

Constitutional Tetrasomy 18p

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We present here the first case of constitutional tetrasomy 18p from India. A 3-year-old female with developmental delay and dysmorphic features revealed 47,XX,+mar karyotype. The small meta-centric marker chromosome was identified as i(18p) with m-FISH followed by m-BAND. Parents and a normal sibling of the proband revealed normal karyotype. There was history of mental retardation and dysmorphic features in four cases on paternal side; however, their karyotype was also normal.

Key words: FISH, Tetrasomy.

Chromosome analysis is indicated for conditions like mental retardation, dysmorphic features *etc.* Within the limits of conventional cytogenetics, various gross chromosomal anomalies are identified. In addition to this, other cryptic and rare constitutional chromosome anomalies are also increasingly uncovered with molecular cytogenetic techniques since the last decade. A patient with dysmorphic features and delayed development was referred to our laboratory for

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chromosomal analysis. Tetrasomy of 18p was established with the help of molecular cytogenetics. We wanted to study extended family members with a history of mental retardation to see if similar chromosomal marker was involved.

Case Report

An 8-month-old female child was referred for chromosomal analysis due to suspected congenital anomaly. The age of the parents at the time of patients' birth were 30 and 32 years for mother and father respectively. The ultrasonography during pregnancy was normal. Her length, weight and head circumference were within the normal limits. Her urine analysis for reducing substance was normal and FeCl₃ test was normal. The results of ultrasonography and fundus examination were also normal. There was no weight gain until the age of 6 months, however, later it was normal. Clinical examination revealed several dysmorphic features. With reference to the percentage of patients with one of 50 different phenotypic features listed in table on the website(1), the presence of the features in index patient was recorded. These features included, develop-mental delay, low set ears, small head, high arched palate, small mouth and chin, epicanthic folds, crossed eyes, long philtrum, down-slanting eyes, asymmetric face, hyper telorism, and hypotonia.

Her family history was remarkable with four cases of mental retardation from paternal side. The paternal aunt, 36/F is mentally retarded (IQ 60) having schizophrenia, dysmorphic features and short stature. Other relatives from previous generations, 40/F, 42/M are siblings with low IQ / mild mental retardation and socially less developed, the male relative is married, with no children. Another relative, a 16/F also has mental retardation.

CASE REPORTS

Karyotypic analysis of above mentioned four affected relatives, and normal individuals i.e. parents, a sibling, and paternal grandfather was normal. Conventional cytogenetic studies were carried out as per standard methods. M-FISH and M-BAND were carried out as per manufacturer protocol (Metasystems, Germany) at Germany.

Based on the results of detailed cytogenetic analysis, the condition was diagnosed as tetrasomy of 18p (*Fig. 1a and 1b*), a known condition from the western countries, but reported for the first time from India. The family is registered on the web site(1) and useful literature was made available to the mother after translation in local language.

Discussion

In order to arrive at an accurate diagnosis of genetic condition, the conventional cytogenetics needs to be substantiated with molecular methods. Use of m-FISH and

m-BAND could simultaneously determine the origin and copy number of the chromosomal fragment in the marker i.e., tetrasomy of 18p. Use of multiplex fluorescent PCR has been reported previously, which gives additional information regarding parental origin of the marker(2). Both paternal(3), and maternal(2,4) origin has been reported. The abnormality of chromosome 18 is either inherited(5) or de novo(6,7).

Pooling the data helps learn about genotype / phenotype correlations and aid in the recognition and diagnosis of tetrasomy 18p. Even in a relatively well-defined condition like Down syndrome, intrinsic variability of the phenotype has been observed. Similarly, tetrasomy 18p seems to display marked variability of phenotypic characteristics. However, combining certain common characteristics may point to a unique picture of an individual with tetrasomy 18p; as a firm definition of the phenotype of tetrasomy 18p has not been

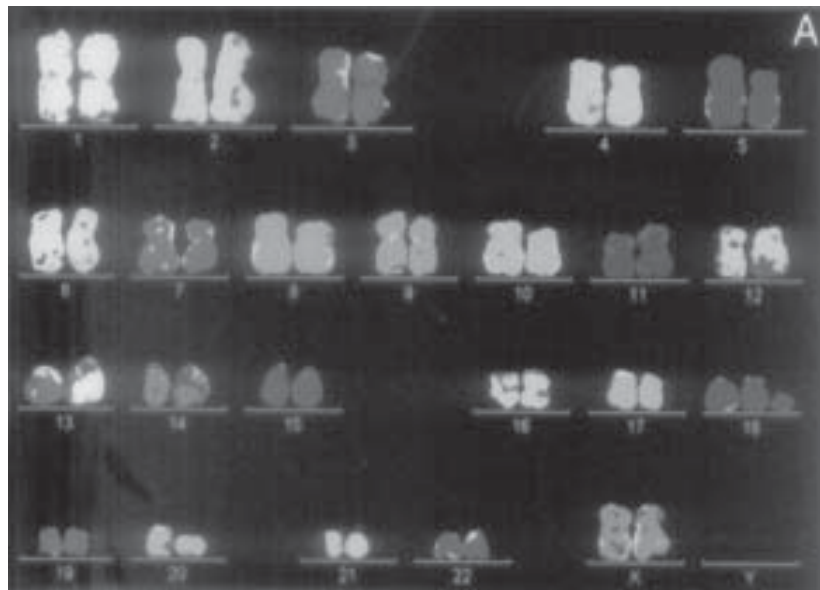


Fig. 1a. M-FISH karyotype depicting three copies of chromosome 18.

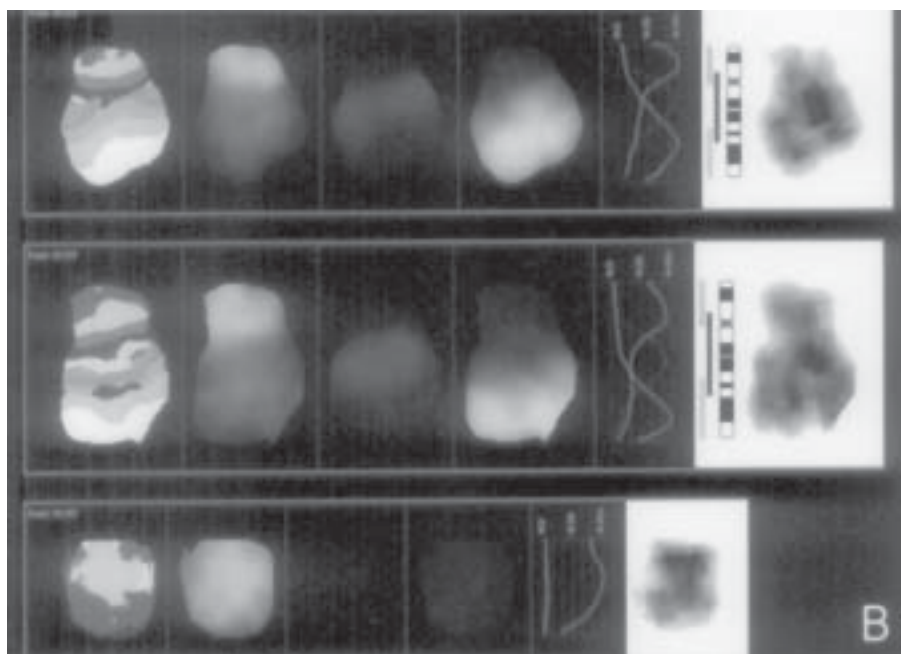


Fig. 1b. M-band image depicting tetrasomy of 18p.

reached unlike Down syndrome. It is important to put on record such rare cases of genetic conditions, as there are relatively small numbers of cases in such category of chromosome anomalies that provides opportunity to explore the mechanisms of anomalies that may be generalizable to other conditions.

This is the first report of constitutional tetrasomy 18p from India. Laboratories dealing with clinical cytogenetics are meager in India compared to the western countries, and rarely equipped with molecular cytogenetics facilities. This fact may have masked the real incidence of many subtle chromosomal abnormalities.

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Subcutaneous Fat Necrosis with Hypercalcemia

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Subcutaneous fat necrosis of the newborn (SCFN) is an uncommon condition and may be complicated by hypercalcemia. A 28-day-old neonate, presenting with SCFN, hypercalcemia and nephrocalcinosis was managed with intravenous saline followed by furosemide, oral prednisolone, potassium citrate and etidronate.

Key words: *Hypercalcemia, Subcutaneous fat necrosis, Nephrocalcinosis*

Hypercalcemia in children is relatively less common when compared to hypocalcemia. Causes of hypercalcemia in infants include causes like hyperparathyroidism and vitamin D intoxication. Identification of the cause is essential for the management of

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hypercalcemia in children. Subcutaneous fat necrosis (SCFN) is a rare cause of hypercalcemia in newborns and infants. The duration of follow-up of these children and management of hypercalcemia with newer drugs are highly debatable. We report a neonate who presented with SCFN and persistent hypercalcemia.

Case report

A 28-day-old neonate, born to a primigravida mother by emergency cesarean section for fetal distress and exclusively breast-fed, was brought with swellings over right elbow, thighs, cheeks and arms of one week duration. On examination, the neonate was pink, active, normothermic with normal vital signs and had reddish purple nodular swelling over arms, thighs and cheeks. The swellings were non-tender, non-fluctuant and firm; the joints were normal. The hemoglobin level was 15 g/dL, leukocyte count 12100/cumm with 40% neutrophils, 43% lymphocytes and 15% eosinophils and platelet count of 250,000/cumm. The blood culture was sterile. Blood levels of urea 38 mg/dL, creatinine 0.7 mg/dL, sodium 136 mEq/L, potassium 3.7 mEq/L, bicarbonate 20 mEq/L, calcium 17.8 mg/dL, phosphorus 7.1 mg/dL, magnesium 2.0 mg/dL, cholesterol 100 mg/dL, total protein 6.9 g/dL, albumin 3.9 g/dL and sugar 90 mg/dL were noted. Urinalysis showed the following: pH 6.5, specific gravity 1.010, albumin 1+ and no deposits. Urine culture was sterile and the random urine sample showed calcium level of 24.4 mg/dL