Recurrent Pregnancy of Down Syndrome

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Abstract

Down syndrome, characterized by an extra chromosome 21 is the most common genetic cause for congenital malformations and learning disability. It is well known that the extra chromosome 21 most often originates from the mother, the incidence increases with maternal age, there may be aberrant maternal chromosome 21 recombination and there is a higher recurrence in young women. In spite of intensive efforts to understand the underlying reason(s) for these characteristics, the origin still remains unknown. We have experienced a case of recurrent pregnancy of Down syndrome, or trisomy 21. We present this case with a brief review of a literature.

Case

Parity: 1-0-2-1

Address and current history: the patient had amenorrhea 19+4 weeks, through ultrasonography, Atypical features were found and suspected of intrauterine fetal death. For further examination and treatment the patient was admitted

Surgical history: One Cesarean section, one induced abortion due to the down syndrome pregnancies

Laboratory findings: Hemoglobin 10.4 g/dL, hematocrit 31%, white blood cells, platelet count was normal. No specific findings on liver function tests and renal function tests. Syphilis and hepatitis antigen test were negative and the patient’s blood type was Rh positive. No abnormal findings on ECG, chest X-ray examination and urinary analysis. APTT coagulation are 20.9sec in a slightly decreased.

Cytogenetic findings: Using Long term flask culture with GTG banding analysis method to the amniocentesis after admission, 47, X( ), +21 was found, yielded cytogenetic diagnosis result was trisomy 21; Down syndrome, respectively. Two independent flasks were observed in a total of 40-50 colonies, 20 colonies of the mid-phase from an analysis, all cells were found competent trisomy 21, or Down syndrome karyotype was observed. Down syndrome is classified as trisomy 21, mosaicism, and translocational by karyotyping, each occurrence frequency were 93%, 2%, and 5%. The patient belonged to the trisomy 21. ETBR karyotype results were 46, XX and 46, XY which were the normal karyotype of both sex. Analysis methods were 1)PHA stimulated T-lymphocyte culture with GTG banding 2)High resolution culture using ETBR, and used peripheral blood of the patient and the spouse.

Obstetrical course: Induction was determined to enforce due to the intrauterine fetal death. Induction of labor using misoprostol caused vaginal bleeding, retained placenta was suspected, therefore curettage was performed. Stillborn height was 128mm, weight 256mg.

Clinical outcome after delivery: Two days after delivery, the patient did not have vaginal bleeding and was discharged.

Discussion

There are three hypotheses about parents’ age and trisomy 21. The age of the father does not affect non-separation of chromosomes and non-separation is related to the age of the mother. From here, the first hypothesis can be made: each germ cell has different period of mutation. The second hypothesis is that non-separation of chromosomes from both parents and the age and the presence of the association, which can be seen as a result of the environment factors. The third hypothesis is that maternal age is increased in non-separation of the parents, regardless of source, the chance of giving birth to children with Down syndrome increases to be, which means ability of removing fetal chromosomal abnormalities as a pregnant women takes ages.

For mechanism of chromosomal non-separation of a mother, it is a leading hypothesis that early mitosis with loss of 21st chromosome homozygotes, or mitosis error after zygote in a normal pregnancy, which causes acquisition of 21st chromosome.

Recurrence rate is about 1% for the couple who has an experience of down syndrome to have another child with down syndrome. In addition, if the down syndrome of the child is caused by parent who are translocational carrier, in this case, recurrence rate will be much higher and will not have relevance with age. If one of the parent has trisomy 21 mosaicism in germ cells, it will be significantly associated to recurrence.
There is a thesis paper, announced in 2006, about mosaicism of recurrent 21 trisomy. In the paper, it reported that down syndrome is caused by fertilization of disomic 21 ovum and monosomic 21 sperm. In this case, fetus of trisomy 21 recurrent pregnancy rate is high, therefore pre-diagnosis is required. Also, evaluation should be based on tissue of reproductive organ due to somatic non-separation of chromosome 21 during fetus mitosis. Therefore, if mother has recurrence pregnancy of trisomy, cytogenetic analysis of the parental tissue is needed.

Based on these, we have presumed of cause of recurrent Down syndrome in this case. First, the pregnant woman was age 39. In this case, there is a delay (especially for 40 years old and above) to meiosis and it can cause error in 1st period of meiosis. Second, possibility recurrence due to 21 trisomy mosaicism in germline, since peripheral blood chromosome test of both pregnant women and the spouse had no abnormality. To this end, in this case in order to explore the exact cause of testicular and ovarian tissue parents additional cytogenetic are needed. We have experienced a pregnant women with two consecutive pregnancy of fetus with 21 trisomy, through this case, we report on the rare recurrence of Down syndrome with literature review

References