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Case Report

Molecular cytogenetic characterization of an inv dup(15) chromosome presenting as a small supernumerary marker chromosome associated with the inv dup(15) syndrome

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ABSTRACT

Objective: To present molecular cytogenetic characterization of an inverted duplication of proximal chromosome 15 [inv dup(15)] presenting as a small supernumerary marker chromosome (sSMC) associated with the inv dup(15) syndrome.
Case Report: A 35-year-old woman underwent amniocentesis because of advanced maternal age at 27 weeks of gestation, which revealed an sSMC that was confirmed by fluorescence *in situ* hybridization (FISH) to be derived from chromosome 15. Prenatal ultrasound findings were unremarkable. A 3434-g male baby was delivered at term with no phenotypic abnormalities. The cord blood analysis revealed a bisatellited dicentric inv dup(15). When followed up at 21 years of age, the proband manifested hypotonia, ataxic gait, developmental delay, intellectual disability, epilepsy, poor speech, and autism consistent with the inv dup(15) syndrome. Array comparative genomic hybridization of the peripheral blood revealed arr 15q11.1q13.2 (20,686,219–30,390,043) × 4, 15q13.2q13.3 (30,390,043–32,445,226) × 3. Conventional cytogenetic analysis of the peripheral blood revealed a karyotype of 47,XY,+inv dup(15)(pter→q13::q13→pter). Quantitative fluorescent polymerase chain reaction analysis showed a maternal origin of the inv dup(15) chromosome. FISH analysis confirmed an inv dup(15) chromosome.
Conclusion: Molecular cytogenetic techniques are useful for rapid diagnosis of an inv dup(15) chromosome associated with the inv dup(15) syndrome.

Introduction

We previously reported prenatal diagnosis and molecular cytogenetic characterization of mosaicism for a small supernumerary marker chromosome 15 [sSMC(15)] without phenotypic abnormalities [1]. In this report, we additionally present a case with an sSMC(15) that was confirmed to be the inverted duplication of

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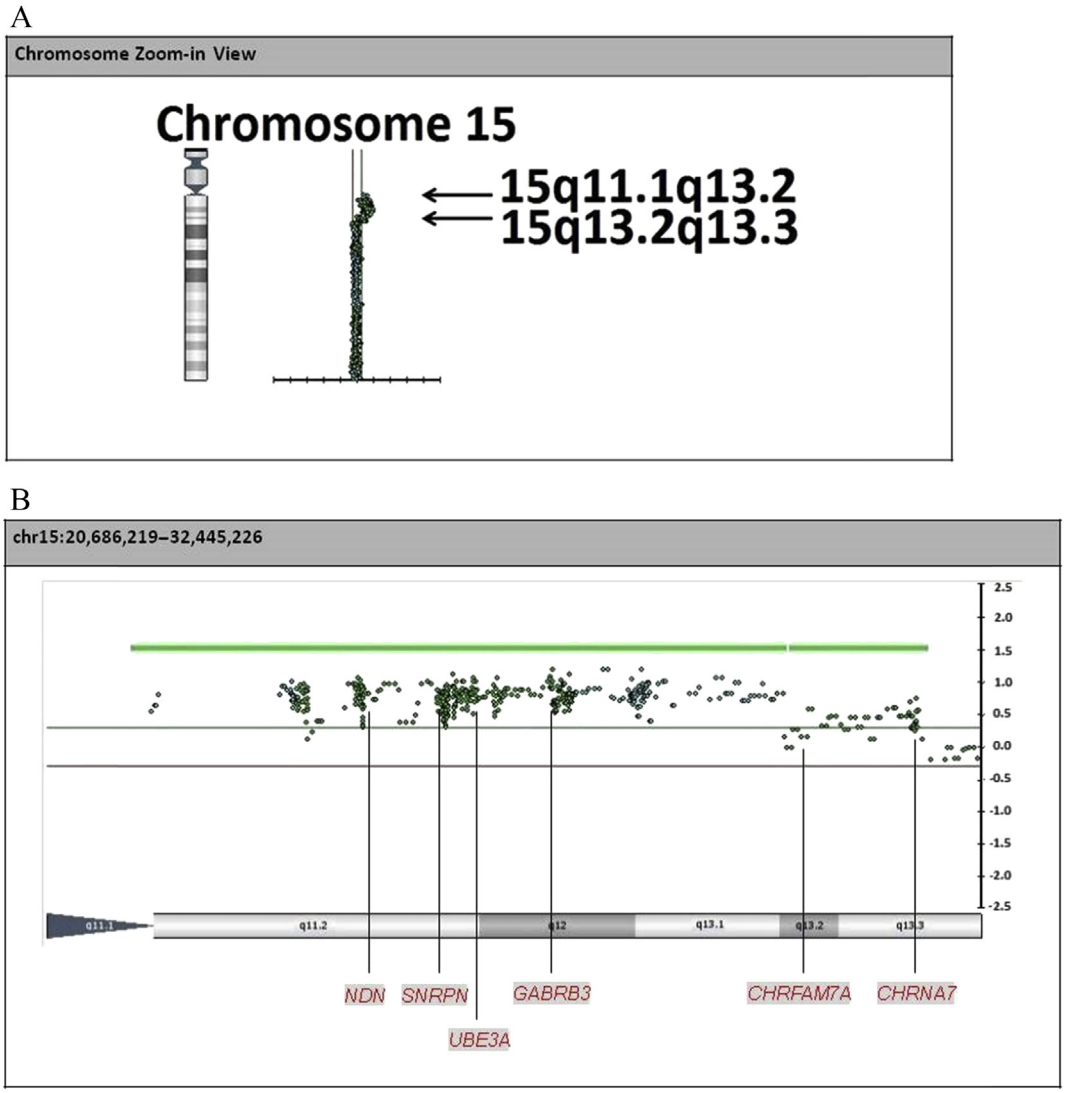

Figure 1. Array comparative genomic hybridization analysis of the proband's blood shows the result of arr 15q11.1q13.2 (20,686,219–30,390,043) × 4, 15q13.2q13.3 (30,390,043–32,445,226) × 3 with an 11.76-Mb gene dosage increase at 15q11.1–q13.3 encompassing the genes of *NDN*, *SNRPN*, *UBE3A*, *GABRB3*, *CHRFAM7A*, and *CHRNA7*. (A) and (B) Chromosome zoom-in view.

proximal chromosome 15 [inv dup(15)] and was associated with the inv dup(15) syndrome.

Case Presentation

A 35-year-old, gravida 3, para 2, woman underwent amniocentesis because of advanced maternal age at 27 weeks of gestation, which revealed an sSMC that was confirmed by fluorescence *in situ* hybridization (FISH) to be derived from chromosome 15. Her husband was 37 years of age, and there was no family history of congenital malformations. Prenatal ultrasound findings were unremarkable. A 3434-g male baby was delivered at term with no phenotypic abnormalities. Cytogenetic analysis of cord blood revealed a bisatellited dicentric sSMC(15), which was confirmed by FISH to be an inv dup(15). The parental karyotypes were normal. When followed up at 21 years of age, the proband had a body height of 161 cm, a body weight of 56 kg. He manifested the inv dup(15) syndrome including hypotonia, ataxic gait, developmental delay, intellectual disability, epilepsy, poor speech, and autism. Array comparative genomic hybridization of the peripheral blood revealed the result of arr 15q11.1q13.2 (20,686,219–30,390,043) × 4, 15q13.2q13.3 (30,390,043–32,445,226) × 3 with an 11.76-Mb gene dosage increase at 15q11.1–q13.3 encompassing 36 Online Mendelian Inheritance in Man (OMIM) genes including *NDN*, *SNRPN*, *UBE3A*, *GABRB3*, *CHRFAM7A*, and *CHRNA7* (Figure 1). Conventional cytogenetic analysis revealed a karyotype of 47,XY,+inv dup(15) (pter→q13::q13→pter; Figure 2). Quantitative fluorescent polymerase chain reaction analysis using the DNAs extracted from the proband's blood sample and the parents' blood samples revealed a maternal origin of the inv dup(15) chromosome (Figure 3). FISH analysis using the bacterial artificial chromosome probes of RP11-307C10 (15q11.2; 22,973,229–23,141,039; fluorescein isothiocyanate, green) and RP11-34H12 (15q13.2; 30,709,003–30,893,021; Texas red, red) confirmed an inv dup(15) chromosome with an order of green–red–red–green (Figure 4).

Discussion

The sSMC occurs in 0.06% of newborn babies of which the inv dup(15) is the most common sSMC and accounts for 50% of all