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Research Letter

A 17q duplication prenatally detected

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This report is about an isolated *de novo* interstitial duplication of chromosome 17q detected in prenatal diagnosis. The duplication spans about 15.6 Mb, and contains at least 15 OMIM genes.

As far as we know, this is the first case which has been detected prenatally; postnatal cases with a similar chromosomal anomaly are rare and the phenotype has been associated with a wide spectrum of clinical signs. This phenotypic variability may be due to the different extents of the duplicated regions, thus an accurate molecular definition of the chromosomal breakpoints is necessary to make better genotype-phenotype correlations [1].

The mother was a 36-year-old healthy woman with two healthy children; amniocentesis was performed at the 16th week of gestation because of her advanced age. Ultrasound gynecological examination did not show any fetal abnormalities except for a slight hypertelorism. Conventional banding chromosome analysis on cultured amniotic fluid cells, with a resolution of about 400 bands, revealed an apparent terminal duplication of chromosome 17q (Fig. 1), that was better characterized using molecular cytogenetic techniques.

Array-comparative genomic hybridization (Array-CGH) using a 44 K oligo platform (Agilent Technologies, Santa Clara, CA, USA) revealed that the duplication was not terminal but interstitial, from position 55,354,004 bp (17q23) to position 71,053,979 bp (17q25) (NCBI36/hg18 map) (Fig. 2). The OMIM genes in the region can be seen in Table 1 and in Fig. 3. Fluorescent *in situ* hybridization, using the whole Chromosome Painting 17 probe (Cytocell, LTD Cambridge, UK), excluded additional cryptic rearrangements; Telvysion 17q (Vysis, Abbott S.p.A., Milan, Italy) probe for the 17q subtelomeric regions showed two normal signals (Fig. 4), confirming array-CGH data. Parental karyotypes and array CGH profiles were normal.

Pregnancy was terminated at the 21st week of gestation. Analysis of the fetal anatomy showed minor facial dimorphisms with hypertelorism, a wide nasal base, a wide mouth and a thin upper lip (Figs. 5–6), along with no specific signs such as microcalcinosis in the adrenal and hepatic parenchyma that can be associated with many other chromosomal anomalies, such as Di George Syndrome, Edwards Syndrome, Patau Syndrome, Down Syndrome, and mosaicism for partial trisomy of chromosome 8 [2–5].

Partial 17q duplication is a rare anomaly, and most of the patients reported in literature have undergone postnatal analysis using classic cytogenetic techniques. The resolution of cytogenetic banding is about 10 Mb, thus a detailed analysis of breakpoints is missing. Duplication 17q has been associated with a severe phenotype but the clinical consequences of this anomaly are far from being clarified, and extensive variability is present among the reported patients. Manifestations of this anomaly include psychomotor/mental retardation, growth retardation, and dysmorphic features such as facial asymmetry with hypertelorism, frontal bossing and temporal narrowness, a broad nasal bridge, epicanthal folds, wide mouth with a thin upper lip, micrognathia, webbed neck, low-set posteriorly angulated ears, and an abnormal hairline. Moreover partial trisomy 17q is associated with polydactyly, long fingers, abnormal positioned feet, cerebellar hypoplasia, multiple cardiac anomalies, limb shortness, hyperlaxity, genital abnormalities, and accessory spleen [6,7].

The partial trisomy of 17q has been described in complex chromosomal rearrangements (Table 2). King et al [8] reported a case of partial trisomy 17q2-qter, detected by amniocentesis which was performed because of polyhydramios and ultrasound diagnosis of fetal anomalies. The chromosome complement of the cultured amniotic fluid cells was 46,XX/46,XX,-21,+der(21),t(17;21) (q21.1; q22.3) in a ratio of 1:15; the infant born showed the unique phenotypic features of mosaic partial trisomy 17q2: frontal bossing, large mouth, brachyrhizomelia, and hexadactyly. Babovic-Vuksanovic et al [9] presented a familial case of dup 17q24-q25.1, whose clinical characteristics resembled Ullrich-Turner syndrome, indicating the presence of genes involved in skeletal development. Kelly et al [6] described an adult with dup

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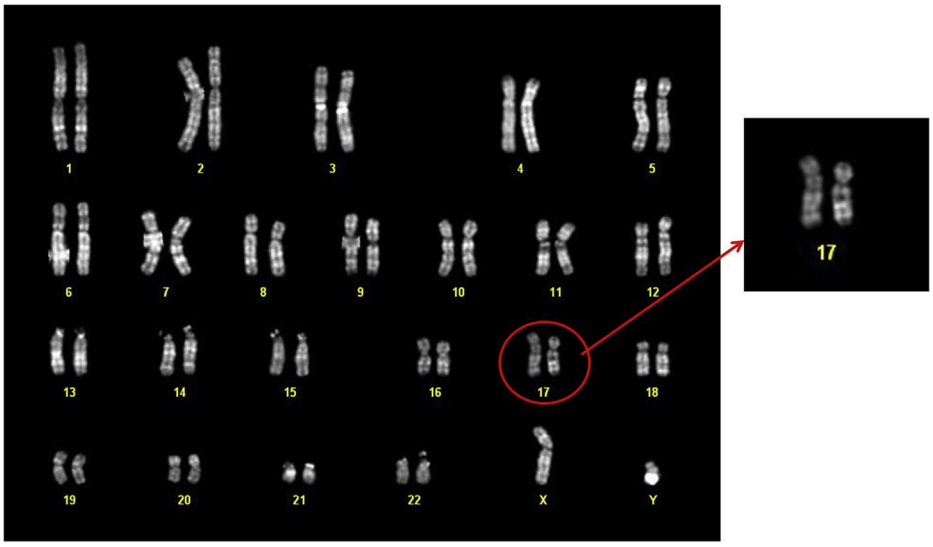

Fig. 1. Cytogenetic analysis of the cultured amniotic fluid cells by Q-banding. Karyotype shows a duplication of the long arm of chromosome 17.

17q24-q25, suffering with epilepsy, sensorineural hearing loss, long fingers, and overlapping toes. In a study Lukusa et al [1] reported a case of a 3 year-old girl, with pure 17q25.3 (2.46 Mb) duplication and a complex clinical presentation comprising main features of dup 17q syndrome and additionally striking distal arthrogryposis.

Most cases of partial trisomy for the distal region of 17q are due to adjacent-1 segregation of reciprocal translocation which were derived from either one of the parents [10–12]; some cases are due to a familial chromosome 17 inversion [13,14], few are *de novo* events [8].

This report shows the first case of a *de novo* isolated 17q duplication detected in a fetus without ultrasound abnormalities. The results of the fetal autopsy did not show the typical phenotypic alterations observed in cases diagnosed postnatally thus the correlation of genotype-phenotype is difficult, particularly during prenatal investigations. The lack of specific data concerning the prognosis of fetuses with dup 17 q makes genetic counseling a difficult task.

The 17q23-qter portion is the region most commonly duplicated in almost all the dup 17q cases reported in literature. This region includes OMIM genes involved in several diseases, such as retinitis pigmentosa, ciliarydyskenesia, microcephaly, and bradyopsia (Table 1). So far, the duplication we have found is the largest described in prenatal diagnosis and it is likely that it was not compatible with life; if the pregnancy had not been interrupted the infant would have probably shown the major clinical signs of dup 17q syndrome immediately after birth.

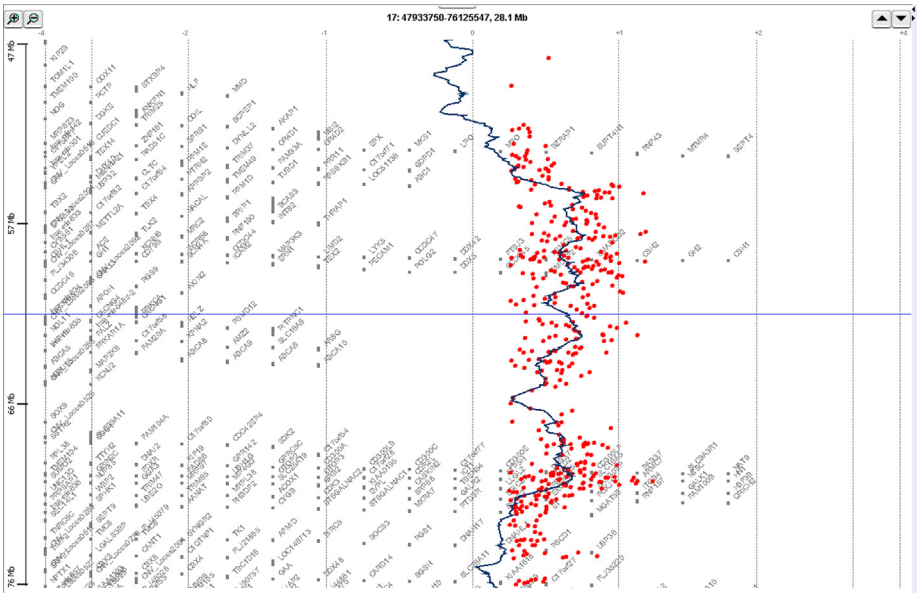

Fig. 2. Array-comparative genomic hybridization profile of the duplicated region. Array-comparative genomic hybridization showing the presence of a duplication of chromosome 17q23-q25 (red dots represent duplicated oligos).

Table 1
OMIM genes located in the duplicated region 17q 23-25.

Gene		Location	Phenotype
Carbonic anhydrase IV	***CA4***	17q23.1	Retinitis pigmentosa 17
Small patella syndrome	***SPS***	17q23.2	Small patella syndrome
Angiotensin i-converting enzyme	***ACE***	17q23.3	Renaltubulardysgenesis Angiotensin I-converting enzyme, benign serum in crease Alzheimer disease, susceptibility to Microvascular complications of diabetes 3 Myocardial infarction, susceptibility to SARS, progression of Stroke, hemorrhagic
Ste20-related kinase adaptor alpha	***STRADA***	17q23.3	Polyhydramnios, megalencephaly, and symptomatic epilepsy
Growth hormone 1	***GH1***	17q23.3	Growth hormone deficiency, isolated, type IA Growth hormone deficiency, isolated, type IB Growth hormone deficiency, isolated, type II Kowarski syndrome
CD79 B antigen	***CD79 B***	17q23.3	A gamma globulinemia 6
Sodium channel, voltage-gated, type IV, alpha subunit	***SCN4A***	17q23.3	Hyperkalemic periodic paralysis, type 2 Hypokalemic periodic paralysis, type 2 Myasthenic syndrome, acetazolamide-responsive Myotonia congenita, atypical, acetazolamide-responsive Paramyotonia congenita
Polymerase, DNA, GAMMA-2	***POLG2***	17q23.3	Progressive external ophthalmoplegia with mitochondrial DNA deletions, autosomal dominant 4
Regulator of G protein signaling 9	***RGS9***	17q24.1	Bradyopsia
Family with sequence similarity 20 member A	***FAM20 A***	17q24.2	Amelogenesis imperfecta and gingival fibromatosis syndrome
Sry-box 9	***SOX9***	17q24.3	Acampomelic campomelic dysplasia Campomelic dysplasia Campomelic dysplasia with autosomal sex reversal
Component of oligomeric golgi complex 1	***COG1***	17q25.1	Congenital disorder of glycosylation, type IIg
Dynein, axonemal, intermediate chain 2	***DNAI2***	17q25.1	Ciliary dyskinesia, primary, 9, with or without situs inversus
Solute carrier family 9, member 3, regulator 1	***SLC9A3R1***	17q25.1	Nephrolithiasis/osteoporosis, hypophosphatemic, 2
Solute carrier family 25 (mitochondrial thiamine pyrophosphate carrier), member 19	***SLC25A19***	17q25.1	Microcephaly, amish type Thiamine metabolism dysfunction syndrome 4 (progressive polyneuropathy type)

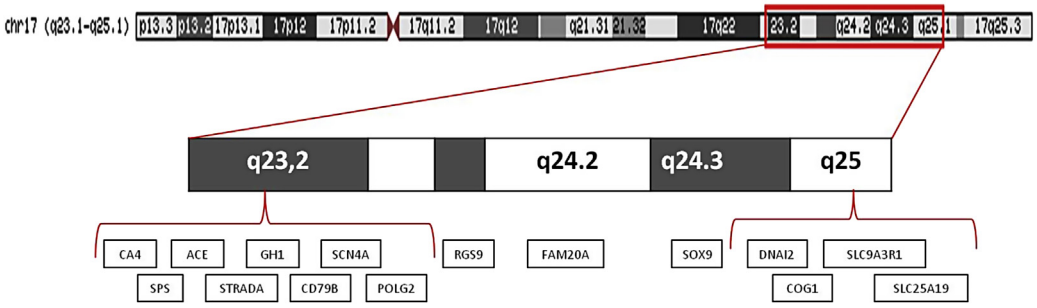

Fig. 3. OMIM genes located in the duplicated region 17q23-25.

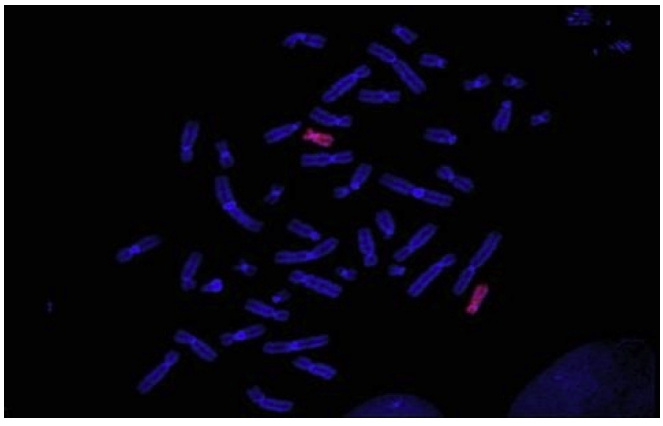

Fig. 4. Fluorescence *in situ* hybridization performed using the probe Whole Chromosome Painting 17 (Cytocell).

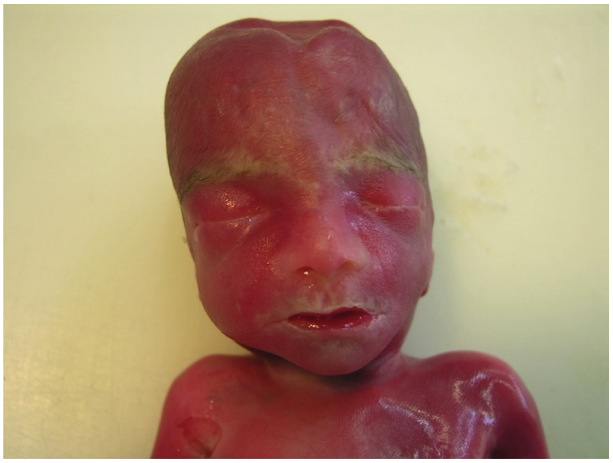

Fig. 5. Hypertelorism and a wide nasal base.

Fig. 6. Apparently normal fetal anatomy.

Table 2
Duplication of 17q region as sole chromosome anomaly reported in literature and in our study.

Study	Duplicated 17q region
Babovic-Vuksanovic et al 1998 [9]	17q24-q25.1
Kelly et al 2002 [6]	17q24-q25
Lukusa et al 2010 [1]	From 17q 25.3 (2,46 Mb)
Our study	17q23-q25 (15.6 Mb)

Conflict of interest

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

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