Causes of Infectious Mononucleosis-like Syndrome in Adult Patients

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Infectious mononucleosis (IM) is a common disease in young adults, typically presenting as fever, sore throat, rash and lymphadenopathy. Diagnosis is based on clinical findings and the presence of atypical lymphocytes. Although IM-like syndromes with atypical lymphocytes are most often associated with Epstein-Barr virus (EBV) or cytomegalovirus (CMV), several other organisms, such as human herpes virus type 6 (HHV-6), parvovirus B19 and human immunodeficiency virus type-1 (HIV-1), cause mononucleosis. Cases of mononucleosis caused by various pathogens have been reported, but analyses of accumulated cases are rare. It is important to analyze the causes of mononucleosis in Japan, as etiology appears to differ by ethnicity, region and era, and the results of such analyses would help in clinical diagnosis. Here, we investigated adult patients who presented with IM-like syndromes and were found to have atypical lymphocytes.

The study group comprised 40 patients examined prospectively at the Department of General Medicine of Juntendo University Hospital, Tokyo, Japan, between 2003 and 2005. The IM-like syndrome in adults was defined to include the following criteria in this study: age of at least 18 years; clinical illness compatible with IM; and ≥3% atypical lymphocytes on a peripheral blood smear. Subjects included 21 men and 19 women, with a mean age of 28.9±6.4 (mean±SD) years. EBV infection was diagnosed based on one or both of the following criteria: (a) presence of EBV viral capsid antigen (VCA) IgM antibody (b) presence of EBV VCA IgG antibody and absence of EBV nuclear antigen (EBNA) (SRL Inc., Tokyo, Japan). CMV infection was confirmed by polymerase chain reaction (PCR) for DNA and the presence of CMV IgM antibody (SRL Inc.). HHV-6 was diagnosed only by PCR for DNA (SRL Inc.), although the possibility of false-positive results remained. Diagnosis of parvovirus B19 infection was confirmed by the presence of specific IgM antibody (BML Inc., Tokyo, Japan). Acute-primary HIV-1 infection was screened by PCR for RNA and was confirmed when the initial HIV-1 antibody test could not be confirmed by Western Blot analysis, but became positive one month later (SRL Inc.).

Table 1 shows the causes of mononucleosis in the present 40 adult patients. More than half of the cases (57.5%) were caused by pathogens other than EBV, including CMV (27.5%), HHV-6 (5.0%), parvovirus B19 (5.0%) and HIV (2.5%). Seven cases (17.5%) were of unknown etiology, which may have included measles, rubella, toxoplasmosis or drug reactions (1). Symptoms, clinical findings and laboratory data were not significantly different between EBV-infected and non-EBV-infected patients.

Although many previous reports have shown that most cases of IM are caused by EBV, we concluded here that more than half of adult IM cases (57.5%) in Japan are caused by pathogens other than EBV, particularly CMV. HHV-6 is known to induce short, acute disease (exanthema subitum) during the first year of life. Primary parvovirus B19 infection usually occurs in children with a typical clinical picture of erythema infectiosum. However, both of these pathogens have been reported to induce IM (2, 3). In order to ensure a satisfactory diagnosis, doctors should be aware of these results. Early and appropriate diagnosis of IM-like syndromes is important in obviating the need to perform unnecessary diagnostic procedures, such as rheumatologic profiles, computed tomographic scans, radionuclide scans and lymph node biopsies.

As seen in our results, primary HIV infection induces the production of atypical lymphocytes. As symptoms of primary HIV infection are nonspecific, it is frequently confused with many other diseases, including IM. At Massachusetts General Hospital, 7 of 563 patients (1.2%) tested for
antibodies against EBV in IM were retrospectively diagnosed with primary HIV-1 infection (4). In one study, only 1 in 4 patients with undiagnosed HIV, but were known to be in high-risk categories, received an appropriate diagnosis of primary HIV infection at their first clinical visit (5). Early diagnosis of primary HIV infection is very important for both the patient and public health, helping to minimize further transmission and to ensure optimal initiation of antiretroviral therapy.

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References


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