

Secondary Hemophagocytic Lymphohistiocytosis in an Infant with Wolman Disease

Wolman Hastalığı Olan Bir Bebeğe Gelişen İkincil Hema-fagositik Lenfohisti-yositozis

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Figure 1. Two-month-old female patient with Wolman disease, showing abdominal distension.

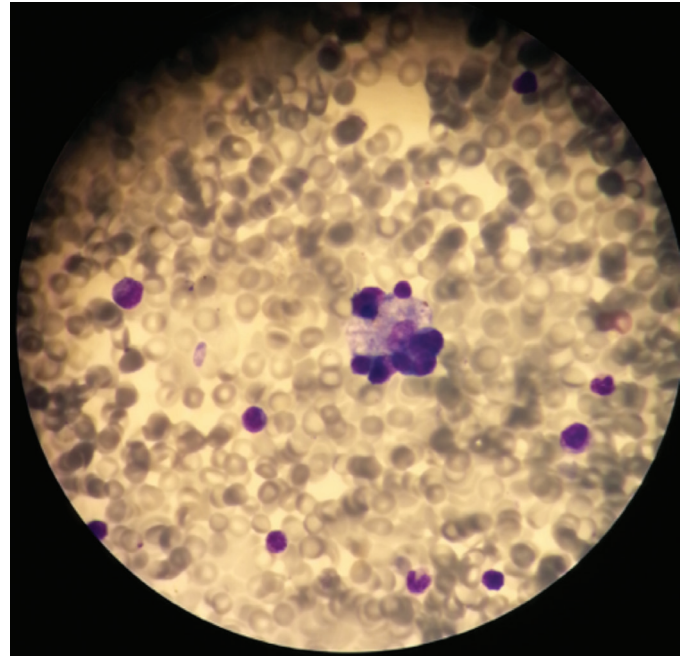


Figure 2. Hemophagocytosis in the bone marrow of our patient.

A 2-month-old girl presented with vomiting, fever, failure to thrive, and diarrhea. She was born to consanguineous parents. She was irritable and pale and she had hepatosplenomegaly (Figure 1). Her weight and height were below the 3rd percentile. Initial hemoglobin count was 7.6 g/dL, white blood cell count was $12 \times 10^9/L$, platelet count was $92 \times 10^9/L$, triglyceride level was 361 mg/dL (reference range: 40–150 mg/dL), and ferritin level was

>1650 ng/mL. According to bone marrow aspiration, numerous examples of hemophagocytosis were observed (Figure 2). She was diagnosed with hemophagocytic lymphohistiocytosis (HLH) because of prolonged fever, organomegaly, bicytopenia, high levels of ferritin, and bone marrow findings. Enzymatic analyses were performed for lipid storage disorders. The lysosomal acid lipase (LAL) activity was <0.02 nmol/punch/h (reference range:



0.07-2.3 nmol/punch/h). Based on reduced LAL activity, she was diagnosed with Wolman disease. Although treatment and supportive therapy were applied, the patient died 1 month later.

Exon 4 heterozygous variation was found at the *LIPA* gene location c:260G>T (GGC>GTC), p.Gly87Val. Sequence analysis of all coding regions of the *LIPA* gene presented heterozygote NM_000235(LIPA_vENST00000336233):c.260G>T(p.Gly87Val) variation in both parents. This variation was reported as a disease-causing variant by Pagani et al. [1].

It was discussed in cases of Wolman disease that the pathophysiological role of cholesteryl ester induces inflammasome activation in macrophages, leading to secondary HLH [2].

Keywords: Wolman disease, Hemophagocytic lymphohistiocytosis, Hemophagocytosis

Anahtar Sözcükler: Wolman hastalığı, Hema-fagositik lenfohistiyositozis, Hemofagositoz

Informed Consent: It was received from the parents.

Conflict of Interest: The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

References

1. Pagani F, Garcia R, Pariyarath R, Stuani C, Gridelli B, Paone G, Baralle FE. Expression of lysosomal acid lipase mutants detected in three patients with cholesteryl ester storage disease. *Hum Mol Genet* 1996;5:1611-1617.
2. Taurisano R, Maiorana A, De Benedetti F, Dionisi-Vici C, Boldrini R, Deodato F. Wolman disease associated with hemophagocytic lymphohistiocytosis: attempts for an explanation. *Eur J Pediatr* 2014;173:1391-1394.