Cancer Prone Disease Section
Mini Review

Variegated aneuploidy related to premature centromere division (PCD)

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Identity

Alias: (Variegated aneuploidy or mosaic aneuploidy) related to (PCD, C-anaphases, premature anaphase, premature chromatid separation or asynchrony of mitotic stages)

Note
The term premature centromere division has also been utilized to describe an unrelated cytogenetic phenomenon, the age related loss of centromeric function in chromosome X.
Variegated aneuploidy has also been described in patients without PCD and patients with Roberts syndrome.

Inheritance
Only 11 patients known.
Premature centromere division (PCD) without variegated aneuploidy has been shown to have an autosomal dominant inheritance, with an estimated frequency of 0.1% of the population.
It has been proposed that patients with variegated aneuploidy related to PCD are homozygotes for this trait, but in several cases one of the parents do not show elevated frequency of PCD.
A recessive inheritance with hormonal factors modifying the expression of PCD in a carrier, isodisomy of one chromosome or loss of heterozygosity has been suggested.

Clinics

Note
Patients show a remarkably constant clinical phenotype probably due to high cellular mortality induced by the aneuploidies; similar clinical findings have also been found in other patients with an expected increased cellular mortality (variegated aneuploidy without PCD and the "ring syndrome").

Phenotype and clinics

the clinical phenotype of the 11 patients described in the literature includes microcephaly (11/11), central nervous system (CNS) anomalies (5/6) with cerebellar defects and migration defects, mental retardation (8/9), prenatal (always noted over 23 weeks of gestation) and postnatal growth retardation (10/10), flat and broad nasal bridge (4/7), apparently low-set ears (5/8), eye abnormalities (8/10), skin abnormalities (3/9) and ambiguous genitalia in male patients (4/6); seizures have been reported in 5 patients; cancer is a major concern in the clinical management of these patients (5/11); birth weight corrected for gestational age ranges from -1.3 to -4.1 SD, birth length from -0.8 to -5.4 SD and OFC from -2.6 to -5.8.

Neoplastic risk

The occurrence of Wilms tumor in three patients, rhabdomyosarcoma in two others and acute leukemia in a fifth characterizes this condition as a chromosomal instability disorder with a high risk of malignancy; interestingly enough, preferential loss of maternal 11p15.5 chromosome region has been repeatedly reported in Wilms tumor as well as in rhabdomyosarcoma.

Prognosis

Although published data is incomplete, at least 4 patients have died before 2 years of age, a fifth deceased at 42 years and one patient aged 18 month has an advanced, relapsed rhabdomyosarcoma; patient's death had been related to pneumonia (one patient), leukemia (one patient), and Wilms tumor (three cases).
Cytogenetics

Inborn conditions

The terms premature centromere division (PCD), C-anaphases, premature anaphase, premature chromatid separation and asynchrony of mitotic stages describe cells in division which have overcome a colchicine-induced metaphase block; the resulting mitotic configuration shows split centromeres and splayed chromatids in all or most of the chromosomes. Control individuals generally show low frequencies of PCD (up to 3% of the mitoses), which seems to have no pathological relevance, but in 0.1% of the population an elevated PCD frequency (>5%) is found in colchicine exposed lymphocyte cultures; this type of PCD shows autosomal dominant inheritance and has traditionally considered to be harmless with the possible exception of some patients with subfertility or repeated abortion.

In few patients high levels of PCD (25-87%) are found in combination with an increased number of cells with mosaic aneuploidies, microcephaly, mental retardation and a variety of malformations; in these patients, trisomy is by far more frequent than monosomy; trisomies of chromosome 8, 18 and X predominate in lymphocyte cultures and trisomy 2, 7, 12 and 20 predominate in fibroblasts; usually, at least one of the parents shows an elevated PCD frequency (range 12.6-42.5) but not variegated aneuploidy.

High levels of PCD have been reported in skin fibroblasts (although in at least one case no aneuploidies where found), hair-root, bone marrow and trophoblastic cells of chorionic villi; there is no data of PCD expression in amniocytes but pseudomosaicism of chromosome 7 and 21 has been reported in amniocytes; cord blood chromosome analysis in one case showed PCD and variegated aneuploidies.

Cytogenetics of cancer

Cytogenetic analysis of one embryonal rhabdosarcoma showed normal karyotype in cultured cells and extensive aneuploidy with some structural aberrations in the only two cells obtained from direct harvest.
**References**


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