Peripheral T-Cell Non-Hodgkin Lymphoma

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INTRODUCTION AND CLASSIFICATION

Peripheral T-cell lymphoma (PTCL) represents a heterogeneous collection of mature T- and NK-cell neoplasms. Most are clinically aggressive and all are uncommon. The descriptor “peripheral” does not refer to an anatomic location but rather the stage of development of the T cell. PTCLs derive from mature, post-thymic T cells as opposed to T-cell acute lymphoblastic leukemia/lymphoma, which derives from immature T cells. The most recent World Health Organization (WHO) classification system for PTCL is shown in Table 1. The histologies are categorized by clinical behavior, with the nodal, extranodal, and leukemic variants grouped together; however, these distinctions are not absolute, and there is substantial overlap in sites of involvement. This review will not focus on cutaneous T-cell lymphoma, which is clinically and biologically distinct from PTCL.

EPIDEMIOLOGY

PTCL accounts for 5% to 10% of all cases of non-Hodgkin lymphoma (NHL) diagnosed in North America. Table 2 shows the relative frequency of various PTCL histologies. In North America and Western Europe, the most common histologies are PTCL–not otherwise specified (NOS); anaplastic large cell lymphoma, T/null-cell type (ALCL); and angioimmunoblastic T-cell lymphoma (AILT). In parts of Asia, however, extranodal NK/T-cell lymphoma, nasal type (NK/TCL) and adult T-cell leukemia/lymphoma (ATLL) are quite prevalent. The epidemiology of individual subtypes will be discussed in more detail in later sections.

CLINICAL AND PATHOLOGIC FEATURES

The median age at diagnosis for most histologies is approximately 60 years, though histologies such as ALCL and hepatosplenic T-cell lymphoma affect adolescents and young adults. There is a 1.5:1 male predominance. Approximately 60% of patients present with stage IV disease. Fifty-six percent of patients will have nodal and extranodal involvement, while 30% have extranodal disease only. Cutaneous involvement is far more common than with B-cell NHL. The majority of patients will have an elevated serum lactate dehydrogenase (LDH), and a substantial percentage will have B symptoms of fever, night sweats, and/or weight loss. With some notable exceptions discussed later, there are few defined risk factors for PTCL.

Many types of PTCL can be confused clinically and pathologically with other types of lymphoma. For instance, PTCL can be confused with T-cell–rich diffuse large B-cell lymphoma, and often only extremely sensitive techniques such as T-cell receptor (TCR) gene rearrangement studies can distinguish the 2 entities. PTCL can also be confused with lymphomatoid granulomatosis, which like PTCL often involves the skin and is Epstein-Barr virus (EBV)-positive. ALCL commonly affects young patients, as do mediastinal diffuse large B-cell lymphoma and Hodgkin lymphoma, resulting in diagnostic confusion. Adding to the confusion, both Hodgkin lymphoma and ALCL can express CD30. One study demonstrated that the concordance of PTCL diagnoses among expert pathologists using histologic criteria alone was extremely low, with concordance rates of 46% for ALCL and 41% for PTCL-NOS. A fairly high level of discordance remained even with the addition of immunohistochemistry: 85% for ALCL and 86% for PTCL-NOS. Specific immunophenotypes for various PTCL histologies are discussed later in the article. In general, however, PTCLs express a constellation of common T-cell antigens such as CD2, CD3, CD5, and CD7. One or more of these antigens, however, is often not expressed, particularly CD5 or CD7. More PTCLs will express CD4 (Thelper phenotype) than CD8 (cytotoxic phenotype), but some may express both or neither. B-cell antigens such as CD20 or PAX5 are generally absent but have been reported in rare cases.

Unlike B-cell lymphomas, there are few cytogenetic abnormalities characteristic of most PTCL subtypes. The general lack of recurring cytogenetic abnormalities in PTCL eliminates a valuable diagnostic tool. Approximately 85% of PTCL cases will have a clonal TCR gene rearrangement. The presence or absence of a clonal TCR rearrangement does not definitively establish or exclude the diagnosis of PTCL and must be considered in the broader clinicopathologic context. Clonal TCR gene rearrangements have been reported in autoimmune and infectious conditions.