Leukaemia Section
Mini Review

T-cell large granular lymphocyte leukaemia
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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 >2x10⁹/L.

Pathology
Involvement of blood, bone marrow, liver and spleen; lymphadenopathy is very rare; not associated with EBV or HTLV I/II.
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.
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.

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 morphological**

Few cases (probably around 60) have been reported in the literature:
- 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 been primarily included under the category of “T-cell chronic lymphocytic leukaemia” 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.

**References**


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