T-γδ LGL Leukemia with Complications

Kazuo Oshimi

Key words: T-γδ cell, LGL leukemia, GLPD, EBV

The interesting fact in this case was the association of T-γδ GLPD and EBV-induced HPS, and that of T-γδ GLPD and a massive infiltration of immature-looking lymphocytes in the liver, spleen and bone marrow at autopsy. Various points should be clarified, particularly on the events which terminally developed in this patient. 1) Was HPS caused by EBV-infected GLPD cells, or caused by EBV incidentally infected in the immunocompromised condition? To reveal this, T-γδ GL should be analyzed for EBV clonality with Southern blotting to use EBV terminal repeats as a probe. When monoclonal EBV band is present, GL are interpreted to be already infected with EBV, and EBV probably played a pathogenetic role to induce GLPD. 2) What were the immature lymphocytes found at autopsy? Were these cells transformed from GLPD cells or originated from cells of a different lineage?

T-αβ GLPD usually exhibits an indolent clinical course, without development of such severe complications as HPS. As far as I know, T-γδ GLPD is also similar to T-αβ GLPD in terms of its clinical course. As was speculated by the authors, HPS was caused by EBV incidentally infected after long-term administration of immunosuppressive agents. This is not an unexpected event, but the possibility that HPS was caused by EBV-infected GL should be ruled out.

The emergence of immature lymphocytes in the terminal period is unusual in T-GLPD. One possible mechanism was a transformation of GL into immature lymphocytes. This has been rarely reported. Tagawa et al (9) reported a case of CD3+CD4+CD8- T-GLPD with transformation during human herpesvirus-6 reactivation, and Matutes et al (10) reported a case of CD3+CD4-CD8+CD56+ T-GLPD that transformed into large T-cell lymphoma. Another possibility of the emergence of immature lymphocytes was that the immature cells originated from a lineage different from GL.

CD56+ T-GLPD was reported to exhibit an aggressive clinical course (5), but this was not true in this case, because the patient did not bear CD56+ GL. CD56+ T-GLPD does not always exhibit an aggressive clinical course, because my three patients with CD56+ T-GLPD did not show an aggressive deterioration (2). Further, some patients with...

Granular lymphocyte-proliferative disorders (GLPD) (1, 2), also known as lymphoproliferative disease of granular lymphocytes (LDGL) (3), or large granular lymphocyte (LGL) leukemia (4) are rare disorders, ranging from indolent benign proliferation of T granular lymphocytes (GL) or natural killer (NK) cells to aggressive proliferation. In T-GLPD, proliferating GL are either αβ T cells or γδ T cells, and its clinical course is usually indolent, with a rare exception of an aggressive clinical course (5). In NK-GLPD, its clinical course is sometimes aggressive, and the disease with an aggressive clinical course is called aggressive NK-cell leukemia.

Tanaka et al (6), reported in this journal a case of T-γδ GLPD complicated with pure red cell aplasia (PRCA) at presentation, and later with Epstein-Barr virus (EBV) infection and hemophagocytic syndrome (HPS). The disease was first diagnosed as PRCA, but T-γδ GLPD developed later, and PRCA was retrospectively considered to be caused by T-γδ GLPD. However, treatment for PRCA was ineffective.

The diagnosis of T-GLPD is not difficult when GL of 2,000 /μL or more are persistently present in the peripheral blood. The diagnosisis difficult when thenumber ofGL is lower. In such a condition, the presence of monoclonal proliferation of T-GL is required for diagnosis (7). The diagnosis of PRCA is not difficult when marked reticulocytopenia is present in the peripheral blood and erythroblasts are almost completely absent in the bone marrow. However, when small numbers of reticulocytes or erythroblasts are present, its diagnosis is difficult. In T-GLPD, these cells tend to remain in small numbers, and it is sometimes difficult to make a definite diagnosis of PRCA.

T-γδ GLPD is strongly suspected when circulating GL show CD3+CD4-CD8- or double negative phenotype. T-γδ GLPD was first described by us (8), and that patient was also associated with PRCA. This disorder is rare, and its association with PRCA is also rare. T-αβ GLPD and T-γδ GLPD in Japan are frequently associated with PRCA (1, 2). Although several theories have been proposed, the mechanism by which PRCA develops in T-αβ GLPD and T-γδ GLPD is not well understood.
CD56+ GL may have leukemic change of NK-like T-cell lymphoma (11), and they may be misdiagnosed as having GLPD.

References


© 2006 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imindex.html