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VIRUS-ASSOCIATED LYMPHOMAS

Epidemiology

Virus-associated lymphomas are an heterogeneous group including different rare subtypes of NHL tipically related to a chronic infection. The major types of virus-associated lymphomas in Western countries include HCV- EBV- and HIV-related lymphomas, while HTLV1-related lymphomas are extremely rare. In Italy it is estimated that up to 10% of NHL may be related to HCV, both indolent lymphomas (mainly marginal-zone lymphomas) and aggressive lymphomas (mainly diffuse large B-cell lymphomas). EBV-related lymphomas include post-transplant lymphoproliferative diaseases (PTLD), Burkitt Lymphomas, EBV lymphoma of the elderly, extranodal NK-T nasal-type lymphoma. The most frequent lymphoma subtypes associated with HIV infection include diffuse large B-cell lymphomas, plasmablastic lymphomas and Burkitt lymphoma.

Signs and symptoms

The clinical presentation of virus-associated lymphoma depends on the specific histologic subtype of NHL and by the characteristics of the underlying infection. Given the general context of immunosuppression, a common additional feature is represented by secondary (bacterial) infection with fever. Systemic symptoms (loss of weight, fever, night sweats, fatigue) are as well commonly detected and may confound the clinical picture.

Diagnosis and risk stratification

The diagnosis of virus-related lymphoma requires both the histologic diagnosis of lymphoma and the demonstration of the underlying viral infection. EBV infection may be detected on the histological specimen by immunohistochemistry (EBER). In addition to a complete work-up for the specific NHL histotype, a comprehensive evaluation of viral infection should be performed. In HIV-related lymphoma the absolute number of CD4+ lymphocyte is of prognostic relevance. In HCV-related DLBCL the viral load (HCV-RNA) has been demonstrated to carry prognostic value.

Treatment

The choice of treatment depends on histologic subtype of NHL, on the stage and tumor burden and on the underlying viral infection. In EBV-related PTLD a cornerstone of treatment is represented by the anti-CD20 monoclonal antibody Rituximab, both as single agent and combined with chemotherapy (R-CHOP). In HCV-related indolent lymphomas without immediate need of conventional immunochemotherapy (absence of bulky or symptomatic disease) the use of direct-acting antivirale (DAAs) alone is nowdays the standard primary treatment. In HCV-associated DLBCL the use of DAAs concurrently or subsequently with immunochemotherapy (R-CHOP) has been demonstrated to be feasible and to ameliorate the outcome of patients. In EBV-related extranodal nasal-type NK/T lymphoma an intensive chemotherapeutic regimen including L-asparaginase (SMILE) is recommended.