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Rare Cause of Liver Cell Failure in Infants: Wolman Disease

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Abstract **Case Report**

Wolman disease is an extremely rare hereditary metabolic lipid storage disorder, characterized by a total deficiency of lysosomal acid lipase (LAL), which leads to the accumulation of cholesteryl esters and triglycerides in the lysosomes, resulting in more or less progressive damage to numerous organs, thus presenting the patient with vomiting, diarrhea, and severe malnutrition. With a fatal outcome in the first months of life if untreated. We present the case of a two-month-old infant admitted for abdominal distension; physical examination revealed jaundice, hepatomegaly, and splenomegaly; biological investigations revealed hepatic cytolysis, anemia, and thrombocytopenia. Imaging studies showed bilateral calcifications of the adrenal glands. The diagnosis of Wolman disease was confirmed by measuring the activity of the collapsed lysosomal acid lipase.

Keywords: Wolman disease, liver Cell Failure, lysosomal acid lipase deficiency, hepatomegaly, calcifications, adrenal glands.

BACKGROUND

Lysosomal acid lipase deficiency is a rare autosomal recessive disorder, caused by mutations in the lysosomal acid lipase gene (LIPA), located on chromosome 10q23.2-q23.3 [1], Wolman disease is an extremely rare and severe subtype with less than 1% of normal lysosomal acid lipase activity, the worldwide prevalence is estimated to be between one in 40,000 and one in 300,000 [2], It occurs in the first months of life with delayed growth and signs of progressive hepatocellular failure due to increased accumulation of TG, mainly in the liver, leading to death in the first 6 months of life if not treated early. We report here a new case because of its rarity to highlight Wolman disease's clinical, biological, radiological, and evolutionary features.

CASE PRESENTATION

A 2-month-old female infant presenting with abdominal distension and jaundice, born to a first-degree consanguineous couple, pregnancy well controlled and carried to term, delivery by vaginal route without incident, birth weight 3000 kg, height 49 cm, head circumference 36 cm. Her medical history dates back to 20 days before her consultation, with the onset of abdominal distension with weight stagnation, vomiting, and diarrhea, all developing in the context of apyrexia and altered general condition. Physical examination revealed icterus with a pale background, weight was 3.2 kg, the abdomen was distended with an umbilical hernia and collateral venous circulation, hepatomegaly extending to the umbilicus, and splenomegaly at 5 cm below the costal margin Figure 1.

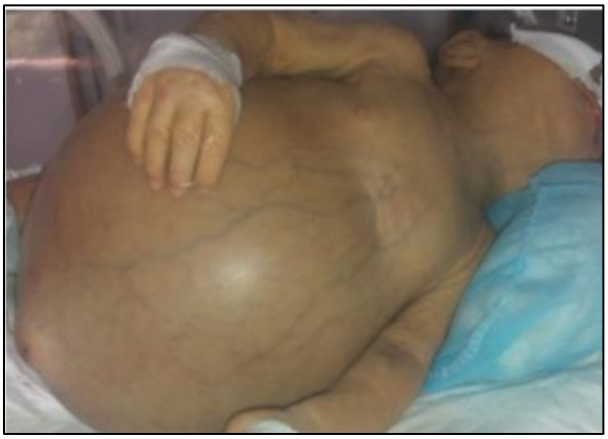

Figure 1: Patient's abdomen with significant distension, collateral venous circulation, umbilical hernia, and jaundice

The biological work-up showed bi-cytopenia with microcytic anemia at 7 g/dl and thrombocytopenia at 66,000/mm3, hepatic cytolysis with AST at 150 U/L,

ALT at 82 U/L, cholestasis with total bilirubin at 105 mg/l, GGT at 60 U/L, ALP at 520 U/L, TP at 22%, albumin at 13 g/l. The lipid profile was normal. A blood smear showed intracytoplasmic foamy lipid vacuoles in lymphocytes Figure 2.

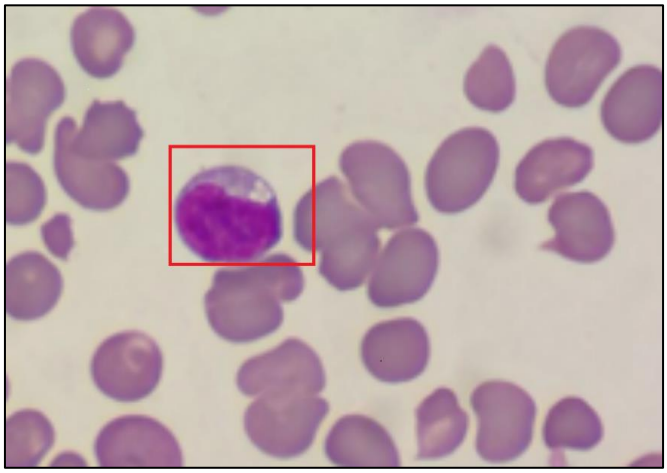

Figure 2: Vacuoles in the cytoplasm of a peripheral blood lymphocyte

Abdominal ultrasound showed massive splenomegaly and hepatomegaly, with bilateral adrenal calcifications, more pronounced on the left side, which was confirmed by the abdominopelvic scan Figure 3.

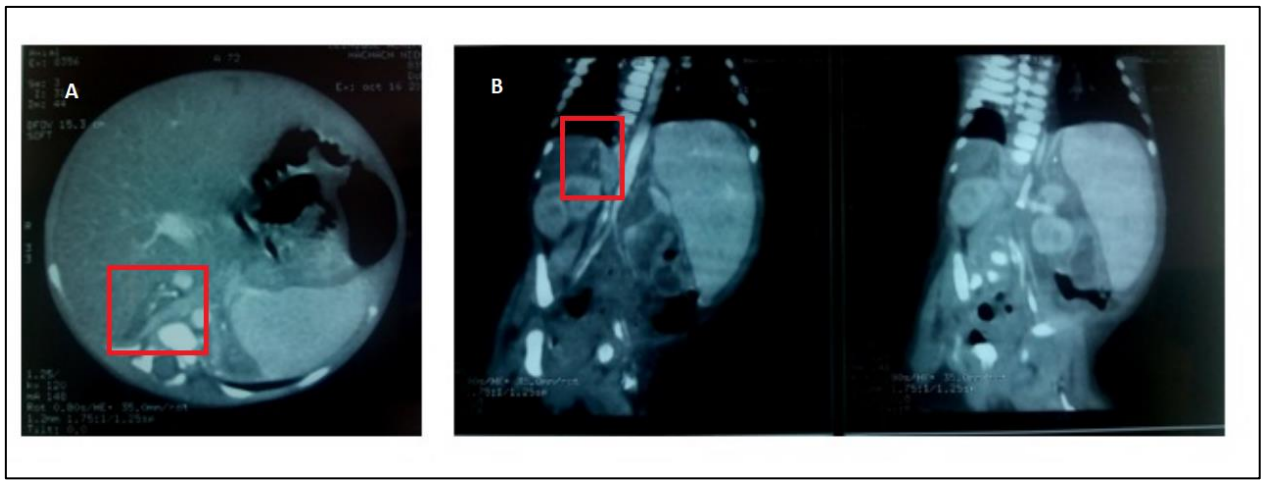

Figure 3: Axial CT section of the abdomen (A) and sagittal CT section of the abdomen (B), showing adrenal gland calcification

Given this clinical picture, a metabolic disorder was strongly suspected, in particular Wolman's disease, which was confirmed by the examination of the leucocyte acid lipase activity, which was low. The baby was treated symptomatically. The outcome was fatal after 20 days.

DISCUSSION

Wolman disease is a rare autosomal recessive lysosomal storage disorder that presents in early childhood. It is caused by a deficiency of lysosomal acid lipase. Which is essential for the metabolism of triglycerides and cholesterol esters. A deficiency of this enzyme leads to elevated levels of triglycerides and cholesterol, resulting in the deposition of excessive amounts of lipid esters in most tissues, particularly the liver, spleen, and adrenal glands. The disease manifests itself in the first weeks of life with vomiting, steatorrhoea, massive hepatosplenomegaly, malnutrition with stunted growth due to feeding difficulties, and malabsorption [3], which together with the severe liver disease contribute to the early death of the patient, usually within the first few months of life [4].

This case illustrates the typical presentation of Wolman disease in infants, with progressive hepatocellular failure, massive hepatosplenomegaly, anemia, and thrombocytopenia. Imaging is an essential part of the diagnostic process. Adrenal calcifications are a pathognomonic sign of Wolman disease, which can be objectified by standard radiography, ultrasound, and (CT) scans. Blood tests will typically show high cholesterol and triglyceride levels [3], which were normal in this case, elevated serum transaminase levels,

anemia, and low platelets. A peripheral blood smear will show an increase in lymphocytes, while a bone marrow aspirate will show vacuolated macrophages, the definitive diagnosis is currently based on the evaluation of enzymatic activity in leukocytes using the Hamilton method, which is absent or less than 1%, Subsequent molecular testing of the LIPA gene for confirmation of the diagnosis of lysosomal acid lipase deficiency [5, 6].

Treatment of Wolman disease is mainly symptomatic and relies on a special diet and close monitoring of the patient's clinical condition. Enzyme replacement therapy (ERT) with sebelipase alfa is currently the treatment of choice in some areas of the world, and is effective in reducing lipid levels in affected organs and improving the quality of life of patients, with improvements in liver function, growth, and quality of life in some patients [7]; however, ERT has limitations, including the high cost of treatment, the need for lifelong administration and potential side effects.

CONCLUSION

Our observation highlights the severity of Wolman disease, which is fatal if untreated in the first months of life. Early recognition of this disease's first signs is essential to establish appropriate management, based on an adapted diet and treatment with ERT, which has changed the prognosis.

Learning points

- Wolman disease is an extremely rare and severe subtype of Lysosomal acid lipase deficiency that remains underdiagnosed.
- The presence of intracytoplasmic foamy lipid vacuoles and Adrenal calcifications seen on ultrasound are important referent elements in Wolman disease.
- The determination of acid lipase activity in leukocytes and fibroblasts, as well as the search for a mutation in the LIPA gene, allows the diagnosis to be confirmed.
- Early recognition of the first signs of this disease is essential for the appropriate management and improved prognosis.

Conflict of Interest: None.

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