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Case Report

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Tumor suppressor candidate 3 gene deletion correlates with mental retardation in a child

Anne Weissenstein, Gloria Villalon, Elisabeth Luchter, Stefan Bittmann

Department of Department of Pediatrics, Ped Mind Institute, Medical and Finance Center Epe, Germany

Address for correspondence:
Stefan Bittmann, MD MA, Department of Pediatrics Ped Mind Institute, Medical and Finance Center Epe, D-48599 Gronau, Germany.
Tel.: +49-2565-97325,
Fax: +49-2565-97324,
E-mail: stefanbittmann@gmx.de

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ABSTRACT

We present the rare case of a 5-year-old boy with developmental delay and microcephalus. Deletion of tumor suppressor candidate 3 gene (TUSC 3) on chromosome 8p was found. It was localized in the gene region 8p22 with the loss of 51.5 kb. The same deletion was found in the 31-years-old father, the mother was negative for this entity. The function of TUSC 3 gene is yet not completely known, and this is one the first published cases in world literature.

KEY WORDS: Child, microcephaly, retardation, tumor suppressor candidate 3

INTRODUTION

The TUSC 3 gene is a candidate tumor suppressor gene. It is expressed in most nonlymphoid human tissues including prostate, lung, liver, colon and many epithelial tumor cell lines. Two transcript variants encoding distinct isoforms have been identified for this gene. TUSC 3 gene may be involved in N-glycosylation through its association with N-oligosaccharyl transferase. A disorder characterized by significantly below average general intellectual functioning and mental retardation associated with impairments in adaptive behavior and manifested during the developmental period is associated in an autosomal recessive hereditary way with TUSC 3 gene mutations. We present a case of a child with TUSC 3 gene deletion and related mental retardation.

CASE REPORT

The boy was born in the 37th week. Pregnancy was uneventful. Birth weight was 3030 g, length 47 cm. APGAR was 10/10 at 5 and 10 min. In the first year of life, a global developmental delay was present. Examination revealed microcephalus, hypotonic muscular function and epicanthus, and minimal craniofacial dysmorphy. The milestones in development "sitting" with 9 months and "free walking" with only 2.5 years were found. Chromosomal analysis was negative in May 2010. At age of 4 years, the patient has spoken only 2 word sentences. Electroencephalography and magnetic resonance imaging was negative. The parents have a daughter aged 3 years, which have no similar entities in the development. Array-CGH analysis revealed a deletion of tumor suppressor candidate 3 gene (TUSC 3) on chromosome 8p, which is extremely rare in children. The same deletion was found in the 31-year-old father, the mother was negative for this entity.

DISCUSSION

Alterations of human chromosome 8p frequently occur in many tumors. MacGrogan *et al*. isolated the TUSC3 gene, which they called N33, within a region on chromosome 8p22 in which a homozygous deletion was associated with metastatic prostate cancer [1,2]. The predicted 347-amino acid protein shares 43% identity with an anonymous C. Elegans gene and 20% identity with the yeast OST3 gene (oligosaccharyltransferase 34-kD subunit) [3]. The protein is predicted to have 4 transmembrane domains and was expressed as a 1.5-kb mRNA in most non-lymphoid cells and tissues examined, including prostate, lung, liver, and colon. Expression was also detected in many epithelial tumor cell lines. The TUSC3 gene encodes a protein involved in the vertebrate plasma membrane magnesium ion transport system. Two transcript variants encoding distinct isoforms have been identified for this gene [4], TUSC3-1 and TUSC3-2. TUSC3-1 and TUSC3-2 contain 348 and 347 amino acids, respectively, and differ only at their extreme C termini, with

TUSC3-1 ending in the sequence DLDFE and TUSC3-2 ending in FLIK. Both isoforms have an N-terminal signal sequence and 4 C-terminal transmembrane domains. Reverse transcription-polymerase chain reaction analysis revealed highest TUSC3 expression in ovary, cervix, placenta, prostate, testis, adipose, and lung, with little to no expression in other tissues examined. The TUSC3 gene contains 11 exons. A defect in the TUSC3 gene is associated with autosomal recessive mental retardation. In 2 patient-cases with non-syndromic autosomal recessive mental retardation [5] identified a homozygous mutation in the TUSC3 gene. The findings implicated a role for N-glycosylation in higher brain functions.

REFERENCES

1. MacGrogan D, Levy A, Bova GS, Isaacs WB, Bookstein R. Structure and methylation-associated silencing of a gene within a homozygously deleted region of human chromosome band 8p22. Genomics 1996;35:55-65.
2. Bova GS, MacGrogan D, Levy A, Pin SS, Bookstein R, Isaacs WB. Physical mapping of chromosome 8p22 markers and their homozygous deletion in a metastatic prostate cancer. Genomics 1996;35:46-54.
3. Pils D, Horak P, Gleiss A, Sax C, Fabjani G, Moebus VJ, *et al*. Five genes from chromosomal band 8p22 are significantly down-regulated in ovarian carcinoma: N33 and EFA6R have a potential impact on overall survival. Cancer 2005;104:2417-29.
4. Zhou H, Clapham DE. Mammalian MagT1 and TUSC3 are required for cellular magnesium uptake and vertebrate embryonic development. Proc Natl Acad Sci U S A 2009;106:15750-5.
5. Molinari F, Foulquier F, Tarpey PS, Morelle W, Boissel S, Teague J, *et al*. Oligosaccharyltransferase-subunit mutations in nonsyndromic mental retardation. Am J Hum Genet 2008;82:1150-7.

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