Case Report
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A Case with Emanuel Syndrome Resulting from a Maternal Balanced Translocation

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Emanuel syndrome is a rare genomic syndrome which is characterized by multiple congenital anomalies and developmental disability. This syndrome is related to the presence of the supernumerary derivative chromosome originating from both chromosome 11 and 22. In most cases, one of the parents is a balanced carrier of a translocation. Our case results from 3:1 meiotic segregation of the maternal translocation carrier and is a rare case in Korea confirmed by genetic analysis.

Key Words: Emanuel syndrome, Supernumerary der(22) syndrome, Congenital abnormalities

Introduction

Emanuel syndrome is characterized by severe intellectual disability, failure to thrive, microcephaly, preauricular tag or sinus, ear anomalies, cleft or high-arched palate, micrognathia, kidney abnormalities, congenital heart defect, and genital abnormalities.[1-4] Affected children are usually identified in the newborn period as the offspring of balanced (11;22) translocation carriers. Carriers of this balanced translocation usually have no clinical symptoms and are often identified after the birth of offspring with an unbalanced form of the translocation, the supernumerary der(22)t(11;22)syndrome. This genomic syndrome was named Emanuel syndrome in 2004 [OMIM 609029]. This syndrome usually arises through 3:1 malsegregation during gametogenesis in a balanced t(11;22), and clustered breakpoints have been reported in numerous unrelated families.[5,6]

Previously, a few cases have been reported as Emanuel syndrome resulting from 3:1 meiotic segregation of the paternal translocation carrier in Korea (Table 1).[7,8] In the current report, we present a female patient with supernumerary der(22) syndrome resulting from 3:1 meiotic segregation of the maternal translocation carrier. Our patient demonstrates the typical clinical manifestations as in the literatures, providing a better understanding of this syndrome.

Case Report

The patient was born after 39 weeks of gestation weighing 2,780 gram, to a 35-year-old mother in a local clinic. Her mother denied any history of illness, smoking, drug use, alcohol use during pregnancy. There is no family history of congenital anomalies, syndromes, or consanguinity. Her prenatal evaluation had been unremarkable. At birth, she was found to have a cleft palate, a

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webbed neck, low-set ears, and micrognathia. Echocardiography revealed secundum atrial septal defect. She also has renal anomalies, a small left kidney and vesicoureteral reflux grade II on left side. On hearing assessment, she was suspicious of having sensorineural hearing loss. Karyotyping using her peripheral blood was done due to her multiple congenital anomalies, which revealed the chromosomal abnormality, 47,XX,+der(22)t(11;22)(q23.3;q11.2) (Fig. 1). In addition, she was admitted to hospital repeatedly due to aspiration pneumonia or urinary tract infection. On the videofluoroscopic swallowing study, the severe velopharyngeal incoordination was noted.

At the age of 6 months, she was transferred to our hospital due to generalized tonic seizure. She could not control her head due to significant central hypotonia. Encephalogram showed diffusely suppressed electrical activities for her age, and diffuse brain atrophy with thinning of corpus callosum was noted on brain magnetic resonance imaging (MRI). To ascertain the origin and trait of this supernumerary marker chromosome, der(22)t(11;22)(q23.3;q11.2), karyotyping for her parents and sister were performed. The mother and her older sister were found to be a balanced carrier; 46,XX,t(11;22)(q23.3;q11.2).

Discussion

Over 100 individuals with Emanuel syndrome have been reported.[1-3] Our patent is the 3rdKorean case, and has the typical features of Emanuel syndrome as described in the literature (Table 1). She has severe global developmental delay. Her long-term prognosis may be related to the associated congenital malformations and repeated infections, and she has to receive multidisciplinary management and intervention for cardiac defect, cleft palate, and seizure. Her older sister is a balanced t(11;22). Therefore, she has to receive prenatal diagnosis by chromosome analysis of fetal cells afterwards.

The t(11;22)(q23;q11) is the only known recurrent, non-Robertsonian constitutional translocation in human being. In more than 99% of cases, one of the parents of a proband with Emanuel syndrome is a balance carrier of t(11;22) and is phenotypically normal. They are often identified after the birth of offspring with an unbalanced form of the translocation, the supernumerary-der(22)t(11;22) syndrome.

This syndrome is easily identified by routine G-band analysis. In the rare instance in which one of the parents is not a balanced translocation carrier, FISH probes for the 22q11.2 deletion and for the telomere of 11q can identify the supernumerary chromosome

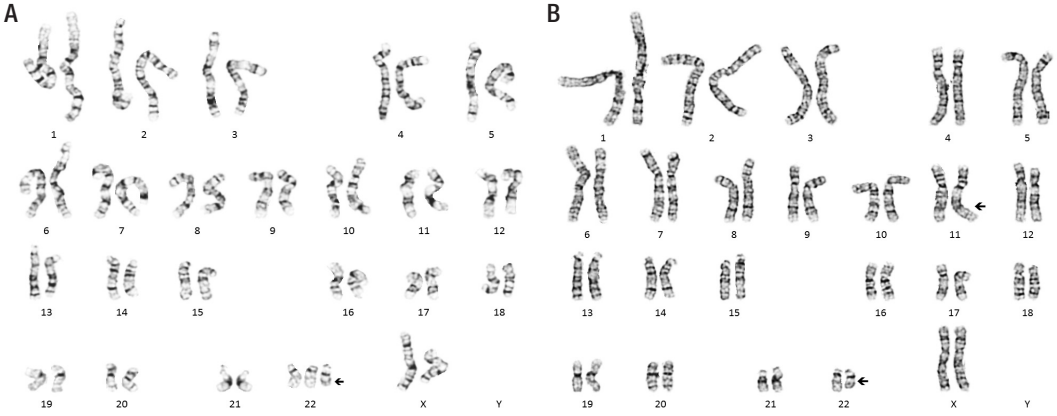

Fig. 1. *A)* The patient's karyotyping shows a supernumerary chromosome, der(22)t(11;22)(q23.3;q11.2). *B)* Her mother's karyotyping shows a balanced non-Robertsonian t(11;22).

Table 1. Karyotypes and characteristics of patients with Korean cases

No. of cases	Karyotypes	Chromosome loci	Inheritance	Chracteristics
1[8]	47,XX,+der(22)t(11;22)	q25;q13.1	Paternal	IUGR, Cleft palate, low set ears, micrognathia, webbed neck, ASD, VSD, pulmonary stenosis, Death
2[7]	47,XX,+der(22)t(11;22)	q23;q11.2	Paternal	Oligohydramnios, IUGR, low set ears, preauricular pit, micrognathia, high-arched palate, winged scapula, ASD, both SNHL, developmental delay, hypotonia
3	47,XX,+der(22)t(11;22)	q23.3;q11.2	Maternal	Cleft palate, low set ears, micrognathia, webbed neck, ASD, both SNHL, vesicoureteral reflux, developmental delay, hypotonia, seizure

ASD, atrial septal defect; IUGR, intrauterine growth retardation; SNHL, sensorineural hearing loss; VSD, ventricular septal defect.

in the karyotype as being derived from chromosomes 11 and 22. The clinical features of Emanuel syndrome arises from duplication of 22q10-22q11 and duplication of 11q23-qter on the supernumerary der(22). Most cases result from 3:1 meiotic segregation of the balanced translocation t(11;22)(q23;q11). There is a single case report of supernumerary der(22) arising from translocation in the paternal germline with probable unbalanced adjacent 1 segregation and maternal non-disjunction of chromosome 22 in meiosis I.[9] Each sib of a proband with a carrier parent will either have supernumerary der(22) syndrome, be a balanced t(11;22) carrier, or be spontaneously aborted as a result of supernumerary der(22) or another meiotic malsegregant.

This syndrome is characterized by multiple anomalies, but mortality is associated with life-threatening congenital malformations such as congenital heart defects, diaphragmatic hernia, or renal insufficiency. Depending on the age and extent of systemic involvement of the subject with Emanuel syndrome, they need to be cared by multiple displinary approaches with developmental assessment on a regular basis. Their siblings of patients need to determine the genetic risk for the offspring with Emanuel syndrome before pregnancy. If the siblings a balanced t(11;22) carrier, it is appropriate to offer genetic counseling that includes discussion of potential risks to offspring and productive option.

In summery, Emanuel syndrome is an inherited chromosome abnormality, characterized by multiple anomalies and developmental delay. In most of cases, a carrier parent has inherited the t(11;22) from one of his or her parents. Therefore parents of a proband with Emanuel syndrome should be offered chromosome analysis.

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