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Cancer Prone Disease Section

Mini Review

Rothmund-Thomson syndrome (RTS)

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Identity

Alias: Poikiloderma atrophicans and cataract

Note

RTS is a chromosomal instability syndrome with an increased risk of cancers.

Inheritance

Autosomal recessive; rare geno-dermatosis with increased frequency in females; more than 200 cases reviewed in the medical literature.

Clinics

Phenotype and clinics

Clinical expression highly variable.

Main features include:

- growth retardation,

- skin defects appearing within the first year of life (90%): atrophic dermatosis, poikiloderma, hyperpigmentation, teleangiectasia,

- 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 (in more than 50%); bone age lower than chronological age,

- juvenile cataract, corneal dystrophy (50%),

- hypodontia,

- hypogonadism (25%),

- proportionate short stature,

- premature aging.

Diagnosis: the diagnosis is difficult before the development of the erythema.

Differential Diagnosis

Differential diagnosis with: Werner syndrome, dyskeratosis congenita, Cockayne syndrome, Anhidrotic ectodermal dysplasia, Bloom syndrome, Fanconi anaemia.

Neoplastic risk

There are more than 30 documented cases of malignancies in RTS patients, predominantly affecting skin (squamous cell carcinoma, basal cell carcinoma) and bone (osteosarcoma).

Etiology is unknown; a DNA repair deficiency has been postulated to account for cancer proneness, but no conclusive results have so far been achieved.

Treatment

Only protection against sunlight is possible; 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), 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

The gene has not been mapped; it has been provisionally assigned to chromosome 8 on the basis of trisomy 8 mosaicism in affected individuals; no linkage studies exploiting homozygosity mapping have been performed due to the few reported families.

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