Biomédica 2014;34:326-9
doi: http://dx.doi.org/10.7705/biomedica.v34i3.1471

PRESENTACIÓN DE CASO

Down syndrome passed from mother to child

Harry Pachajoa[1,2], Antonio José Riascos[3], Diego Castro[3], Carolina Isaza[4], Juan Carlos Quintero[3]

[1] Centro de Investigaciones en Anomalías Congénitas y Enfermedades Raras (CIACER), Facultad de Ciencias de la Salud, Universidad Icesi, Cali, Colombia
[2] Departamento de Pediatría, Fundación Clínica Valle del Lili, Cali, Colombia
[3] Departamento de Ginecología y Obstetricia, Hospital Universitario del Valle, Cali, Colombia
[4] Departamento de Morfología, Facultad de Salud, Universidad del Valle, Cali, Colombia

Down syndrome is the leading cause of inherited intellectual disability; it is characterized by mental retardation associated to physical growth delay and certain physical traits or features. It is caused by the presence of a third copy of chromosome 21, being this trisomy the most common chromosomal aneuploidy. Women with Down syndrome are less fertile, and pregnancy in these women is rare, although the information on exact statistics of reproduction in these patients is very limited, and they often have difficulties with miscarriage, premature birth, and difficult labor.
We report the case of a preterm newborn with Down syndrome passed from her mother; this pregnancy was a result of sexual assault, which is an event that can and should be prevented in this population.

Key words: Down syndrome, fertility, heredity, genetics, intellectual disability.

doi: http://dx.doi.org/10.7705/biomedica.v34i3.1471

Transmisión de síndrome de Down de madre a hijo

El síndrome de Down es la principal causa de discapacidad intelectual congénita; se caracteriza por retraso mental asociado a retardo del crecimiento y del desarrollo psicomotor, así como a algunas características físicas típicas. Se debe a la presencia de una tercera copia del cromosoma 21, siendo esta trisomía la aneuploidía cromosómica más común. Las mujeres con síndrome de Down tienden a ser menos fértiles y el embarazo en ellas es poco frecuente, aunque los datos estadísticos de este evento son limitados, y se asocia, además, a dificultades que terminan en aborto, parto prematuro y parto difícil.
Se reporta el caso de un recién nacido prematuro con síndrome de Down, hijo de madre con el mismo diagnóstico, producto de un embarazo resultado de violación, evento que debe ser prevenido de forma oportuna en esta población de alto riesgo.

Palabras clave: síndrome de Down, fertilidad, herencia, genética, discapacidad intelectual.

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Down syndrome is the most common cause of inherited intellectual disability. The clinical picture of these patients is characterized by mental retardation in association to development delay and peculiar physical features. They are also at increased risk of having various other medical problems. This disorder is the result of the presence of a third copy, or at least part of it, of chromosome 21. This aneuploidy is the most common chromosome abnormality, occurring in one of every 700 live births; an advanced maternal age is recognized as the most important risk factor (1,2).

Although reports of the syndrome have been identified from a long time ago, even in artwork done by prehispanic cultures more than 2,000 years ago (3), it was not until 1866 that the syndrome was clinically described by Langdon Down, and only in 1959, that Lejeune and Jacobs, independently, determined the cause of the disease (4,5).

Corresponding author:
Harry Pachajoa, Calle 18 N° 122-135, Pance, Cali, Colombia
Teléfono: (572) 555 2334, extensión 8032
hmpachajoa@icesi.edu.co

Recibido: 14/03/13; aceptado: 16/04/14

Author's contributions:
Harry Pachajoa: literature search, data interpretation and writing
Antonio José Riascos and Diego Castro: clinical history and charts review and writing
Carolina Isaza: karyotyping, data analysis, figures and writing
Juan Carlos Quintero: prenatal follow-up and ultrasounds and manuscript review

There is evidence of normal sexual development in females with Down syndrome, but, nevertheless, fertility is greatly compromised in about 50% of them (6). Here we report the case of a newborn diagnosed with Down syndrome born to a mother with the same condition, who was pregnant as the result of sexual assault.

Case report

A preterm 35 week-old male was born to a 20-year-old mother, product of pregnancy due to rape. The mother had Down syndrome, which led to the indication of C-section delivery. The pregnancy elapsed normally with adequate prenatal controls, except that during ultrasound follow-up fetal growth in low percentiles was detected.

Birth weight was 2,020 g, length was 47 cm, head circumference, 33 cm, the Ballard score corresponded to 38 weeks, and the Apgar score was 9-10. Just like the mother, the newborn presented clinical features of Down syndrome, including flat facies with hypertelorism, up-slanting palpebral fissures, flat nasal bridge, bilateral medial epicanthal folds, micrognathia, microcephaly, low-set ears with an overfolded helix, brachydactily and single palmar creases. A short sternum, poor muscle tone, joint hyperflexibility and a weak cry were also evident in the baby.

For routine cytogenetic analysis, karyotype was determined in both mother and child. A blood sample of 0.3 ml was incubated in culture medium for complete separation of lymphocytes (20% fetal calf serum in Roswell Park Memorial Institute 1640 with 2.5% phytohemagglutinin and 2% L-glutamine and 1% pen-strept in an incubator at 37°C for 72 hours). Metaphases were harvested by adding colcemid for 60 minutes, followed by the addition of hypotonic potassium chloride (0.075 M) (treatment for 10 minutes and fixation, using standard 3:1 methanol-acetic fixative - Merck). Chromosome preparations were stained with G-banding. Chromosomal analysis of son revealed 47, XY, +21 (figure 1), and mother revealed 47, XX, +21 (figure 2).

Discussion

People with Down syndrome rarely reproduce, although the information on exact statistics of reproduction in these patients is very limited. Fifteen to thirty percent of women with trisomy 21 are fertile and they have about 50% risk of passing down the disease to their offspring. Pubertal development among these females appears to be normal, with a mean age of 12.6 years at menarche, which does not differ from that of non-affected females. There are no significant differences in terms of menstrual problems or irregularities either, although these patients

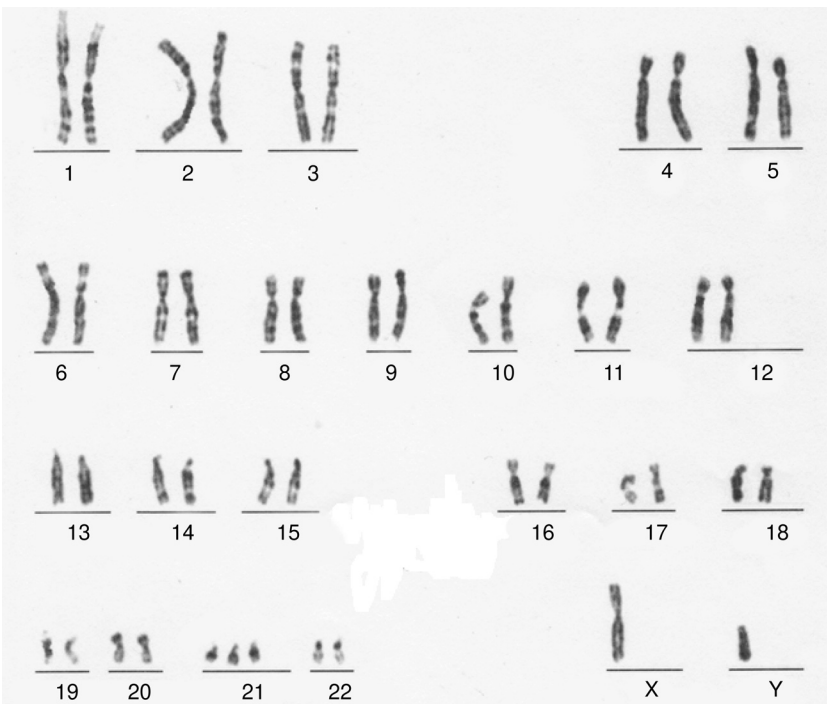

Figure 1. G-banded karyotype of the newborn showing trisomy 21 (47, XY, +21)

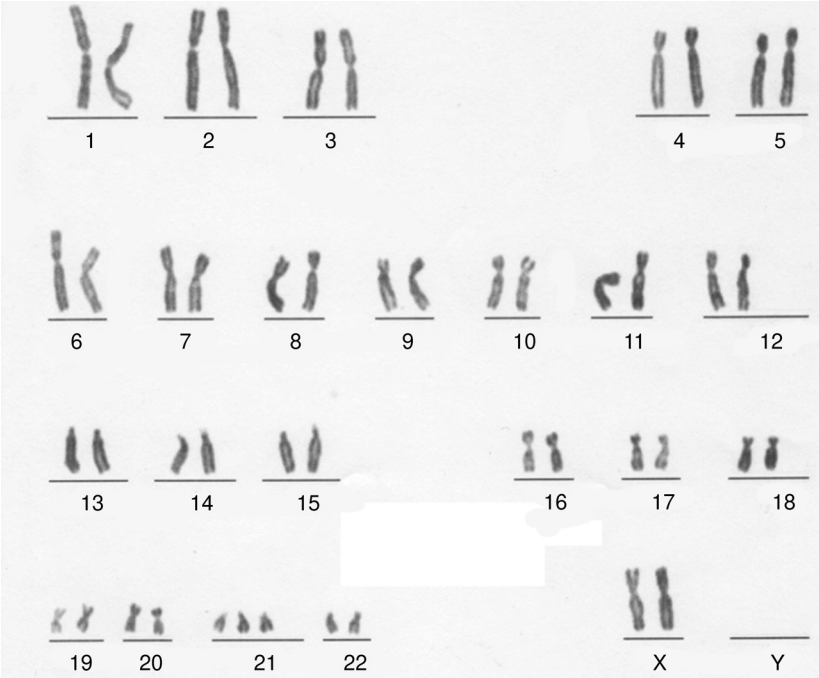

Figure 2. G-banded karyotype of the mother revealing trisomy 21 (47, XX, +21)

are at increased risk of having hypothyroidism, which could affect the normal endocrine function altering the menstrual cycle. Moreover, in some patients menarche may be somewhat earlier, which could be related to obesity. Usually, the follicle stimulating hormone (FSH) and the luteinizing hormone (LH) rise normally with maturation, with levels equivalent to those in non-affected women (7). Although earlier studies have reported high rates of ovarian abnormalities and anovulatory cycles, a recent study among 10 to 27 year-old women found that 88% of cycles had a biphasic temperature curve, indicating that there was ovulation (8).

Pregnancy in women with trisomy 21 is associated with perinatal complications and with the presentation of aneuploidy in the offspring. In a review on reports of pregnancy among females with Down syndrome, Manila, *et al.,* described the outcomes of 31 cases: 13 were uncomplicated pregnancies that resulted in normal live births with no complications; in 10, the mother passed the syndrome to the child; 3 terminated in abortion or stillbirth, and the remaining were associated to other undetermined malformations and cognitive deficits with karyotype negative for trisomy 21 (9). It is important to take into account results like those reported in this study when offering counseling to families of women diagnosed with Down syndrome who are facing a pregnancy (6).

On other hand, it is also important to acknowledge the fact that pregnancy in patients with Down syndrome is usually an indicator of sexual violence and abuse. The increase in life expectancy of these patients imply new challenges that require a comprehensive approach based on protocols to address and manage situations of physical abuse, including those events resulting in pregnancy, which in turn imply even major diagnostic challenges, and clinical and ethical issues.

It is relevant to create guides focused on a more integrated care of patients with Down syndrome. Additionally, it is important to suggest definitive contraception options, especially for women, taking into account the health risk associated to pregnancy in these patients, and underlining the importance of preventing harmful situations, such as physical abuse.

Conflict of interest

None declared by the authors.

Financing

Universidad del Valle and Universidad Icesi.

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