

Leukaemia Section

Mini Review

T-cell prolymphocytic leukemia (T-PLL)

Martin Yuille

Institute of Cancer Research, Academic Department of Haematology and Cytogenetics, Haddow Laboratories, 15 Cotswold Road, Sutton, Surrey SM2 5NG, UK (MY)

Published in Atlas Database: October 1999

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/TPLL.html>
DOI: 10.4267/2042/37557

This article is an update of: Michaux L. T-cell prolymphocytic leukemia (T-PLL). *Atlas Genet Cytogenet Oncol Haematol.* 1997;1(2):83-84.

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Clinics and pathology

Disease

Chronic T-cell lymphoproliferative syndrome.

Phenotype/cell stem origin

Disease affecting mature T-cells; T-cell prolymphocytes usually express CD3, CD5 and CD7; they have either a T-helper (CD4+/CD8-) or a T-suppressor (CD4-/CD8+) phenotype; a small number of cases may co-express CD4 and CD8; this finding is more prevalent in the small cell variant of T-PLL than in classic T-PLL.

Epidemiology

Very rare disease; represents 20% of prolymphocytic leukemias; the disease occurs at advanced age, typically in the 7th or 8th decade; slight male predominance.

Clinics

Splenomegaly is common; lymphadenopathy at presentation is unusual but more frequent than in B-PLL; blood data: high leucocyte counts usually exceeding $100 \times 10^9/l$; T-cell prolymphocytes have the same morphologic features than B-cell prolymphocytes; a small cell variant of T-PLL has been described.

Prognosis

Evolution: progresses rapidly and is generally more aggressive than B-PLL; prognosis: poor response to chemotherapy is observed; median survival is approximately 7 months from diagnosis.

Cytogenetics

Cytogenetics morphological

Few cases have been reported in the literature.

So far; karyotypes are usually complex.

14q11 abnormalities: very frequent, either as an inv(14)(q11q32) or as a translocation t(14;14)(q11;q32); another reported change involving 14q11 is a translocation t(X;14)(q28;q11), similar to the translocation observed in ataxia-telangiectasia, involving the Mature T-cell Prolymphocyte 1 (MTCPI) gene located at Xq28.

Other recurrent changes involve chromosome 8 either as i(8)(q10) or as der(8) t(8;8).

Finally, some aberrations involving 12p have been reported.

Genes involved and proteins

Note

As with other T-cell neoplasms, T-PLL exhibits clonal rearrangement of T-cell receptor genes; translocation t(X;14)(q28;q11) may result into fusion of MTCPI with TRA/D genes; finally, the TCL1 locus on chromosome 14q32 might also be involved.

In Ataxia Telangiectasia- a rare recessive pleiotropic disease (including elevated cancer predisposition) mapping to 11q23 and caused by mutations of the ATM gene - a recurrent malignancy is observed that is similar to T-PLL; its frequency in A-T patients is higher than in the non-A-T related form; A-T related TPLL has a similar course, a similar immunophenotype and similar cytogenetics (with the notable exception

that 11q23 breakpoints are recurrent in the sporadic but not the A-T related form of the disease); an initial report of ATM mutations in T-PLL demonstrated the principle that ATM was a candidate cancer gene in sporadic forms of malignancies prevalent in A-T; the identification of lesions in ATM associated with T-PLL has shown that:

Homozygous truncating mutations are present in some cases; this suggests ATM can appear to act like a conventional tumour suppressor with biallelic inactivation in the tumour cell.

Missense mutations cluster in the carboxy-terminal phosphatidyl-3-kinase (PIK) domain; this suggests impairment of this domain can contribute to - and may constitute a distinct step in - tumourigenesis.

Rearrangement of the gene is frequent; some rearrangements are consistent with a translocation event, in agreement with cytogenetic data implicating 11q23 in T-PLL; others involve transposition of a segment of the ATM gene elsewhere in the genome.

One allele only is mutated (by rearrangement) in some cases; this is probably not associated with a concomitant epigenetic event such as abnormal promoter methylation.

No T-PLL case has been reported with germline ATM mutation; this may reflect the small numbers investigated; all the same, the hypothesis is excluded that this rare disease is due solely to germline ATM mutation.

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This article should be referenced as such:

Yuille M. T-cell prolymphocytic leukemia (T-PLL). *Atlas Genet Cytogenet Oncol Haematol*. 1999; 3(4):187-188.
