Rothmund-Thomson syndrome (RTS)

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Identity

Alias: Poikiloderma atrophicans and cataract

Note
Is a chromosomal instability syndrome with an increased risk of cancers.

Inheritance
Autosomal recessive; rare geno-dermatosis with increased frequency in females; 260 cases reported in the English medical literature.

Clinics

Note
Clinical expression highly variable.

Phenotype and clinics

Main features include:
-Growth retardation.
-Skin defects appearing within the first year of life (90%) and persisting throughout life: atrophic dermatosis, poikiloderma, hyperpigmentation, telangiectasia.
-Sparse hair which may progress to partial or total alopecia: dystrophic nails.
-Photosensitivity.
-Congenital skeletal defects - hypoplasia or absence of the radii and thumbs, osteopenia, cystic or sclerotic changes of the long bones - (>50%); bone age lower than chronological age.
-Juvenile cataract, corneal dystrophy (50%).
-Hypodontia.
-Hypogonadism (25%).
-Proportionate short stature.
-Premature aging.

Detailed definition of the clinical profile in a contemporary cohort of 41 RTS patients evidences some differences in the distribution of the clinical findings (figure 1), which should be kept into account to optimize diagnostic criteria.

Diagnosis: the diagnosis is difficult before the development of the erythema; differential diagnosis with:
-Werner syndrome,
-Dyskeratosis congenita,
-Cockayne syndrome,
-Bloom syndrome,
-Fanconi anaemia,
-Anhidrotic ectodermal dysplasia.

Neoplastic risk

Patients have an enhanced risk of bone cancer, specifically osteosarcoma (30 out of 300 - 10% - in the literature) and nonmelanoma skin cancers (squamous cell carcinoma, basal cell carcinoma) with an estimated prevalence around 5%.

Etiology: deficiency of RECQL4 helicase (see below), a protein involved in some aspect of replication and transcription, repair and recombination may suggest a mutational mechanism for cancer development, but the specificity for mesenchymal tumors is currently unknown.

Treatment

Only protection against sunlight is possible by means of sunscreens with both UVA and UVB protection; dermatologic therapies; surgical correction of skeletal malformations and cataracts;
regular and careful work-up of signs and symptoms of both cutaneous and internal malignancy; caution is warranted in administering chemotherapy to affected individuals due to their sensitivity to chemotherapeutic agents.

**Evolution**
The disease tends to progress during the first years of life, but becomes static so that patients may have a normal lifespan; the mortality from neoplastic disease during the second or third decade is very significantly increased.

**Cytogenetics**

**Inborn conditions**
Spontaneous/induced chromatid breaks were found increased in only a very few studies; In contrast with (mainly negative) chromatid results, consistent clonal/non clonal structural chromosomal abnormalities
were evidenced in most studies, often involving chromosome 8, in cultured lymphocytes and in fibroblasts; low frequency trisomy 8 mosaicism has been reported in both lymphocyte and primary fibroblast cultures as well as in uncultured blood and buccal smears, indicating this characteristic chromosomal abnormality is present in vivo; a propensity to centromere misdivision with development of clones carrying isochromosomes, such as i(8q), i(8p), i(12p), i(12q) is peculiar of RTS.

Cytogenetics of cancer
Marked chromosomal instability has been detected in mesenchymal tumours developed by RTS sibs.

Other findings
Note
Reduced unscheduled DNA synthesis, 37% of normal after exposure to ultraviolet C or gamma irradiation.

Genes involved and proteins
Note
Mutations of RECQL4 gene, a member of the RECQ helicase gene family, have been identified in a limited number of RTS patients. Molecular testing is available on a research basis and useful in confirming the diagnosis in suspected RTS patients carrying RECQL4 mutations.

References


This article should be referenced as such: