Neurofibromatosis type 1 (NF1)
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Identity

Other names: Von Recklinghausen neurofibromatosis; Peripheral neurofibromatosis
Inheritance: autosomal dominant with almost complete penetrance; frequency is 30/10^5 newborns (and 1 of 200 mentally handicapped persons): one of the most frequent genetically inheritable disease; neomutation in 50%, mostly from the paternal allele; highly variable expressivity, from very mild to very severe; expressivity is also age-related.

Clinics

NF1 is a hamartoneoplastic syndrome; hamartomas are localized tissue proliferations with faulty differentiation and mixture of component tissues; they are heritable malformations that have a potential towards neoplasia.

The embryonic origin of dysgenetic tissues involved in NF1 is ectoblastic.

Phenotype and clinics

Diagnosis is made on the ground of at least 2 of the following:
- Café-au-lait spots (6 or more, over 0.5 cm of diameter (in pre-puberty));
- 2 or more neurofibromas or 1 plexiform neurofibromas (mainly cutaneous);
- 2 or more Lisch nodules (melanocytic hamartomas of the iris);
- Freckling in the axillary/inguinal region (Crowe's sign);
- Glioma of the optic nerve;
- Distinctive bone anomalies (scoliosis, pseudoarthroses, bony defects (orbital wall)...);
- Positive family history.
- Other features:
  - Macrocephaly;
  - Epilepsy;
  - Mental retardation in 10 %; learning diabilities in half patients;
  - Sexual precocity and other endocrine anomalies;
  - Hypertension (renal artery stenosis).

Neoplastic risk

5% of NF1 patients experience a malignant neoplasm Neurofibromas, especially the plexiform variety; polyclonal (benign) proliferation; may be present at birth or appear later, may be a few or thousands, small or enormous, occur in the skin and in various tissues and organs; neurofibromas localized to the spine are extremely difficult to manage.

Neurofibrosarcomatous transformation (malignant) of these in 5-10 %.

Schwannomas (optic nerve, see above), meningiomas, astrocytomas, ependymomas.

Childhood MDS (myelodysplasia) and ANLL, often with monosomy 7 (monosomy 7 syndrome, 'juvenile myelomonocytic leukaemia'): risk, increased by X 200 to 500, is still low, as childhood MDS is rare; M > F; most often before the age of 5 yrs; no increased risk of leukaemia in the adult.

Pheochromocytomas.

Various other neoplasias, of which are rhabdomyosarcomas.

Treatment

Early diagnosis, lifetime monitoring and surgery are essential.

Cytogenetics

Inborn condition
No special feature.

Cancer cytogenetics
According to the cancer type in most cases.

Myelodysplasia and ANLL: monosomy 7.
Genes involved and Proteins

**NF1**

**Location:** 17q11.2

**Protein**

**Description:** the protein has been called neurofibromin; GTPase activating protein; tumour suppressor.

**Mutations**

**Germinal:** nucleotide substitutions, small deletions or insertions on one allele.

**Somatic:** the second allele remains normal in the benign tumours and is often lost in the malignant tumours.

**To be noted**

Beside neurofibromatoses 1 and 2 (NF2), other types of neurofibromatoses are numbered and named 3 to 9, some of them being known to involve other loci.

References


*This article should be referenced as such:*