# T-cell Prolymphocytic Leukemia

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**KEYWORDS**

• T-cell prolymphocytic leukemia • T-cell • Leukemia • Alemtuzumab

**KEY POINTS**

- T-cell prolymphocytic leukemia is a rare and aggressive leukemia.
- The current therapeutic approach includes immunotherapy followed by a hematopoietic stem cell transplant in eligible cases.
- Genomic and molecular studies may increase our understanding of this disease, with the promise of novel therapeutic options.

## INTRODUCTION

T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive T-cell malignancy first described by Catovsky and colleagues[1] more than 40 years ago. Although termed 'prolymphocytic,' the disease is characterized by the proliferation of post-thymic T-lymphocytes. T-PLL can be distinguished from other lymphoid diseases by the evaluation and integration of clinical features, morphology, immunophenotyping, cyto-genetics, and molecular features. The current therapeutic approach relies on immunotherapy followed by a hematopoietic stem cell transplant (HSCT) in selected cases. Clinical outcomes are generally poor, although insights from genomic and molecular studies may increase our understanding of this disease, with the promise of additional effective therapeutic options.

## EPIDEMIOLOGY

T-PLL accounts for 2% of mature lymphocytic leukemia in adults.[2] The median age at presentation is 61 years and there is a male predominance.[3] Three cases of children with T-PLL have been reported, although incomplete diagnostics were reported in

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1 case.[4–6] Patients with ataxia telangiectasia are at increased risk of developing T-PLL (as well as other lymphoid malignancies) with a younger median age at presentation of approximately 31 years.[7] An individual with Nijmegen breakage syndrome developing T-PLL has been reported.[8] Aside from these findings, no other genetic or environmental risk factor has been robustly identified thus far.

## CLINICAL FEATURES

Most patients with T-PLL present with a brief history of B symptoms, hepatosplenomegaly (splenomegaly is often massive) and a marked lymphocytosis (typically >100 $\times$ $10^9$/l).[3] Lymphadenopathy, although present in a majority of patients, is rarely bulky. Anemia and thrombocytopenia are seen in up to one-half of patients.[3] Erythematous or nodular skin rashes involving the trunk or limbs, peripheral edema, and pleuroperitoneal effusions may be seen in up to one-quarter of patients with T-PLL.[9] T-PLL may also involve the face, where it manifests as purpura and edema, often in a periorbital distribution.[10,11] Central nervous system involvement is rare. A minority of patients have no symptoms at diagnosis. This 'indolent' phase can persist for a variable length of time, and can be as long as years. Disease progression may be rapid when it occurs.

## LABORATORY DIAGNOSIS

The diagnosis of T-PLL relies on an integrated evaluation of clinical features, peripheral blood, morphology, immunophenotyping, bone marrow, cytogenetics, and molecular tests.

### *Morphology*

The 'typical' morphology observed in 75% of cases consists of medium sized lymphoid cells with partial chromatin condensation, a visible nucleolus, and a round or oval nucleus (**Fig. 1**).[2,9] A slight basophilic cytoplasm is present, often with protrusions and an absence of granules. A 'small cell variant' is seen in 20% of cases. These small cells possess condensed chromatin with a small nucleolus (observed only by electron microscopy). Finally, the 'cerebriform (Sézary cell–like) variant' is seen in

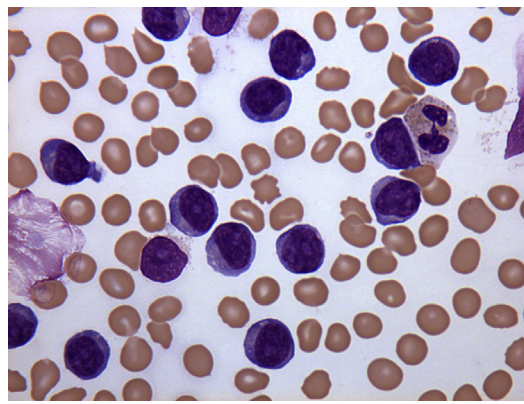

**Fig. 1.** Peripheral blood smear from a patient with T-prolymphocytic leukemia demonstrating a 'typical' morphology. The T-prolymphocytic leukemia cells are medium sized lymphoid cells with partial chromatin condensation and a visible nucleolus. The cytoplasm is basophilic with protrusions and an absence of granules.