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Case Report

Detection of mosaic 15q11.1-q11.2 deletion encompassing *NBEAP1* and *POTEB* in a fetus with diffuse lymphangiomatosis

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ABSTRACT

Objective: We present cytogenetic and molecular cytogenetic diagnoses of mosaic deletion of chromosome 15q11.1-q11.2 in a fetus with diffuse lymphangiomatosis.

Case Report: A 33-year-old woman underwent amniocentesis at 22 weeks of gestation because of fetal diffuse lymphangiomatosis involving left-side chest, abdominal cavity, thigh and vulva, and intrauterine growth restriction. Amniocentesis revealed a karyotype of 46,XX,del(15) (q11.1q11.2)[9]/46,XX[26]. The mother had a karyotype of 46,XX. The father had a karyotype of 46,XY. The parents elected to terminate the pregnancy. A 610-g female fetus was delivered at 23 weeks of gestation with large cystic lymphangioma over the left abdomen, thigh, and vulva. The umbilical cord had a karyotype of 46,XX,del(15)(q11.1q11.2)[24]/ 46,XX[16]. The placental tissue had a karyotype of 46,XX,del (15)(q11.1q11.2)[23]/ 46,XX[17]. Array comparative genomic hybridization analysis of the umbilical cord and placenta revealed a 2.42-Mb deletion of 15q11.1-q11.2 encompassing the genes of *NBEAP1* and *POTEB*.

Conclusion: Deletion of 15q11.1-q11.2 encompassing *NBEAP1* and *POTEB* may be associated with diffuse lymphangiomatosis.

Introduction

Diffuse lymphangiomatosis is a rare congenital malformation of the lymphatics caused by primary lymphatic dysplasia and a lymphatic proliferative process that may involve soft tissues, visceral organs, bones, retroperitoneum, and eyes [1–3]. The cause of diffuse lymphangiomatosis is poorly understood, and the genetic basis of this disorder has rarely been investigated. We present perinatal detection of mosaic 15q11.1-q11.2 deletion encompassing *NBEAP1* and *POTEB* in a fetus with diffuse lymphangiomatosis. Our finding may provide a novel genotype–phenotype correlation of this disorder.

Case report

A 33-year-old gravida 1, para 0 woman underwent amniocentesis at 22 weeks of gestation because of abnormal fetal ultrasound findings. Her husband was 35 years old, and there was no family history of lymphangiomatosis. Level 2 fetal ultrasound

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examination revealed unilateral diffuse lymphangiomatosis involving left-side chest, abdominal cavity, thigh and vulva, and intrauterine growth restriction (IUGR). Amniocentesis revealed a karyotype of 46,XX,del(15)(q11.1q11.2)[9]/ 46,XX[26]. The mother had a karyotype of 46,XX. The father had a karyotype of 46,XY. The parents elected to terminate the pregnancy. A 610-g female fetus was delivered at 23 weeks of gestation with large cystic lymphangioma over the left abdomen, thigh, and vulva. Postnatal cytogenetic analysis revealed a karyotype of 46,XX,del(15)(q11.1q11.2)[24]/46,XX[16] in the umbilical cord and a karyotype of 46,XX,del(15)(q11.1q11.2)[23]/46,XX[17] in the placental tissue (Figure 1). Array comparative genomic hybridization (aCGH) analysis of the umbilical cord using Roche ISCA Plus Cytogenetic Array (Roche NimbleGen, Madison, WI, USA) revealed a result of a 2.39-Mb deletion of 15q11.1-q11.2 or arr 15q11.1q11.2 (20,225,177-22,617,226)×1.15 encompassing 79 genes including two Online Mendelian Inheritance in Man (OMIM) genes of *NBEAP1* and *POTEB*. The log2 ratio was −0.8 equivalent to 85% mosaicism for the deletion. aCGH analysis of the placental tissue revealed a result of a 2.42-Mb deletion of 15q11.1-q11.2 or arr 15q11.1q11.2 (20,200,762-22,617,226)×1.2 encompassing 79 genes including two OMIM genes of *NBEAP1* and *POTEB* (Figure 2). The log2 ratio was −0.75 equivalent to 80% mosaicism for the deletion. aCGH analysis of the maternal peripheral blood revealed a result of a 0.44-Mb microdeletion of 15q11.2 or arr 15q11.2 (22,179,070-22,617,226)×1.19 encompassing 16 genes including no OMIM gene. aCGH analysis of the paternal peripheral blood revealed a result of a 0.99-Mb microdeletion of 15q11.1-q11.2 or arr 15q11.1q11.2 (20,213,575-21,205,149)×1.18 encompassing 23 genes including no OMIM gene and a result of 0.47-Mb microdeletion of 15q11.2 or arr 15q11.2 (22,083,345-22,557,608)×1.16 encompassing 18 genes including no OMIM gene.

Discussion

The peculiar aspect of the present case is the association of 15q11.1-q11.2 deletion with diffuse lymphangiomatosis involving the deficiency of *NBEAP1* and *POTEB*. *POTEB* (OMIM 608912) belongs to the pote ankyrin domain family *POTE* (prostate-, ovary-, testis-, and placenta-expressed gene) [4,5]. POTE protein is associated with apoptotic cells and plays a role in apoptosis [6,7]. *NBEAP1* (OMIM 601889) or *BCL8* (B-cell CLL/lymphoma 8) is involved in translocation t(14;15)(q32;q11-13) breakpoint affecting band 15q11-13 in diffuse large-cell lymphoma [8]. *NBEAP1* belongs to an evolutionarily conserved human gene family that encodes proteins with protein kinase A anchoring function [9].

The present fetus and her family had copy number variation (CNV) at 15q11.1-q11.2. However, only the present affected fetus had deficiency of *NBEAP1* and *POTEB* and diffuse lymphangiomatosis. Whether such a correlation is a coincidence or a pathogenetic effect is unclear and will require more investigations to prove.

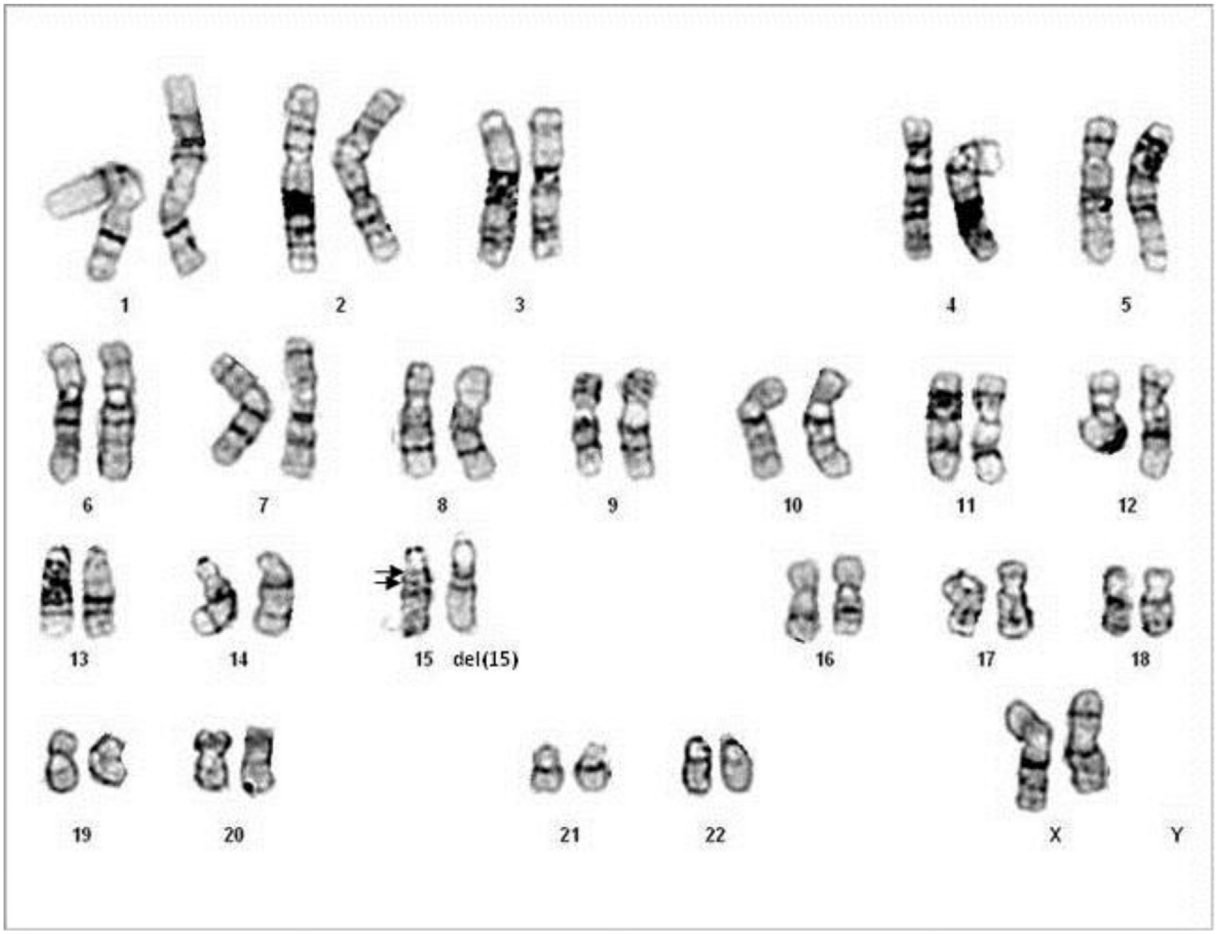

Figure 1. A karyotype of 46,XX,del(15)(q11.1q11.2). The arrows indicate the breakpoints.

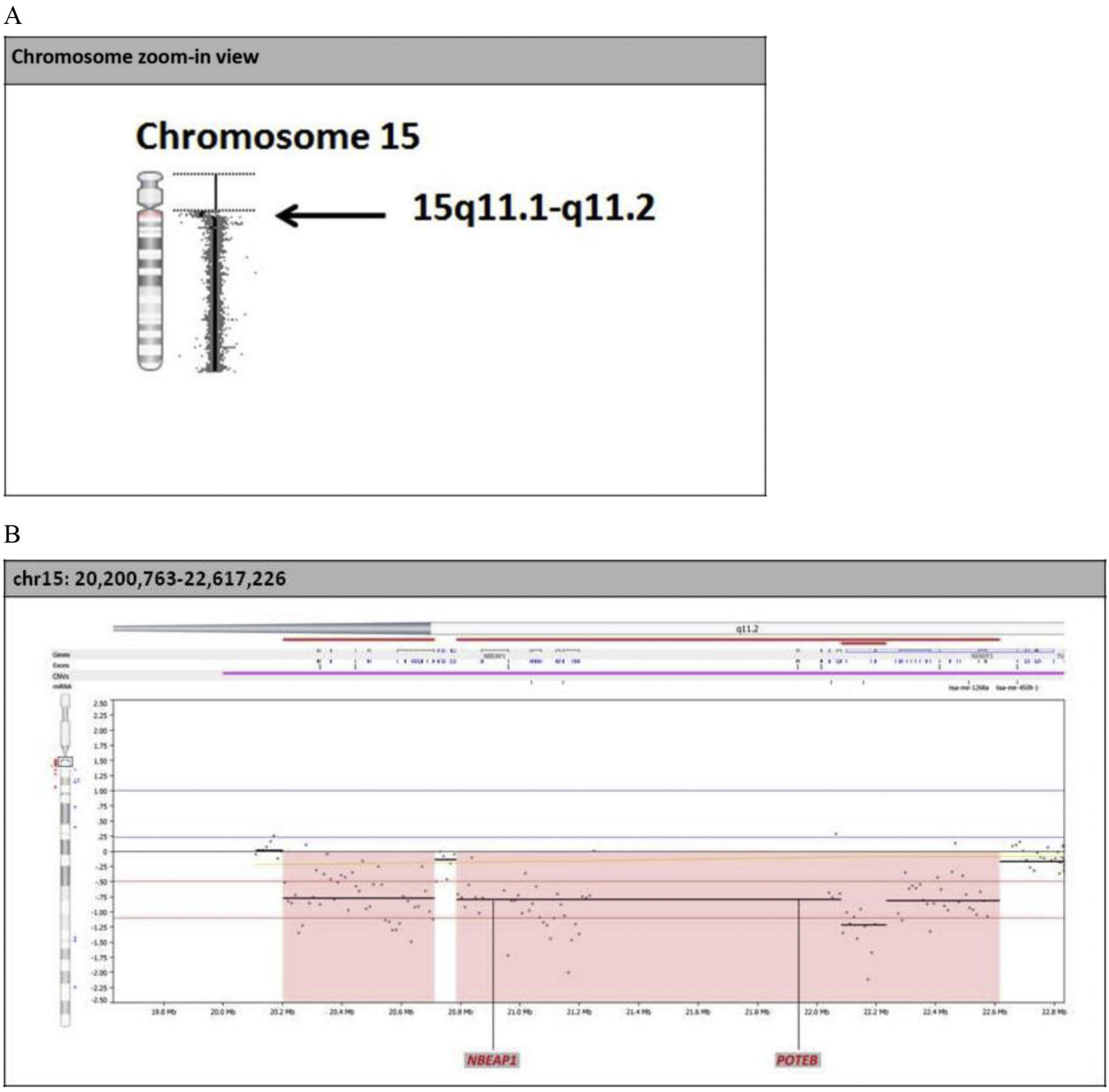

Figure 2. Array comparative genomic hybridization analysis on the placental tissue reveals a result of a 2.42-Mb deletion of 15q11.1-q11.2 encompassing *NBEAP1* and *POTEB*. (A) Chromosome zoom-in view; (B) chromosome 15.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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