

T-cell large granular lymphocyte leukaemia

Clinics and Pathology

Disease	T-cell large granular lymphocyte leukaemia (T-LGL)
Note	T-LGL is also called T-cell chronic lymphocytic leukaemia, Tgamma lymphoproliferative disorder and large granular lymphocytosis.
Phenotype / cell stem origin	Clonal proliferation of CD3+ CD4- CD8+ CD56± CD57+ TCRab+ mature T cells with rearranged TCRab genes; rarely, variable expression of both CD4 and CD8 or expression of TCRgd.
Etiology	Sometimes associated with B cell chronic lymphoproliferative disorder such as hairy cell leukaemia and chronic lymphocytic leukaemia; rarely may follow solid organ transplantation.
Epidemiology	2-5% of all chronic lymphoproliferative disorders in the West, and 5-6% in the Chinese population.
Clinics	Often asymptomatic, and incidentally found to have lymphocytosis and moderate splenomegaly; frequently accompanied by severe neutropenia (sometimes with recurrent infections); anaemia due to red cell aplasia, and sometimes thrombocytopenia; associated with immune mediated disturbances such as cytopenia, rheumatoid arthritis, Sjogren's syndrome, circulating autoantibodies and immune complexes, and hypergammaglobulinaemia; indolent clinical course.
Cytology	Large granular lymphocytes (LGLs) with the nucleus of a small lymphocyte but abundant cytoplasm and fine or coarse azurophilic granules; ultrastructural examination may reveal characteristic parallel tubular arrays; the LGLs are often $>2 \times 10^9/L$.
Pathology	Involvement of blood, bone marrow, liver and spleen; lymphadenopathy is very rare; not associated with EBV or HTLV I/II. <p>In the bone marrow, the infiltration is usually interstitial with occasional focal aggregates; in some patients, the involvement may be minimal and not readily detectable on histologic sections; the lymphocytes are small to medium-sized with abundant cytoplasm, and the granules are not apparent in histologic sections.</p> <p>In the spleen, the red pulp is expanded; the infiltrate is predominantly sinusoidal but may also involve the pulp cords; in the liver, there is a sinusoidal pattern of infiltration with portal involvement in severe cases; in the lymph node, the infiltrate primarily involves the paracortical regions and medullary cord</p>
Treatment	Cyclosporin A (particularly for pure red cell aplasia and other immune mediated disturbances); other treatments include methotrexate, cyclophosphamide, chlorambucil, corticosteroids and deoxycoformycin (pentostatin) with variable success; and splenectomy for grossly enlarged and incapacitating splenomegaly.
Prognosis	An indolent disease, with morbidity mostly attributed to neutropenia or anaemia; mortality is uncommon; an aggressive form of T-LGL with

dysregulated expression of [Fas ligand](#) has been reported; large cell transformation has also rarely been described.

Cytogenetics

Cytogenetics Few cases (probably around 60) have been reported in the literature :
Morphological The apparent lack of cytogenetic data probably arises from rarity of

the disease and difficulty in obtaining metaphases from the terminally differentiated T-cells.

Some cases have probably been included under the category of ³T-cell chronic lymphocytic leukaemia² or other T-cell lymphoproliferative disorders.

The most frequent structural abnormality appears to be deletion of the long arm of chromosome 6, [del\(6q\)](#), with 2 cases of del(6)(q21) and 1 case of del(6)(q21q25) reported as part of complex karyotypic aberrations, and two cases of del(6)(q21q26) as the sole chromosomal abnormality.

Genes involved and Proteins

Note As with other T-cell lymphoproliferative disorders, T-LGL exhibits clonal rearrangement of the TCR genes; in most cases, the [TCRA](#) [TCRD](#) genes are rearranged, but rarely, the [TCRG](#) gene is rearranged while the [TCRB](#) gene is in germline configuration.

Unlike other T-cell malignancies, karyotypic aberrations in T-LGL rarely involve the TCR gene loci; so far, only one case each with possible involvement of the TCRG gene at 7p14-p15 in an inv(7)(p15q22) and the TCR A/D genes at 14q11 in an [inv\(14\)\(q11q32\)](#) has been described.

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