepatosplenomegaly	c.688C>G (p.Arg230Gly), c.1829_1831del (p.Arg610del)	4,8 (20%)	211	6887
7	M	59	ASMD B	No	interstitial pulmonary	homozygous c.96G>A (p.(Trp32*)	0.2 (1,5%)	185	
8	M	52	ASMD B	No	Hepatosplenomegaly	c.1826GCC[1] (p.Arg610del), c.1382_1383del (p.His461fs)	0,74 (3%)	275	17816
9	F	33	ASMD B	yes	Familiar study	homozygous.1829_1831del,(p.Arg610del)	2.5 (11%)	127	3670

Clinical Manifestations

- The patient with type A displayed neurological symptoms and a cherry-red spot. The two pediatric patients with types A and AB had congenital dermal melanocytosis.
- All patients presented with interstitial lung disease at the time of diagnosis, despite the majority being asymptomatic.
- All patients exhibited splenomegaly; seven (77.8%) also presented with hepatomegaly, and three (33.3%) demonstrated abnormal liver function tests, with a mean AST of 87 U/L ± 97 and ALT of 70 U/L ± 100.Only one had advanced hepatic fibrosis.
- Five (55.6%) had thrombocytopenia
- Regarding dyslipidemia, mean LDL was 144 mg/dL (± 45), HDL 25 mg/dL (± 10), and triglycerides 148 mg/dL (± 83). No ischemic events occurred. One patient had hypertrophic cardiomyopathy.
- Olipudase therapy was administered to 83.3% of the patients without adverse effects.



Patient 6 CT scan: extensive interstitial lung involvement withwith areas of ground-glass opacities and septal thickening. He was assymptomatic

CONCLUSIONS

- ASMD is a rare genetic disorder likely underdiagnosed due to limited clinician awareness and milder forms. This study highlights the diverse clinical spectrum across ages.
- It should be considered in differential diagnoses of interstitial lung disease and hepatosplenomegaly.
- Biomarkers like LysoSM levels help differentiate ASMD types, aiding diagnosis.
- Further registries are crucial to better understand disease progression and the real-world impact of Olipudase therapy.

COI disclosure: No author has conflicts of interest regarding the content included in the present study.

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REFERENCIA:
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