

## Hairy Cell Leukemia (HCL) and Hairy Cell Leukemia Variant (HCL-V)

### Clinics and Pathology

Phenotype / cell stem origin	cells from hairy cell leukemia (HCL) and hairy cell leukemia variant (HCL-V) have a distinct immunophenotype which is of a mature but not terminally differentiated activated B-cell. Although some similarities exist between these two conditions like the expression of B-cell activation marker CD103, CD11c and IgG heavy chain expression, differences exist between these two diseases. HCL is positive for CD25 (anti IL2 receptor) and HC2 while HCL-V is negative for CD25 and HC2.
Epidemiology	first described as leukaemic reticulo endotheliosis, HCL predominantly affects middle aged males (male /female ratio = 4) while male predominance is not observed in HCL-V but they are older
Clinics	HCL patients present with splenomegaly, cytopenia(s) and variable proportions of circulating hairy cells. Monocytopenia is constant, lymphadenopathy is rare and the bone marrow is "dry tap" in most cases. HCL-V patients show most of the above features but have high white blood cell counts normal numbers of monocytes and aspirable bone marrow.
Cytology	The typical hairy cell is large in size, has an eccentric and sometimes kidney shaped nucleus and abundant cytoplasm with long villi which is associated with alterations in the cytoskeletal architecture. HCL-V has a central round nucleus, a prominent nucleolus, cytoplasmic villi and is intermediate in morphology between HCL and <a href="#">B-prolymphocytic leukaemia</a> . HCL cells show strong acid phosphatase reaction which is resistant to tartaric acid.
Pathology	The bone marrow and spleen histology is identical in HCL and HCL-V. The bone marrow shows a distinct pattern of interstitial infiltration by lymphoid cells with spaces among them ('fried egg ' pattern). Reticulin is invariably increased in HCL but not in HCL-V. Spleen histology shows expansion and infiltration of the red pulp with naked white pulp.
Treatment	Interferon alpha produces good partial responses in HCL but invariably the disease relapses. The purine analogs 2 deoxycorformycin and 2-deoxyadenosine induce responses in >95% of patients, most of them complete and durable. HCL-V is not responsive to the above treatments with only half achieving transient partial responses to the purine analogs with splenectomy being the best palliative therapeutic measure.

- Evolution** HCL and HCL-V are characterised by a chronic clinical course with the symptoms deriving from cytopenias, and abdominal distension due to splenomegaly. Few patients undergo transformation.
- Prognosis** HCL has a good prognosis .In a large series 80% of patients survived at 12 years.  
HCL -V has a poorer prognosis and in the only largest series reported the median survival is 9 years.

## Cytogenetics

**Cytogenetics** Several reports describe nonclonal or oligoclonal abnormalities in Morphological HCL and in some with clonal abnormalities translocations involving the 14q32.3 the site of the [IGH](#) locus, rearrangements of 14q22-24 and abnormalities of chromosomes 11 and 12 have been described. One study reported a 40% incidence of chromosome 5 abnormalities.

HCL-V is often characterised by a complex karyotype.

Translocation [t\(14;18\)\(q32;q21\)](#) observed in [follicular lymphoma](#) and [t\(2;8\)\(p12;q24\)](#) observed in variant [Burkitt lymphoma](#) have been reported in HCL-V.

**Cytogenetics** Deletion of the [p53](#) tumour suppressor gene mapping to chromosome Molecular 17p13 occurs with a high incidence in both HCL and HCL-V. But a significant difference is observed in the proportion of cells with a deleted allele in HCL-V compared to HCL(P<0.01) and correlates with the well known tendency for transformation and poor response to therapy characteristic of HCL-V

## Genes involved and Proteins

**Note** Molecular studies suggest that hairy cells have aberrations in the constant region of the IgM intron which could be responsible for errors in class switching and explain the pattern of Ig heavy chain expression in HCL which does not fit the the class switching model which occurs in normal B-cell differentiation.

Over expression of the [BCL-1](#) gene on chromosome 11q13 and encoding Cyclin D-1 has been demonstrated by Northern blot for RNA and Western blot and immunocytochemistry for protein expression in over 70% of patients with HCL investigated (including 1HCL-V), but with no evidence for chromosomal or molecular rearrangement of the BCL-1 locus.

The steady state m-RNA and protein levels of the leucocyte specific gene pp52 coding for a cytoskeletal protein and binding to filamentous actin (F-actin) is elevated in HCL.The gene maps to chromosome 11p15.5. Colocalisation of pp52 with F-actin occurs at the base of the villi. Interferon alpha (IFN alpha) a highly effective agent in the treatment of HCL has been shown to reduce pp52 m- RNA and blunt the villi.

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