Persistent hypogammaglobulinemia following mononucleosis in boys is highly suggestive of X-linked lymphoproliferative disease--report of three cases.

Hypogammaglobulinemia is a common symptom in different immunodeficiencies. It is, however, not usually associated with Epstein-Barr virus (EBV) infections. The X-linked lymphoproliferative disease (XLP) on the other hand shows immunological changes in response to the EBV. Here we report three previously healthy boys, all of which developed persistent hypogammaglobulinemia following severe acute infectious mononucleosis. All three patients revealed T-cell abnormalities including inverted CD4/CD8 and increased CD8(+) T-cell numbers. The number of IFN-gamma-producing T cells were markedly increased in the two patients studied so far. In addition, patient 2 showed mainly T cells, instead of B cells, to be infected with the EBV. Apart from an uncle of patient 3, who died of malignant lymphoma, family history was unremarkable in all cases. All three patients exhibited mutations in the SH2D1A gene, establishing the diagnosis of XLP. Protein expression was found on immunoblot analysis in one patient with a missense mutation. Development of persistent hypogammaglobulinemia after severe primary EBV infection seems to be a specific diagnostic sign for XLP even in males with unremarkable family history.