

Cancer Prone Disease Section

Mini Review

Dyskeratosis congenita (DKC)

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Identity

Alias

Zinsser Cole Engeman syndrome ; Hoyeraal Hreidarsson syndrome

Note

Hoyeraal Hreidarsson syndrome is a more severe variant.

Inheritance

X-linked recessive form constitute more than 80% of cases and 91% of DKC patients are males.

Clinics

Note

The disease is characterised by a multisystem failure, affecting essentially tissues with a high proliferation rate: skin, mucous membranes, bone marrow.

Phenotype and clinics

Short stature (16%).

Cutaneous signs:

Hyperpigmentation, telangiectasia, atrophy (poikiloderma);

Dystrophic nails and palmoplantar keratoderma, hyperhidrosis;

Mucosal leucoplakia;

Dental caries or loss (18%);

Blepharitis, conjunctivitis, epiphora (36%);

Sparse eyebrows / eyelashes;

Alopecia (16%);

Urethral stricture, phimosis (7%).

Bone marrow failure, peripheral pancytopenia (93%).

Others signs:

Oesophageal stricture (14%);

Pulmonary fibrosis (19%);

Liver cirrhosis (5%);

Hypogonadism (8%);

Abnormal bone trabeculation, osteoporosis (4%)

Immune abnormalities: reduced or increased immunoglobulin level, T- and/or B-lymphocyte deficiency.

Mild Mental Retardation, learning difficulties (21%).

Prognosis

The major part of patients die before 20 years, mainly from infectious complications of immune deficiency.

90% of patients have haematological abnormalities when 30 year-old, and bone marrow failure is the main cause of early morbidity in 71% of cases. It can evolve toward aplastic anemia or myelodysplasia.

The mucosal leucoplakia can transform into spinocellular carcinoma.

Other carcinomas can develop during the third decade of life: lung, colon, larynx, oesophagus, pancreas, Hodgkin disease.

Cytogenetics

Inborn conditions

An excess of chromosome breakages has been reported in DKC but this finding is controversial; not frequently, rearrangements comparable to what is observed in Fanconi anemia are described: chromosome instability and breakage (di- and trivalent chromosomes), either spontaneous or induced by clastogenic agents (mitomycin C). Cells with a high turn-over (skin fibroblasts, lymphocytes, bone marrow cells, digestive tract) would be particularly sensitive to chromosome rearrangements and DNA damage.



Leucokeratosis of the tongue, poikiloderma of the foot and the trunk, onychopathy. Courtesy Daniel Wallach.

Genes involved and proteins

DKC1

Location

Xq28

Protein

Description: DKC1 encodes for Dyskerin, a 514 aminoacid protein

Expression: Widespread tissue repartition.

Function: Dyskerin is the nucleolar pseudouridine synthetase component of the box H+ACA snoRNAs. It also interacts with the RNA component of human telomerase. Chromosome instability could be linked to increased telomere shortening due to an alteration in telomerase-dependant telomere maintenance. DKC1 plays a role in ribosomal RNA synthesis and in ribosome biogenesis; DKC is a human ribosomopathy.

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