TRISOMY 8 MOSAICISM SYNDROME IN TWO CHILDREN FROM BULGARIA

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ABSTRACT

Trisomy 8 is defined as the presence of 3 full copies of chromosome 8 in all human cells. Mosaic trisomy 8 describes the situation that occurs when only a portion of these cells contains three copies of chromosome 8, while others contain the usual two copies of that chromosome.The condition is also referred to as trisomy 8 mosaicism(T8mS) or mosaic Warkany syndrome.There was identified trisomy 8 mosaicism syndrome in 2 dysmorphic boys. The chromosomal analysis in peripheral blood showed trisomy 8p47, XY+8{56}/46,XY{20} and 47,XY+8{3}/46, XY{53}.They had typical clinical features : moderate mental retardation , dysmorphic faces with low set abnormally shaped ears, strabismus and ptosis, bone and tissue abnormalities, sole creases- furrowed appearance, hydrocephaly , agenesis of the corpus callosum and cryptorchidism. Although the low percent /12%/ of mosaicism trisomy 8 in our cases, the clinical picture was expressive.This confirmed the opinion that the percentage of cells with trisomy 8 does not appear to correlate with the types of symptoms in the affected persons.

INTRODUCTION

Trisomy 8 is defined as the presence of 3 full copies of chromosome 8 in all human cells. Mosaic trisomy 8 describes the situation that occurs when only a portion of these cells contains three copies of chromosome 8, while others contain the usual two copis of that chromosome.The condition is also referred to as trisomy 8 mosaicism(T8mS) or mosaic Warkany syndrome.
Full trisomy 8 occurs in about 0,7% of spontaneous miscarriages. It is estimated to occur in about 0,1% of the recognized pregnancies. When seen at birth it is always due to mosaic trisomy 8 as opposed to full trisomy 8.The study of Nielsen et al.(1991) found one child with T8mS among 34 910 newborns.To present are known about 75 cases.

Common characteristics of the syndrome are distinct facial features including low set or abnormally shaped ears and bulbous- tipped nose, eye abnormalities, strabismus ,corneal clouding , bone and tissues abnormalities, various structural heart problems, palate abnormalities, hydronephrosis, cryptorchidism, mild to moderate mental delays and deep hand and feet creases.These characteristics tend to vary widely from person to person.
The presence of 3 copies of chromosome 8 arises from process nondisjunction during the process of cell division, meiosis or mitosis after fertilization.Depending on when the nondisjunction happened , the person may have few or many cells with trisomy 8.
Nondisjunction is a cell division error that occurs by chance. The parent hasn`t control over this process and cannot influence the number of chromosomes their child receives at or after conception. Unlike Down syndrome T8mS hasn` t been strongly associated with mother's or father's age of conception.

Most people with T8mS do not have a family history of the condition, since it usually occurs by chance.
The aim of our work was to diagnose and investigate patients with trisomy 8 mosaicism syndrome.

MATERIAL AND METHODS

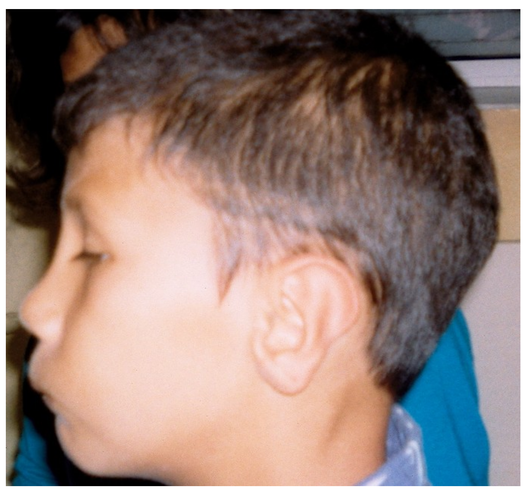
There were investigated 2 boys : S.T.G. (date of birth: 18.08.98) and D.A.D.(date of birth: 19.11.98), patients of University Children's Hospital , Sofia.
There was used an integral approach including clinical and laboratory investigations including history of the disease, physical examination, antropometric parameters, somatic and neurological status, rentgenography, EEG, CAT of the brain, US of the heart, kidney , liver and spleen, haematological and biochemical investigations with routine methods . Urine metabolic screening, organic acids, acylcarnitine , carnitine were proceeded with Tandem MS, aminoacids- with HPLC. For karyotyping – G- banding in peripheral intravenous blood. Mathematical – statistical methods.

RESULTS

DESCRIPTION OF THE CASES

Case I: S.T.G.(date of birth : 18.08.98) is a 9 year`s old boy with a Gipsy origin , born from third normal pregnancy, after which the mother had 7 spontaneous miscarriages.The birth weight was 2500gr and lenghth–47 cm. He had dysmorphic face : microcephaly, microretrognathy , a lot of frenulums of the tongue and alveolar ridges , for which he was operated. He had thorax deformity , camptodactily, excavated nails, hypertrichosis and sole creases- furrowed appearance. He had bronchitis and bronchial asthma. He started to walk at 4 year`s old and said words after 5 year`s old. His IQ= 42 /Wechsler/-moderate mental retardation with aggressive and autoaggressive behaviour.The CAT showed internal hydrocephaly.The metabolic screening was normal.The chromosomal analysis showed trisomy 8p47, XY+8{56}/46,XY{20}.
Case II : D.A.D.(date of birth: 19.11.98) is a 9 year`s old boy from Bulgarian-Turkish origin , born from first pregnancy with vacuum extraction. During his childhood he showed food allergy , recurrent bronchitis and asthma. He had mental , speech retardation and vitiligo at 7 year`s old. The general condition of the boy was good with weight-24 kg, height-128 cm , head circumference 53cm.His face was dysmorphic with strabismus , ptosis of left eye lid, upturned nose, thicker and downturned lower lip, alopecia areata, low-set ears with incisure of the helix, high palate, camptodactily and contractures of the fingers, kyphosis.The metabolic screening was normal. The EEG was normal.CAT - internal hydrocephaly and agenesis of corpus callosum.The chromosomal analysis in peripheral venous blood showed:47,XY+8{3}/46, XY{53}.The investigation of the parents proceeds.

Case I .S.T.G



Case II .D.A.D.

DISCUSSION

There was identified trisomy 8 mosaicism syndrome in 2 dysmorphic boys.
They had typical clinical features : moderate mental retardation , dysmorphic faces with low set abnormally shaped ears, strabismus and ptosis, bone and tissue abnormalities, sole creases- furrowed appearance, hydrocephaly and agenesis of the corpus callosum.

The creases on the palms and soles of people with T8mS are the most unique characteristic of the condition. On the palms there could be found more arches than usual on the fingertips and a single crease running across the palm. The creases are often deep and vertical with furrowed appearance on the soles of the feet, as in the our cases.These changes could make think for Trisomy 8 mosaicism syndrome.

The patients with T8mS often have distinct facial features including the wide upturned nose, thicker and downturned lower lip and low set and prominent ears that may not be shaped in the usual way. Our patient had incisure of the helix, an inusual shape of the ears.

It was interesting finding that one of the children had a lot of frenulums between the tongue and alveolar ridge , as the Mohr type 2 syndrome. The other patient had skin changes, which progressed (café au lait, vitiligo, alopecia areata) .

The bone and tissue abnormalities include narrow shoulders, absent knee caps, abnormally shaped toes, higher joints, slender palms, extra missing ribs and curving of the spine.They were present in our cases too.

The eye abnormalities seen in the syndrome as strabismus and ptosis were both presented in the children. There was not found corneal clouding.

Our children had no heart problems and hydronephrosis but their genitalia were underdevelopped and cryptorchidism was present .

Although the low percent 12% of mosaicism trisomy 8 in our cases, the clinical picture was expressive.This confirmed the opinion that the percentage of cells with trisomy 8 does not appear to correlate with the types of symptoms in the affected persons.

The diagnosis T8mS in our cases was confirmed in blood chromosome testing. The diagnosis could be confirmed in skin biopsy too.
Our laboratory diagnosed 6 cases with T8mS with this method for 25 years.
The 7 spontaneous miscarriages of the mother ,who had 2 other healthy children from the first husband, showed that her second partner was carrier of trisomy 8 but the father of the ill child refused to be investigated .

Trisomy 8 can be detected on CVS but the diagnosis was not always confirmed at the following amniocentesis . For unknown reasons, amniocentesis might not provide the most accurate results with a view of T8mS.This make difficult the genetic counseling of T8ms and the providing information to the couples during pregnancy.
There is no cure for T8mS. The treatment is symptomatic .Our patients visited a Center for Mentally retarded children , where they proceeded physical rehabilitation, education and consultation with a logopedist and psychologist . The clinical examination and treatment proceeds.

CONCLUSION

We identified Trisomy 8 mosaicism syndrome in two dismorphic boys.The diagnosis was confirmed in peripheral blood cells .The clinical examination and the treatment proceeds.

REFERENCES

Benlian P, Foubert L, Gagne E et al, Complete paternal isodisomy for chromodsome 8 unmasked by lipoprotein lipase deficiency, Am J. Hum. Genet , 1996, 59:431-436
De Pater JM, Schuring-Blom GH, Nieste-Otter MA et al, Trisomy 8 in chorionic villi-unpredictable results in follow up. Prenatal Diagnosis, 2000, 20 (5) : 435-7
Hahnemann JM, Vejerslev LO Accuracy of cytogenic findings on chorionic villus sampling (CVS)-diagnostic consequences of CVS mosaicism and non-mosaic discrepancy in centers contributing to EUCROMIC 1986-1992. Prenat Diagn, 1997 Sept; 17(9):801-20
Hahnemann JM, Vejerslev LO, European Collaborative Research on Mosaicism I CVS(EUCROMIC)-Fetal and Extrafetal Cell lineages in 192 gestations with CVS mosaicism involving single autosomal trisomy, 1997 Am J Med Genet 70; 179-187
Hsu Ly, Yu MT, Neu RL, van Dyke DL, Benn PA, Bradshaw CL et al, Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20 and 21; karyotype/phenotype correlations, Prenatal Diagnosis , 1997, 17(3):201-42
Karadima G et al,Origin of nondisjunction in trisomy 8 and trisomy 8 mosaicism.Eur J Hum Genet.1998 Sep-Oct; 6 (5):432-8
Karanjawala ZE, Kaariainen H, Ghosh S et al.Complete maternal isodisomy of chromosome 8 in an individual with an early –onset ileal carcinoid tumor , Am J Med Genet 2000 Jul 31; 93(3): 207-10
Ledbetter DH, Engel E, Uniparental disomy in humans:development of an imprinting map and its implications for prenatal diagnosis Human Molecular Genetics, 1995, 4: 1757-1764
Meck J, Chen TJ, Wong L-J et al.Cytogenetic and molecular evidence of constitutional mosaic trisomy 8 and hematologic abnormalities in a phenotypically normal woman Georgetown Univ.Med Ctr, Wash, DC
Robinson WP , Bernasconi F, Lau A, Mc Fadden DE, Frequency of meiotic trisomy depends on involved chromosome and mode of ascertainment, Am J Med Genet, 1999 May 7:84 (1) : 34-42
Saks E, Mccoy MC, Damron J et al, Confined placental mosaicism for trisomy 8 and intra-uterine growth retardation , Prenatal diagnosis, 1998, 18(11) :1202 : 4
Webb AL, Wolstenholme J, Evans J et al.Prenatal diagnosis of mosaic trisomy 8 with investigations of the extent and origin of trisomic cells.Prenat Diagnosis, 1998, 18(7): 737-41
Wolstenholme J, Confined placental mosaicism for trisomies 2, 3, 7, 8, 9, 16, and 22: their incidence, likely origins, and mechanisms for cell lineage compartimentalization.Prenatal Diagnosis, 1996,16(6):511-24