Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Cancer Prone Disease Section

Mini Review

Sotos syndrome (SOS)

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Identity

Alias: Cerebral gigantism
Inheritance: Generally sporadic, a few inherited cases. The familial case reported in 2003 was proved to have NSD1 mutation.

Clinics

Phenotype and clinics

Excessive growth, advanced bone age, typical facial gestalt, developmental delay.
In infancy growth is rapid, but settles down above the >97th centile in early childhood.
The adult height remains close to normal.
Large hands and feet.
Characteristic facial gestalt: macrocephaly (>97th centile), frontal bossing, prognathism, hypertelorism, and antimongoloid slant of the palpebral fissures.
Occasional hypotonia and delay in motor and language development.
Cardiac, urogenital, musculoskeletal, and ophthalmologic anomalies are observed.

Neoplastic risk

Relatively high. Neoplasms in SoS are found with a frequency of 2.2-3.9%.

Cytogenetics

Inborn conditions

Routine chromosome analysis usually shows normal karyotype. Chromosomal abnormality concering 5q35 were reported. In addition, several chromosomal translocations other than 5q have been published.

Genes involved and proteins

NSD1

Alias
Nuclear receptor binding SET domain protein 1
Location
5q35
Note
Haploinsufficiency of NSD1 is a major cause of SoS.
Protein
Note: NSD1 contains at least six functional domains (SET [su(var)3-9, enhancer-of-zest, trithorax], PWWP [proline-tryptophan- tryptophan- proline] -I, PWWP-II, PHD-I [plant homeodomain protein-finger], PHD-II, and PHD-III) and ten putative nuclear localization signals, and encodes 2696 amino acids.
Mutations
Note: Among a total of 87 point mutations reported, 56 were proved to be de novo. So far 69 protein truncation mutations and 18 missense mutations were identified in 225 SoS patients. Protein truncation mutations spread through the entire NSD1 coding regions, but missense mutations clustered at a latter half part of NSD1 where most of functional domains are located. In SoS, five missense mutations were identified in the SET domain, three in PHD domains and two in the PWWP domains.
Frequencies of microdeletions involving NSD1 are quite different among different populations. In the Japanese population about a half of cases (49/95) had microdeletions, whereas microdeletions are observed only in 9% of cases (9/100) analyzed in European populations.

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