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Case report/Kazuistyka

Tetraploidy in the era of molecular karyotyping – What we need to remember

Tetraploidia w erze kariotypowania molekularnego - o czym należy pamiętać

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ARTICLE INFO

Article history:
Received: 08.05.2013
Accepted: 11.06.2013
Available online: 14.06.2013

Keywords:
- Tetraploidy
- Newborn
- Karyotyping

ABSTRACT

Tetraploidy is a condition in which there are four complete sets of chromosomes in a single cell. In humans, this would be 92 pairs of chromosomes per cell. A great majority of pregnancies with a tetraploid fetus end in miscarriage, or if the pregnancy goes to full term, the infant dies shortly after birth. Longer surveillance is rarely described. The only method for confirming tetraploidy is karyotyping, in many cases using classical G-banding methods. In this paper we would like to present another living individual with tetraploidy and to revise the syndrome in the light of its diagnostics in the era of molecular karyotyping, with array Comparative Genomic Hybridization (aCGH, arrayCGH).

Introduction

Tetraploid is a term used to describe organisms having four instead of two paired (homologous) sets of chromosomes. It is a known genetic aberration in humans, but because of its high intrauterine lethality (it is found in 1–2% of early miscarriages), only several clinical reports of infants diagnosed with tetraploidy are available [1–10]. The clinical consequences of tetraploidy are varied and include limited life expectancy and multiple congenital anomalies (MCA). A reliable diagnosis can be established only by cytogenetic analyses, which allow the visualization of chromosomes for chromosomal rearrangements, including numerical and structural aberrations.

In this paper we report a 1.5-year-old boy with complete tetraploidy and review clinical features described in this aberration so far in order to raise clinicians' awareness of the symptoms, and point to G-banded karyotyping as a first-tier test.

Case presentation

The proband is the second child of healthy, non-consanguineous parents. His family history is unremarkable. Prenatal

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http://dx.doi.org/10.1016/j.pepo.2013.06.002

ultrasound revealed no abnormalities. He was born at week 40 of gestation with a weight of 2415 g and scored 5-8-8 points on the Apgar scale. Facial dysmorphism, microphtalmia, skin defects of the scalp, and a loud systolic murmur over the heart were noted at birth. Moreover, he presented with severe breathing difficulties and therefore was referred to the Department of Neonatology and Intensive Care of the Children's Memorial Health Institute in Warsaw.

In the physical examination, numerous dysmorphic features were found: long cranium, sparse, fair hair, loss of skin on top of the head (on an area of 2 cm × 2 cm), hypoplastic, low-set and rotated ears, long face, high forehead, short palpebral fissures, lack of the right eyeball and small left eyeball, long nose with pressed nasal tip and hypoplastic alae nasi, narrow upper lip, microstomia, short neck (Fig. 1). Moreover, high palate, club foot, long toes and arachnodactyly with long fingernails, abnormal position of the thumbs (Fig. 2), hypoplastic external genitalia (micropenis, small testes in the scrotum) were noted. The boy presented with muscle hypotonia and low spontaneous activity.

Echocardiography revealed a significantly and atypically rotated heart, patent ductus arteriosus (PDA), and atrial septal defect (ASD). No abnormalities were noted in abdominal ultrasound, while transfontanellar study revealed small cysts with a diameter of 2–4 mm in the floor of the lateral ventricles and an uneven outline of the plexus choroideus.

After obtaining informed consent, peripheral blood samples were taken from the patient. Chromosome analysis at the 550-band level was performed on peripheral blood lymphocytes according to standard procedures using trypsin and giemsa for G-banding. It showed regular tetraploidy with the karyotype 92,XXYY (Fig. 3). This result was then verified in fibroblast analyses, which confirmed this ploidy.

Taking into consideration this diagnosis, it was decided to abstain from further cardiologic and ophthalmic tests. The boy was transferred to the care of the Warsaw Hospice for Children (WHD). At 24 days of life the patient was discharged from the hospital in good condition to his home.

At present, at the age of one year and 8 months, he still is at home under the care of the WHD. He is profoundly psychomotor retarded, blind, responds only to sound stimuli. His weight is about 10 kg, is teat-fed and partially probe-fed. The dominant problems in the child's care are severe, recurrent respiratory infections.

Fig. 1 – Male patient with regular tetraploidy, facial appearance

Fig. 2 – Male patient with regular tetraploidy

Discussion

Tetraploidy is a condition in which there are four complete sets of chromosomes in a single cell. In humans, this would be 92 sets of chromosomes per cell, *i.e.*, 92,XXXX (in females) or 92,XXYY (in males). The most probable origin of tetraploidy is chromosome duplication in a somatic cell in an early-cleavage-stage embryo, a postzygotic event. Fertilization of a rare diploid ovum by an equally rare unreduced sperm may be possible. Another rare event is fertilization of one egg by three sperms, but this will develop as hydatidiform moles rather than a tetraploid fetus, because of the genomic imprinting effect [11].

A great majority of pregnancies in which the fetus has tetraploidy end in miscarriage (5–6% of genetically abnormal miscarriages), or if the pregnancy goes to full term, usually results in the infant's death shortly after birth. Longer surveillance is rarely described. The patient presented herein is the twelfth live-born case with regular tetraploidy described in the literature so far [1–10]. Six were females and six were males. Except for four cases, all were born at term (38–42 weeks of gestation).

Numerous abnormalities were observed in the live-born children (Table I). The most common were: intrauterine hypotrophy and postnatal growth retardation, high and prominent forehead, low-set and dysplastic ears, as well as feet/hand abnormalities. Over 50% of these children had microphthalmia and microcephaly. They presented with a somewhat characteristic facial appearance caused by a beaked nose and micrognathia/retrognathia (Figs. 1 and 2).

As presented in Table I, the spectrum of congenital anomalies observed in children with tetraploidy is not