

cancer incidence and the involvement of EBV in some of these tumors, especially lymphomas. This group includes PIDs with mutations in genes WAS (Wiskott–Aldrich syndrome, X-linked), ATM (Ataxia telangiectasia syndrome, AR), and TNFRSF6 (ALPS-FAS, AD and AR).^{2,4,6}

The message for all pediatricians is to consider EBV as a causative agent in clinical pictures similar to those described by Bolis et al. In addition to the immune system impairment associated with treatment for several diseases, we must also consider these situations as a red alert for primary immunodeficiencies in pediatric patients. Recognizing PIDs may be essential to achieve a better management for patients with atypical EBV infections.

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Conflicts of interest

The author declares no conflicts of interest.

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Authors' reply: Atypical manifestations of Epstein–Barr virus: red alert for primary immunodeficiencies[☆]



Resposta dos autores: manifestações atípicas do vírus de Epstein-Barr: alerta vermelho para imunodeficiências primárias

Dear Editor,

Human primary immunodeficiency disease (PID) is a condition where mutations in single immune system genes predispose individuals to certain infectious agents. The human herpesviruses are a challenge of immune competence, since most of these agents are widespread in the population; they are often acquired silently or with mild symptoms in childhood and then carried for life as asymptomatic latent infections. PID patients are therefore likely to be exposed to these viruses relatively early in life and will have to deal with them both as a primary infection

and as a persistent condition.¹ For individuals who are immunocompromised, due to a genetic immunodeficiency or immunosuppressive drug therapy, viral infections may result in severe complications and even life-threatening disease.²

PID is considered a rare disease, with an overall incidence of 4.6 cases of PIDs per 100,000 person-years in the last 35 years.³ However, neither the true incidence nor the true prevalence of PID are known. Although there have been estimates of these parameters from geographically limited studies, those estimates were based only on diagnosed cases. Therefore, PID may be far more common than previously estimated. Surveys suggest prevalence rates for diagnosed PID as 1:2000 for children, 1:1200 for all persons, and 1:600 households.⁴

Specific gene mutations in PID patients are responsible for susceptibility to Epstein–Barr virus (EBV) infections, as highlighted in the letter to the editor of the *Jornal de Pediatria* entitled “Atypical manifestations of Epstein–Barr virus: red alert for primary immunodeficiencies”. Although PID and atypical complications of EBV infection are not very common, pediatricians should indeed correlate these two conditions as mentioned in the previous letter, since EBV infects more than 95% of the adult population worldwide.⁵ PID incidence has increased in the last decades,³ and patients with immunodeficiency are the group most exposed to atypical complications of EBV among healthy people.

The strongest predictor of PID is family history. Moreover, when an immunodeficiency disease is suspected, initial laboratory screening should include a complete blood count with

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differential and measurement of serum immunoglobulin and complement levels.⁶

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