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Peripheral T-cell lymphoma – Not otherwise specified

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Abstract

Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) does correspond to a heterogeneous group of nodal and extranodal mature T-cell lymphomas, with a low prevalence in Western countries. PTCL-NOS accounts for about 25% of all PTCL, which represent over 15% of all lymphomas. In the lymph node, PTCL-NOS shows paracortical or diffuse infiltrates with effacement of the normal architecture, with a broad cytological spectrum and a frequently observed inflammatory background. Some morphological variants include: lymphoepithelioid or Lennert's type, T-zone, and follicular. PTCL-NOS is characterized by an aberrant T-cell phenotype, with frequent loss of CD5 and CD7. A CD4+/CD8− phenotype predominates in nodal cases. CD4/CD8 +/+ or −/− is at times seen, as is CD8, CD56 and cytotoxic granule expression. Ki-67 rate is typically high. TCR β-chain is usually expressed; *TCR* genes are most often clonally rearranged.

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PTCL-NOS typically occurs in adults (median age 55–60 years), with a higher prevalence in males. It presents more often as disseminated disease, occasionally with eosinophilia, pruritis or hemophagocytic syndrome. Patients often have B symptoms, generalized lymphadenopathy, bone marrow infiltration, and extranodal involvement, with high or high-intermediate IPI score in 50–70% of cases. Prognosis is poor, with a 5-year OS of 20–30%. Some variables, like ST2(L), CXCR5, CXCR3, EBV infection, cytotoxic granule expression, high proliferative index, NF-κB expression, were proposed as prognostic indicators, but the IPI score, and its variant called PIT, remains the most effective prognostic factor.

Patients with PTCL-NOS should be treated with anthracycline-containing chemotherapy, followed by radiotherapy in cases of stage I–II disease. This strategy is associated with an overall response rate higher than 60%, but the 5-year overall survival is only 20–30%. Upfront high-dose chemotherapy supported by autologous or allogeneic SCT is an investigational approach, with a 4-year overall survival of about 40%. Patients with chemosensitive relapse respond favorably to high-dose chemotherapy and ASCT, with long-term survival rates of 35–45%. Graft-versus-lymphoma effect following allogeneic SCT has been observed; and reduced intensity conditioning emerges as an attractive strategy for frail patients. Most patients with PTCL-NOS are enrolled in prospective trials to explore new approaches, and new agents, like gemcitabine, alemtuzumab and pralatrexate, are being investigated.

Keywords: Peripheral T-cell lymphomas; CD52; Allogeneic transplant; Reduced intensity conditioning

1. General information

1.1. Definition

In the current WHO Classification [1], peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) does correspond to a heterogeneous group of nodal and extranodal mature T-cell lymphomas, which does not fit with any of the specifically defined entities derived from mature T lymphocytes. This is a group of lymphomas uncommon in Western countries, whose classification is very difficult because of the lack of reliable immunophenotypic markers of T-cell malignancies. Some distinct clinical syndromes with recognizable morphologic features of T-cell malignancies have been described, and they should be considered separately. Peripheral T-cells in various stages of transformation have been postulated as the normal-cell counterparts for peripheral T-cell lymphomas (PTCL).

1.2. Incidence and risk factors

PTCL constitute less than 15% of all NHLs in the United States and Europe but they are more common in the Far East. In a recent international collaborative effort, the most common diagnoses of PTCL by the World Health Organization classification for lymphomas [1] were PTCL-NOS (25.9%), angioimmunoblastic T-cell lymphoma (18%), systemic anaplastic large-cell lymphoma (12.1%) and extranodal NK/T-cell lymphoma, nasal type (10.4%) [2]. The present article will focus on PTCL-NOS.

No risk factors have been clearly identified in PTCL-NOS. Epstein-Barr virus (EBV) is positive in approximately 30% of cases of PTCL-NOS, although the role in pathogenesis is unknown. No particular correlation between PTCL-NOS and inherited immunological deficiency disease, or other immunological disorders has been reported. There are no convincing data regarding the role of chronic antigenic stimulation in the genesis of PTCL. However, the inflammatory background and the follicular dendritic cell proliferation observed in these malignancies suggest a pathogenesis mediated by different chemokines. Several chemical substances, such as solvents, pesticides and fertilizers as well as dusts and particles, hair, smoking and diet, have been suggested as possible aetiological factors in general for non-Hodgkin lymphoma (NHL) [3]. Among other pesticides, 2,4-D [4], organophosphate insecticides [5] and phenoxy herbicides [6] have been suggested as aetiological agents. Although the highest risk is related to the occurrence of large-cell lymphomas, all histologic subtypes of NHL occur in individuals whose work involves application of pesticides [7,8].

2. Pathology and biology

2.1. Morphology

In the lymph node, PTCL-NOS shows paracortical or diffuse infiltrates with effacement of the normal architecture. The cytological spectrum is extremely broad, from highly polymorphous to monomorphous. Clear cells and Reed–Sternberg-like cells can also be seen. High endothelial venules may be increased. An inflammatory background is often present. The differential diagnosis with angioimmunoblastic T-cell lymphoma (AITL) may require extensive immunophenotyping. In the new WHO classification, some morphological variants have been included: lymphoepithelioid or Lennert's type, T-zone and follicular. In particular, the latter consists of atypical clear cells forming intrafollicular aggregates (mimicking follicular lymphoma), small nodular aggregates in a background of progressively transformed germinal centres (mimicking nodular lymphocyte-predominant Hodgkin lymphoma) or enlarged perifollicular zones/nodular aggregates surrounding hyperplastic follicles (mimicking nodal marginal zone lymphoma). Although this variant shows a follicular T-helper derivation, it has not been included