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Cancer Prone Disease Section

Mini Review

Naevoid basal cell carcinoma syndrome (NBCS)

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Identity

Other names: Gorlin syndrome; Gorlin-Goltz syndrome; Multiple basal cell nevi, odontogenic keratocysts, skeletal anomalies; Fifth phacomatosis; Hydrocephalus, costovertebral dysplasia, sprengel anomaly.
Inheritance: autosomal dominant with complete penetrance, but variable expressivity; 40% are de novo mutations; frequency is about $2/10^5$ newborns.

Clinics

NBCS is a hamartoneoplastic syndrome; it is also a chromosome instability syndrome; hamartomas are localized tissue proliferations with faulty differenciation and mixture of component tissues; they are heritable malformations that have a potential towards neoplasia.

Phenotype and clinics

Multiple basal cell carcinomas, appearing as early as 15 yrs;
Jaw keratocysts;
Dyskeratotic palmar/plantar pits;
Skeletal malformations (of ribs, spina bifida occulta...);
Soft tissue calcifications (falx cerebri, ovarian fibroma, diaphragma sellae...);
Facial dysmorphia.

Neoplastic risk

Mainly multiple basal cell carcinomas;
Other proliferations (see below) in 60% of patients;
Other malignancies: medulloblastoma, ovarian fibrosarcoma;
Benign proliferations: ovarian fibroma, meningioma, rhabdomyoma, cardiac fibroma.

Treatment

Tumour exereses.

Evolution

Extensive number of basal cell carcinomas.

Prognosis

According to the tumours (basal cell carcinomas are not life threatening, but may be devastating).

Cytogenetics

Inborn condition

Spontaneous and induced chromosome instability.
Delay in the cell cycle.
NBCS is therefore a chromosome instability syndrome.

Cancer cytogenetics

Poorly documented.

Genes involved and Proteins

Complementation groups

None so far.

PTCH

Location: in 9q22.3 (between FACC and XPAC!!)

Protein

Description: glycoprotein with transmembrane domains, extra cellular loops and intracellular domains.
Localisation: transmembrane protein.
Function: part of a signalling pathway; probable cell to cell adhesion role; may have a repressive activity on cell proliferation; as NBCS syndrome is a chromosome instability syndrome, this protein may have a role in DNA maintenance, repair and/or replication.

Mutations

Germinal: most germ-line mutations in NBCS patients lead to protein truncation, which suggests that developmental anomalies seen in NBCS may be due to haplo-insufficiency; no obvious genotype-phenotype correlations.

Somatic: mutation and allele loss events in basal cell carcinoma, in NBCS and in sporadic basal cell carcinoma are, so far, in accordance with the two-hit model for neoplasia, as is found in retinoblastoma.

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