

Chromosome 3p Duplication: A Rare Chromosomal Anomaly

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ABSTRACT

Partial trisomy 3p results from either unbalanced translocation or *de novo* duplication. Common clinical features consist of dysmorphic facial features, congenital heart defects, psychomotor and mental retardation, abnormal muscle tone and hypoplastic genitalia. In this paper, we report a case of partial trisomy 3p with rare clinical manifestations. A full-term, female newborn was admitted to our hospital with complaints of repeated seizures and developmental retardation. On evaluation, chromosome 3p duplication was detected.

Keywords: Partial trisomy 3p, unbalanced translocation, seizures, developmental retardation, chromosome 3p duplication

Chromosome 3p duplication is an anomaly that occurs with an extra copy of genetic material on the short arm (p) of third chromosome. Another name for chromosome 3 duplication is trisomy 3p. It is a rare chromosomal disorder, where a portion of the short arm (p) of chromosome 3 is duplicated, so there are three copies of it rather than the normal two.

The severity along with the signs and symptoms depends on location and the size of duplication. Features that often occur in people with chromosome 3p duplication include developmental delay, behavioral problems, intellectual disability and distinctive facial features. Chromosome 3p duplication can be inherited from a parent with balanced translocation or *de novo* origin^{1,2}. Treatment is based on the signs and symptoms on individual basis.

Signs and symptoms are brachycephaly, square face, frontal bossing, flat back of skull, small jaw,

full cheeks, malformed auricles, widely spaced eyes, bushy eyebrows, downward slanting of eyes, short nose, large mouth, short upper lip, cleft lip and palate, short neck, short hand, stubby feet, excessive whorls, hemivertebrae, reduced muscle tone, seizure, congenital heart defect, esophageal atresia, hypoplastic kidney, ureteric duplication, growth retardation, speech retardation, mental retardation, feeding difficulty.

“*De novo*” duplications occur randomly during the formation of the egg or sperm. In these cases, a person would have no family history of the condition but could pass the duplication on to children. Other cases of chromosome 3p duplication are the result of a balanced translocation in one of the parents. Carriers of a balanced translocation generally do not have any unusual symptoms or health problems; however, they have an increased risk of having children with chromosomal abnormalities.

CASE REPORT

A 2½-year-old female child, a product of non consanguineous marriage with proper antenatal check-up and normal antenatal ultrasonography (USG) delivered through normal vaginal delivery (NVD) at hospital. Baby had not cried immediately after birth and was admitted to neonatal intensive care unit (NICU) and discharged after 3 days. At 2½ years, the baby came to the hospital with c/o delayed developmental milestones, repeated episodes of seizures at 20-25 days interval from the age of 7 months and poor weight gain. Baby recognized mother at 6 months, started neck holding at

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CASE REPORT

7 months, bi-syllable sound at 2 years, walked with support at 2 years. Baby was having head circumference of 40 cm, weight was 9 kg, mid-arm circumference was 12 cm, antimongoloid slant of eyes, brachycephaly, small jaw, broad and short nose, short neck, epicanthic fold, large mouth (Fig. 1), malformed auricle (Fig. 2),



Figure 1. Facial anomaly.



Figure 2. Ear anomaly.

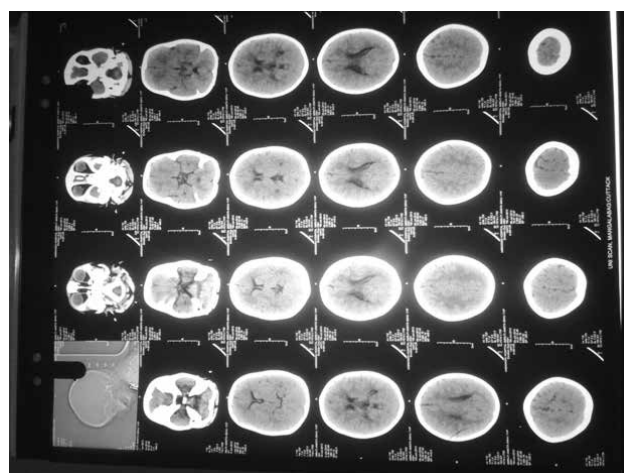


Figure 3. CT scan of brain.

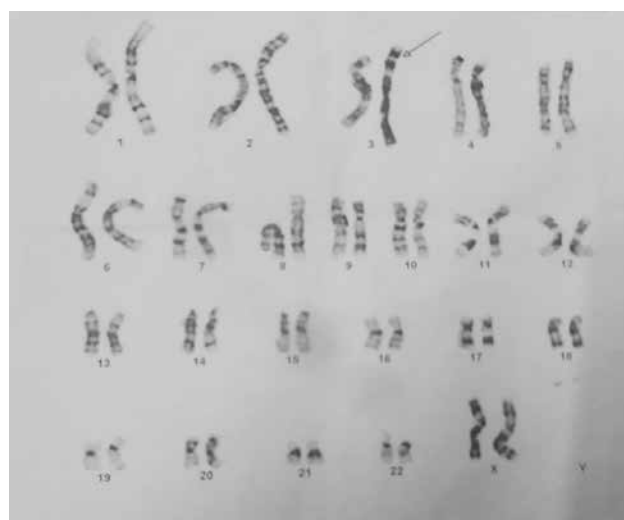


Figure 4. Chromosomal anomaly showing 3p duplication.

reduced muscle tone, seizures, growth retardation, mental retardation and speech retardation. On evaluating the child, complete blood count was normal. Electroencephalograms (EEG) showed normal sleep-wake cycle and normal EEG, CT brain showed no apparent anomaly (Fig. 3). On chromosomal analysis there was presence of duplication of segment between 3p22 and 3p25 (Fig. 4). For recurrent seizures, child was treated with levetiracetam and valproate, dietary modification advice and developmental counseling was properly given.

DISCUSSION

Our bodies are made of billions of cells. In each cell is a set of structures called chromosomes that carry all of the instructions (genes) for the cell to function. We generally have 23 pairs of chromosomes and inherit one in each pair from each parent. Sometimes,

a section from one chromosome of a particular pair changes places with a section from a chromosome of another pair. When the two breaks do not pass through a gene and there is no gain or loss of material when the chromosomes are looked at under a microscope, it is called a balanced translocation.

Some people discover from a blood test when they have had a child with special needs or health problems caused by a chromosome disorder. Some people have repeated miscarriages or other fertility problems. Some people have a blood test as part of family investigations. Others find out by chance when they have a chromosome test for other reasons. Occasionally, a balanced translocation is found in a baby during pregnancy. Translocations can be new or they can be passed down in families from parent to child through the generations. New translocations occur when sperm or egg cells are forming or just after fertilization during the copying of the early cells that will become an embryo, then a fetus and then a baby. One study suggests that most new balanced translocations arise during sperm production and particularly in older fathers. They are not caused by men's lifestyle, environment or work. Duplication of the short arm of chromosome 3 is associated with severe delay in mental development. More than 50% of children die within the first 2 years of life. Duplications may be due to paternal or maternal balanced translocation.

The list of signs and symptoms mentioned in various sources for trisomy 3p include³⁻⁵:

- **Skull:** Brachycephaly, holoprosencephaly, flat back of skull, temporal indentations.
- **Face:** Square face, frontal bossing, small jaw, facial clefts, full cheeks.
- **Eyes:** Widely spaced eyes, iris coloboma, small eyes, telecanthus, bushy eyebrows, downward slanting space between eyelids, cyclopia, epicanthal folds.
- **Nose:** Short nose, broad nose, flat nose, prominent philtrum, choanal atresia.
- **Ear:** Malformed auricles.
- **Mouth:** Large mouth, short upper lip, cleft lip, cleft palate.
- **Neck:** Short neck.
- **Extremities:** Short hands, stubby hands, short feet, stubby feet, camptodactyly, syndactyly, brachymesophalangy, clubfoot, excessive fingertip whorls, joint contractures.
- **Cardiac defects:** Congenital heart defects including tetralogy of Fallot, ventricular septal defect, hypoplastic heart and transposition of the great vessels.
- **Central nervous system:** Seizures.
- **Muscles:** Severe hypotonia.
- **Gastrointestinal:** Esophageal atresia, atresia of the colon and rectum.
- **Miscellaneous:** Hemivertebrae, reduced muscle tone, accessory nipples, esophageal atresia, atresia of colon, rectal atresia, hypogonadism, hypospadias, small penis, undescended testes, duplication of ureters, kidney hypoplasia, kidney cysts, hypercholesterolemia, growth retardation, motor retardation, speech retardation, mental retardation and feeding difficulty.

There are several different specialized tests that can be used to diagnose a chromosome 3p duplication. These include:

- **Karyotyping:** A karyotype is a laboratory test that produces an image of a person's chromosome. This test can be used to diagnose large duplications.
- **FISH:** A laboratory technique that is used to detect and locate a specific DNA sequence on a chromosome. A chromosome is exposed to a small DNA sequence called probe that has a fluorescent molecule attached to it. The probe sequence binds to its corresponding sequence on the chromosome. This test can be used in combination with karyotyping for duplications that are too small to be seen on karyotype. However, FISH is only useful if the person ordering the test suspects there is a duplication of a specific region of 3p.
- **Array CGH:** A technology that detects duplications that are too small to be seen on karyotype.

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