

# Successful treatment of Epstein-Barr virus-related acute retinal necrosis in a patient with X-linked lymphoproliferative disease

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## Introduction

- X-linked lymphoproliferative disease (XLP) is a rare disorder with severe immune dysregulation and susceptibility to Epstein-Barr virus (EBV) infection caused by mutations in the SH2D1A/SAP gene.
- Clinical manifestations include fulminant infectious mononucleosis, lymphoma, hemophagocytic lymphohistiocytosis, and dysgammaglobulinemia

## Case

- A 13-month-old previously healthy boy presented with fever, cough, multiple cervical lymph node enlargements, whole-body rash, red lip, conjunctival injection and hand, foot edema (Figure 1).
  - intravenous immunoglobulin for **Kawasaki disease**.
- Hx: Born as a twin and his 10-year-old brother had B-cell lymphoma in a 10-year-old brother.
- He continued spiking fevers.
- Rapidly increasing cervical lymph nodes and hepatosplenomegaly + leucocytosis and elevated liver enzymes → **r/o HLH or refractory Kawasaki disease**. (Figure 2&3).
- Initial EBV PCR value was 2,117 IU/mL and increased to 79,143 IU/ml one week later. He showed respiratory difficulty due to airway lymphoproliferation and was eventually intubated (Figure 2&3, Table 1)
- His lymph node and bone marrow biopsy
  - **EBV-positive large B cell lymphoma**
  - Rituximab & Chemotherapy (Figure 4)
- At eye evaluation before hematopoietic cell transplantation → **Acute retinal necrosis in both eyes & EBV detection in the aqueous humor** by PCR (Table 1 & Figure 5)
  - **Intravenous & intravitreal foscarnet injection 13 times for three months**
  - **Umbilical cord blood transplantation (UCBT) with intravenous foscarnet**
  - Retinal necrosis improved without vision loss
- His older brother was diagnosed with relapsed lymphoma and EBV viremia.
- Diagnostic exome sequencing (DES) in both brothers
  - **Exon 3-4 deletion of SH2D1A gene on Xq25**
  - **X-linked lymphoproliferative syndrome (XLP-1)**
- Their mother and sister were the carriers (Figure 6).



Figure 1. Patient's feature at admission



Figure 2. Patient's feature at ICU admission

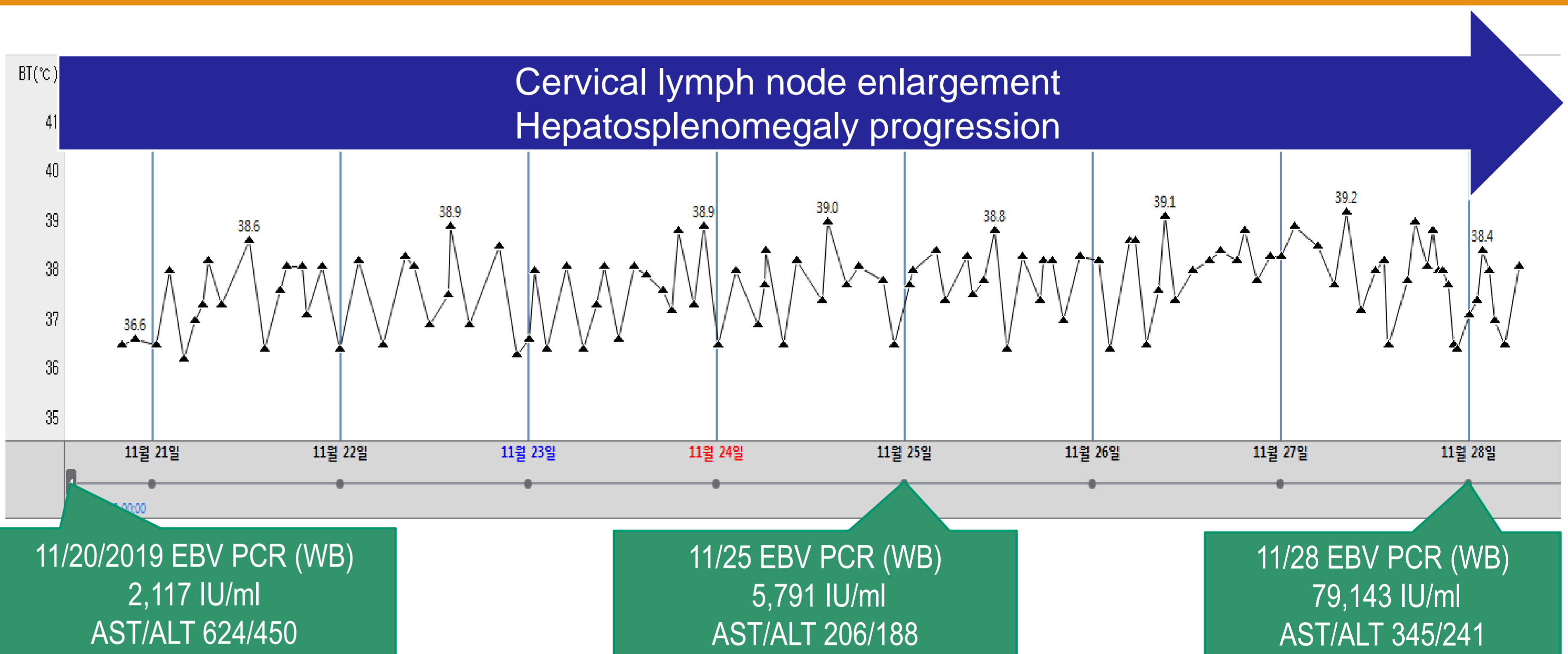


Figure 3. Patient's fever pattern and laboratory results

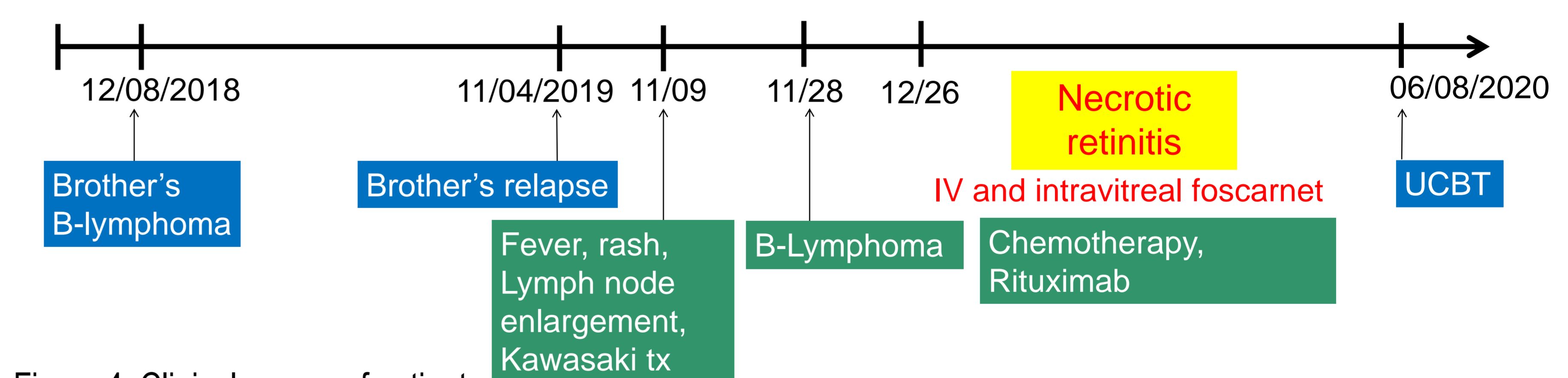


Figure 4. Clinical course of patient.

Table 1. EBV titer of the patient

Whole blood	IU/ml
11/20/2019	2,117
11/25/2019	5,791
11/28/2019	79,143
12/02/2019	21,756
12/09/2019	195
12/16/2019	ND
Vitreous humor	IU/ml
02/11/2020	653,251
03/10/2020	147,616
05/26/2020	214

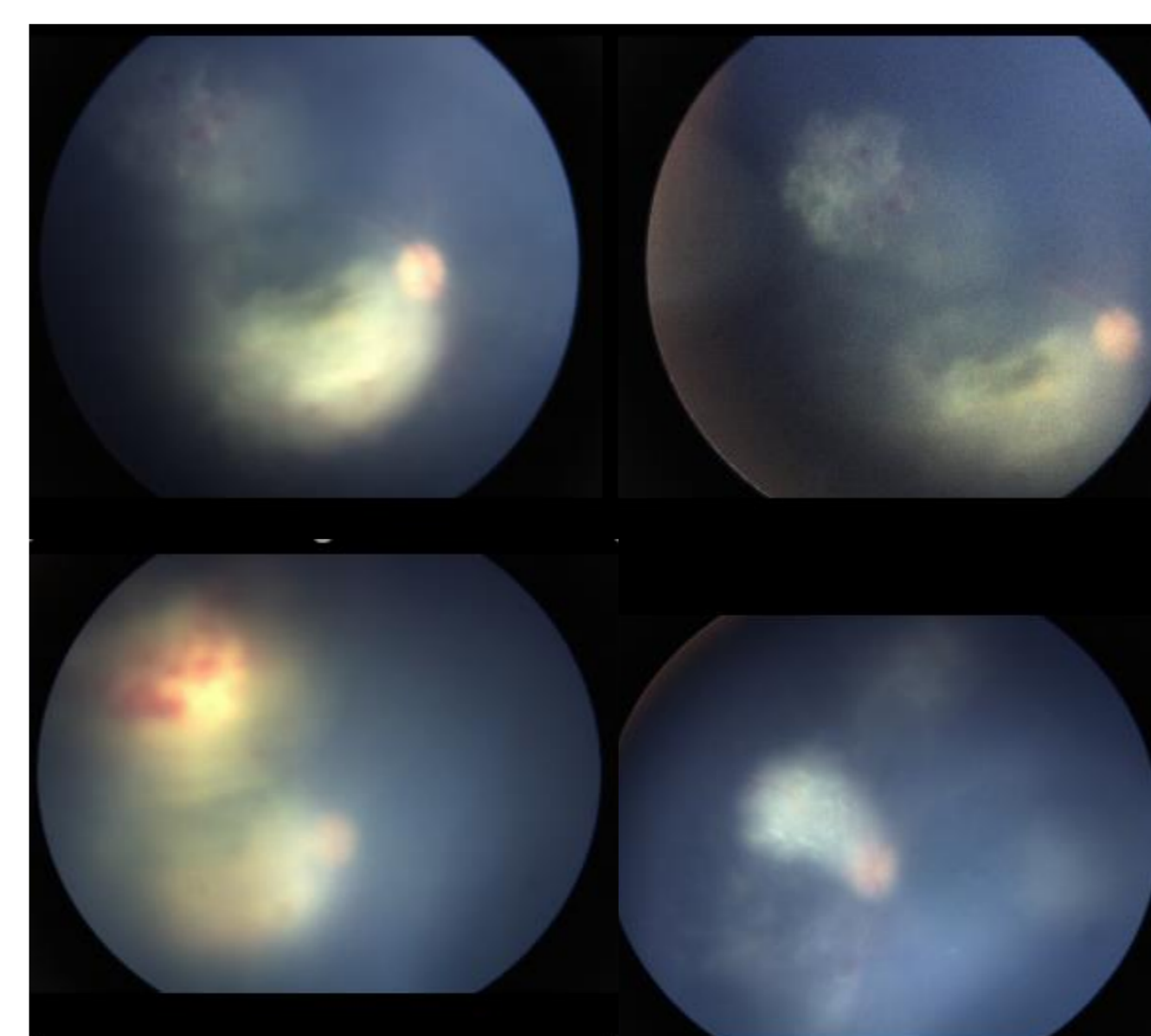


Figure 5. Acute retinal necrosis (diffuse retinal whitening and opacification)

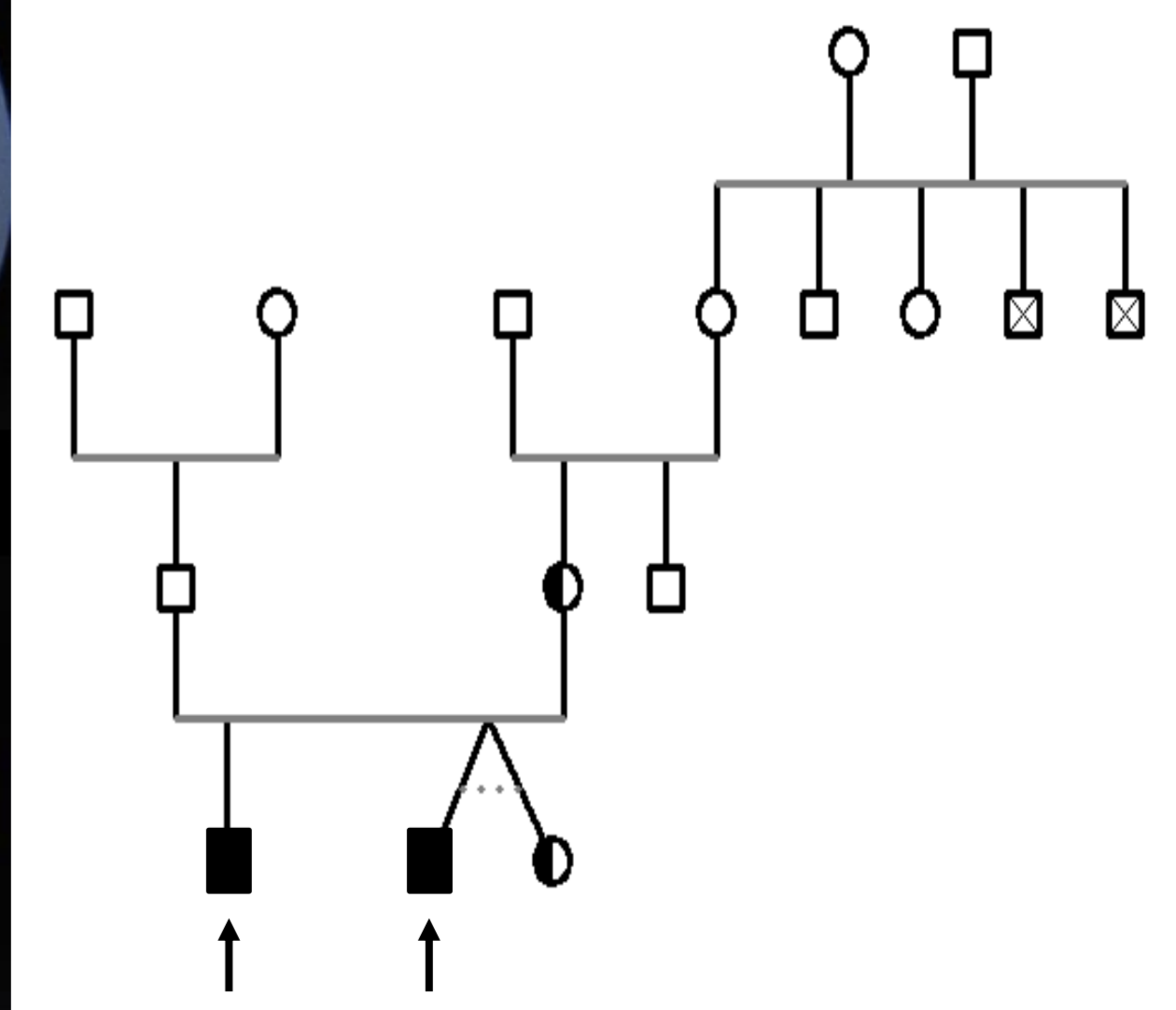


Figure 6. Pedigree of the patient.

## Conclusions

- EBV involvement in the eyes should be considered in XLP-1 patients with XLP-1 and have serious EBV infection.