

Leukaemia Section

Mini Review

Mycosis fungoides/Sezary's syndrome

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Clinics and pathology

Phenotype/cell stem origin

The cell of origin is a peripheral CD4+ T-lymphocyte. The immunophenotype of the neoplastic clone is CD3+ CD5+ CD4+ CD25-. Rare CD8+/CD4- cases were observed. Clonality studies demonstrated a monoclonal rearrangement of the T-cell receptor (TCR).

Epidemiology

This is the most common form of cutaneous T-cell lymphoma. The annual incidence is around 0,3 cases per 100.000 in western countries. The median age at diagnosis is between 55 and 60 years, with a 2/1 male-to-female ratio.

Clinics

The disease usually shows cutaneous patches, plaques, tumors or generalized erythroderma (Mycosis fungoides). Pruritus is a common symptom. Extracutaneous manifestations are more frequent in the presence of locally advanced disease (cutaneous tumors). The presence of erythroderma with circulating malignant cells (Sezary's cells) in the peripheral blood (PB) and in the bone marrow is consistent with Sezary's syndrome, which is usually associated with lymphadenopathy. Other sites of involvement in disseminated disease include the lungs, the gastrointestinal tract, the liver and the central nervous system.

Pathology

The tumor cell is a small lymphocyte with cerebriform nucleus, clumped chromatin and inconspicuous nucleoli. Epidermotropism by neoplastic CD4+ lymphocytes with the formation of Pautrier's microabscesses is the hallmark of the disease.

Treatment

Phototherapy, radiation therapy and alpha interferon are the mainstay of treatment of cutaneous disease. Chemotherapy using various regimens was employed in cases displaying disseminated disease and in Sezary's syndrome with limited success.

Prognosis

The clinical stage is the most important indicator. Patient with limited cutaneous disease have an excellent prognosis. Patient with cutaneous tumours, generalized erythroderma, with Sezary's syndrome or extracutaneous disease usually have a short survival, ranging from 1 to 4 years.

Cytogenetics

Note

The neoplastic cells have a low mitotic index and stimulation with phytohemagglutinin and interleuchin-2 (IL-2) and IL-7 were used. The probability of detecting an abnormal clone largely correlates with the clinical stage, being very low in those patents with limited disease. Chromosome aberrations are detectable by conventional cytogenetic analysis in up to 60% of the cases with PB involvement (Sezary' syndrome). Two recurrent structural changes were identified, namely der(1)t(1;10)(p2;q2) and der(14)t(14;15)(q;q?). Other recurrent abnormalities include loss of chromosome material at 1p22 and 1p36, involvement of chromosome 10 and 17p. The involvement of regions containing the T-cell receptor subunits, were observed rarely.

Cytogenetics molecular

The absence of breaks involving the TCR regions was confirmed by fluorescence in situ hybridization.

Comparative genomic hybridization studies showed chromosome imbalances in 56% of the cases. DNA losses occurred at 1p (38%), 17p (21%), 10q (15%), and 19 (15%). DNA gains involved 4q (18%), 18 (15%) and 17q (12%). 1p33-36 and 10q26 may represent regions of minimal recurrent deletion. On chromosome 1p, two regions of minimal common deletion at 1p36 (D1S228 marker) and 1p22 (D1S2766 marker) were defined by allelotyping.

The microarray technology allowed for the identification of gains of distinct oncogene copy numbers in the majority of cases: RAF1 at 3p25; CTSB at 8p22; PAK1 at 11q13; and JUNB at 19p13. Amplification of the latter oncogene was found in some cases with strong nuclear expression of the corresponding protein product.

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