Nephrocalcinosis is a complication described in up to 10% of cases,[4] highlighting the need of monitoring to guide treatment planning and prevent sequelae.

As for treatment, there is no standardized approach to the management of systemic sarcoidosis in the pediatric population. Steroid therapy is the first-line treatment, as is the case in adult patients.[3,6] In refractory or steroid-dependent cases, there is the option of adding an immunosuppressive agent such as methotrexate or anti-TNF-$\alpha$.[6]

## References


1. Nathan N, Sileo C, Calender A, Pacheco Y, Valeyre D, Clement A. Paediatric sarcoidosis. Paediatr Respir Rev. 2019;29:53–9.
2. Sherief LM, Amer OT, Mokhtar WA, Kamal NM, Ibrahim HM. Pediatric sarcoidosis presenting as huge splenomegaly. Pediatr Int. 2017;59:366–7.
3. Nathan N, Marcelo P, Houdouin V, Epaud R, de Blic J, Valeyre D, et al. Lung sarcoidosis in children: update on disease expression and management. Thorax. 2015;70:537–42.
4. Hoffmann AL, Milman N, Byg KE. Childhood sarcoidosis in Denmark 1979–1994: incidence, clinical features and laboratory results at presentation in 48 children. Acta Paediatr. 2004;93:30–6.
5. Hurst JR, Verma N, Lowe D, Baxendale HE, Jolles S, Kelleher P, et al. British Lung Foundation/United Kingdom Primary Immunodeficiency Network Consensus Statement on the Definition Diagnosis, and Management of Granulomatous-Lymphocytic Interstitial Lung Disease in Common Variable Immunodeficiency Disorders. J Allergy Clin Immunol Pract. 2017;5:938–45.
6. Eklund A, du Bois RM. Approaches to the treatment of some of the troublesome manifestations of sarcoidosis. J Intern Med. 2014;275:335–49.



Álvaro Cobreros-Pérez[a,*], Rocío Galindo-Zavala[b], Begoña Carazo-Gallego[c], Laura Martín-Pedraz[b], Esmeralda Núñez-Cuadros[b]

[a] *Unidad de Gestión Clínica de Pediatría, Hospital Materno Infantil, Hospital Regional Universitario de Málaga, Málaga, Spain*
[b] *Unidad de Reumatología Pediátrica, Unidad de Gestión Clínica de Pediatría, Hospital Materno Infantil, Hospital Regional Universitario de Málaga, Málaga, Spain*
[c] *Unidad de Infectología Pediátrica, Unidad de Gestión Clínica de Pediatría, Hospital Materno Infantil, Hospital Regional Universitario de Málaga, Málaga, Spain*

* Corresponding author.
*E-mail address:* alvaro_cobre@msn.com
(Á. Cobreros-Pérez).


https://doi.org/10.1016/j.anpede.2020.02.011


# Lysosomal acid lipase deficiency: A rarely recognised cause of dyslipidaemia and liver dysfunction☆

## Deficiencia de lipasa ácida lisosomal: una causa poco reconocida de dislipemia y disfunción hepática

*Dear Editor:*

Lysosomal acid lipase (LAL) deficiency is an ultra-rare, progressive, autosomal recessive disorder resulting from an inborn error of lipid metabolism at the lysosomal level. It is characterised by the accumulation of cholesteryl esters and triglycerides in different tissues (liver, spleen, intestine, adrenal glands and mononuclear phagocyte system cells).[1–3] We describe 2 cases of LAL deficiency diagnosed in childhood with different clinical presentations.

The first case corresponded to a boy aged 22 months referred to the metabolic disorder clinic for evaluation of hepatomegaly, splenomegaly and hypercholesterolaemia with normal liver enzyme levels. The key finding of the abdominal ultrasound scan was hepatomegaly due to fat accumulation and moderate splenomegaly. The evaluation for lysosomal storage disorders did not yield relevant results. Clinical suspicion of LAL deficiency led to performance of a LAL assay in a skin biopsy sample, which revealed substantially reduced enzymatic activity in fibroblasts. Genetic testing confirmed the diagnosis of LAL deficiency with the finding of 2 heterozygous mutations in the *LIPA* gene. At age 2 years, the patient started treatment with bile acid binding resins, switching to statins 6 months later due to the persistence of marked hypercholesterolaemia, which improved the lipid profile without achieving normalisation. From age 3 years, the patient experienced elevation of liver enzymes. An elastography performed during the follow-up revealed stage 2 liver fibrosis. At age 12 years, the patient started enzyme replacement therapy with a recombinant human lysosomal acid lipase, which achieved normalisation of liver enzyme levels and the lipid profile despite discontinuation of statin therapy.

The second case corresponded to a boy aged 10 years referred to the metabolic disorder clinic for evaluation of persistent hypertransaminasaemia and hypercholesterolaemia from age 3 years that was currently in treatment with statins. The examination of a liver biopsy sample revealed unspecified chronic hepatitis with moderate intraportal and portoportal fibrosis. Clinical suspicion of LAL deficiency motivated performance of a LAL activity assay in dry blood, in which enzymatic activity was undetectable. Genetic testing confirmed the diagnosis of LAL deficiency with detection of a homozygous mutation in the *LIPA* gene. The patient started enzyme replacement therapy with recombinant human LAL at age 11 years, which achieved normalisation of

☆ Please cite this article as: Marín Andrés M, Ros Arnal I, Cebolla Sanz JJ, Pérez Delgado R, García Jiménez MC. Deficiencia de lipasa ácida lisosomal: una causa poco reconocida de dislipemia y disfunción hepática. An Pediatr (Barc). 2021;94:50–51.

liver enzyme levels and the lipid profile that was sustained after discontinuing treatment with statins.

Lysosomal acid lipase deficiency is due to a reduction or complete absence of enzymatic activity due to mutations in the *LIPA* gene.[4] This lack of activity results in the intralysosomal accumulation of cholesteryl esters and triglycerides, leading to microvesicular steatosis, progressive liver disease and dyslipidaemia associated with rapidly progressing atherosclerosis, which are the characteristic features of this disease. A lack of clinical suspicion may lead to misdiagnosis, delaying initiation of appropriate treatment and follow-up. Generally speaking, the possibility of LAL deficiency should be contemplated in patients with unexplained persistent abnormalities in liver function tests or the lipid profile.[1–3]

In the first case, the diagnosis was reached through the measurement of LAL activity in fibroblasts through obtention of a skin biopsy. Advances in diagnostic techniques that have made it possible to study enzymatic activity in dry blood possible allows the assessment of this disease with considerably less invasive and more accessible methods, as demonstrated by the second case. If enzymatic activity is found to be nearly undetectable, genetic analysis of the *LIPA* gene should be considered with the purpose of identifying the causative mutation and confirm the diagnosis.[1,4]

Traditionally, the management of LAL deficiency was based on the control of dyslipidaemia through a low-fat diet and lipid-lowering drugs.[1,2] However, the use of lipid-lowering drugs is not always effective and does not correct the enzymatic defect or prevent lipid accumulation.[1,3] In 2015, the use of sebelipase alfa (a recombinant human lysosomal acid lipase) was approved in Europe for enzyme replacement therapy. This drug is used with the aim of restoring a LAL activity nearing physiological levels through the administration of exogenous enzyme, thus halting disease progression.[1,2,5] The fact that enzyme replacement therapy is now available makes awareness of LAL deficiency in health care professionals all the more relevant for the purpose of early diagnosis and treatment of the disease.

## References


1. Kohli R, Ratziu V, Fiel MI, Waldmann E, Wilson DP, Balwani M. Initial assessment and ongoing monitoring of lysosomal acid lipase deficiency in children and adults: consensus recommendations from an international collaborative working group. Mol Genet Metab. 2019;129:59–66.
2. Camarena C, Aldamiz-Echevarria LJ, Polo B, Barba MA, García I, Cebolla JJ, et al. Actualización en deficiencia de lipasa ácida lisosomal: diagnóstico, tratamiento y seguimiento de los pacientes. Med Clin (Barc). 2017;148:429.e1–10.
3. Strebinger G, Müller E, Feldman A, Aigner E. Lysosomal acid lipase deficiency – early diagnosis is the key. Hepat Med. 2019;11:79–88.
4. Carter A, Brackley SM, Gao J, Mann JP. The global prevalence and genetic spectrum of lysosomal acid lipase deficiency: a rare condition that mimics NAFLD. J Hepatol. 2019;70:142–50.
5. Erwin AL. The role of sebelipase alfa in the treatment of lysosomal acid lipase deficiency. Therap Adv Gastroenterol. 2017;10:553–62.



Marta Marín Andrés[a,*], Ignacio Ros Arnal[b], Jorge Javier Cebolla Sanz[c], Raquel Pérez Delgado[a], María Concepción García Jiménez[a]

[a] *Unidad de Neurometabolismo, Hospital Universitario Miguel Servet, Zaragoza, Spain*
[b] *Unidad de Gastroenterología, Hepatología y Nutrición Pediátrica, Hospital Universitario Miguel Servet, Zaragoza, Spain*
[c] *Instituto de Investigación Sanitaria Aragón, Grupo de estudio de enfermedades metabólicas y neoplasias hematológicas, Zaragoza, Spain*

* Corresponding author.
*E-mail address:* marta_marin91@hotmail.com
(M. Marín Andrés).


https://doi.org/10.1016/j.anpede.2020.02.010


# Suicide attempt with selective serotonin reuptake inhibitor antidepressants*

## Intento autolítico con antidepresivos inhibidores selectivos de la recaptación de serotonina

*Dear Editor:*

Intentional drug poisoning with suicidal intent is an important cause of morbidity and mortality in adolescents.[1]

The drugs involved most frequently in these cases are paracetamol, ibuprofen and, third in frequency, selective serotonin reuptake inhibitors (SSRIs).[2,3] The frequency of the latter has been increasing in recent decades because these drugs are used for first-line treatment of major depression and anxiety disorders in this age group.[4]

The aim of our study was to assess the clinical manifestations, laboratory findings and electrocardiographic features associated with intentional ingestion of SSRIs with suicidal intent in adolescents.

We conducted a single-centre retrospective observational study in patients aged less than 18 years managed between February 2013 and May 2018 in the paediatric emergency department (PED) of a tertiary care hospital that is a reference centre for psychiatric disorders with a discharge diagnosis of ''intentional drug poisoning'' or ''suicide attempt''. We selected patients in who the main drug ingested in the episode was a SSRI (Table 1). We defined

* Please cite this article as: Cuenca Carcelén S, Moral Larraz A, Sanchíz Perea A, Alonso Cadenas JA, de la Torre Espí M. Intento autolítico con antidepresivos inhibidores selectivos de la recaptación de serotonina. An Pediatr (Barc). 2021;94:51–52.