HEMATOLOGIC MANIFESTATIONS IN HIV INFECTION

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Hematological abnormalities are among the most common complications of infection with HIV that are regularly encountered in the clinical setting. Cytopenias, particularly anemia and thrombocytopenia, non-Hodgkin's (NHL) and Hodgkin lymphomas (HL), and Kaposi sarcoma occur with increased frequency in patients infected with HIV (25-40% of all HIV-infected patients at some stage in their illness) and may be causative in almost one-third of HIV-related deaths. The development of these malignancies is related to a number of factors, including antigen stimulation, genetic abnormalities, cytokine dysregulation, immunosuppression and concurent infections with other viruses such human herpesvirus 8 (HHV-8) and Epstein-Barr virus (EBV), which foster malignant transformation. Coagulation abnormalities are occasionally a clinical problem.

Aggressive lymphomas such as diffuse large B-cell lymphoma (DLBCL) and primary central nervous system lymphoma (PCNSL) have decreased since the introduction of combination antiretroviral therapy (CART), though these and other HIV-associated malignancies continue to have a major impact on the morbidity and mortality pf persons with HIV. Recently, because of highly active antiretroviral therapy (HAART), cytopenias are seen less frequently except in patients with advanced disease and in patients undergoing chemotherapy.

In HIV-infected patients, anemia is normochromic/normocytic and is due to suppression of marrow by virus or therapy, some patients with significant anemia requiring frequent transfusion. Eritropoietin administration is an alternative in patients with eritropoietin low levels. Microangiopathic hemolysis (and endothelial dysfunction with cytokine dysregulation) is associated with thrombotic thrombocytopenic purpura, whose treatment of choice is plasmapheresis or plasma exchange. A mild neutropenia is relatively common due to marrow suppression by virus or therapy and splenic sequestration, and may experience increased frequency of significant bacterial infections. G-CSF is the most widely used hematopoietic growth factor. Lymphopenia with CD4 decrease may be masked by CD8 lymphocytosis, and it is improved by antiviral therapy. Thrombocytopenia is common be decreased survival (immune distruction), suppression of marrow (virus, therapy) or splenic sequestration. Patient with ITP and HIV infection respond to steroid, intravenous immunoglobulins, vincristin monthly, and HAART.

The common HIV-associated lymphomas are DLBCL, which includes PCNSL, and Burkitt lymphoma (BL), whereas primary effusion lymphoma (PEL), plasmablastic lymphoma (especially of the oral cavity type) and classic HL are far less frequent; occasionally, follicular lymphoma and peripheral T-cell lymphoma can also be seen. The systemic HIV-associated NHL are tipically seen in advanced HIV infection (CD4<100 cells/μL), frequently involve extradodal sites, and constitutional B symptoms are common. The risk of systemic or primary CNS lymphoma in HIV-infected persons is closely associated with the CD4 count (<50 cells/μL), and usually is a late manifestation of AIDS. HIV-associated DLBCL is divided into centroblastic and immunoblastic variants. The neoplastic cells in PEL range from large immunoblastic to anaplastic large cell lymphoma-type cells. HIV-associated BL is divided into 3 separate entities: classic BL, BL with plasmacytoid differentiation, and "atypical" BL. Classic HL is mostly the mixed cellularity subtype, and EBV is positive in virtually all cases. EBV is the most commonly found oncogenic virus in HIV-associated lymphomas: nearly all cases of PCNSL and HL, 80-90% of DLBCL with immunoblastic features, most cases of PEL (in addition to HHV-8 which is present in all cases), 30-50% of BL, 50% of plasmablastic lymphoma cases.

Patients with CD4 count <100 cells/μL are at increased risk of serious opportunistic infections and death. PCNSL, PEL, plasmablastic lymphoma, and relapsed lymphoma are associated with a poor prognosis, and a median survival less than 1 year. In the pre-CART era, patients with HIV-associated lymphoma had a median survivals of 5-6 months. The outcome of HIV-associated lymphoma has undergone significant improvement in recent years because of widespread use of CART. Both DLBCL and BL are highly curable diseases for the most part.

The treatment of HIV-associated lymphoma has evolved in line with improved control of HIV replication and preservation of immune function. In NHL, HAART associated with combination systemic chemotherapy, and intrathecal therapy for prophylaxis of CNS lymphoma represent the standard of treatment; the role of rituximab is controversial. In PCNSL whole-brain radiotherapy in combination with corticosteroids offers a 2-4 months survival (due to opportunistic infections). For HL can be used ABVD with HAART combination.

Patients with HIV-associated malignancies remain at risk of treatment-related toxicity, major infectious complications (including tuberculosis and hepatitis B), and interaction between antiretroviral and chemotherapeutic agents necessitates careful attention to supportive care. The optimum therapy for many is still unclear, partially relating to the significant succes in the development of HAART therapy, which has prolonged the lives of patients with AIDS.