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Case Report
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Atypical Features in a Neonate with *de novo* 17p11.2p13.2 Duplication Syndrome - A Case Report

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Abstract

17p duplication is a rare chromosomal abnormality which is either inherited from parents or can occur *de novo*. The clinical spectrum depends on the size and location of the duplication. The present case report is a case of neonate born to non consanguineous couple with antenatal findings of Fetal Growth Restriction (FGR), unilateral hydronephrosis. Postnatally the neonate had low birth weight, facial dysmorphism and unilateral hydronephrosis with additional findings of 11 pairs of ribs, excessive Mongolian spots, brachydactyly, preaxial polydactyly. Chromosomal microarray has revealed 17p11.2p13.2 duplication. As parental karyotype is normal, it is *de novo* duplication. This case highlights the rarity of the syndrome and presence of additional clinical features not reported previously in cases with 17p duplication syndrome.

Keywords: Non allelic homologous recombination; Low-copy repeats; 17p duplication; Preaxial polydactyly; Mongolian spots

Introduction

Chromosome 17 constitutes about 3% of total human genome with 1,300 to 1,400 genes [1]. It has second highest gene density and rich in protein-coding genes [2,3]. Deletions and duplications of various regions of chromosome 17 have been reported [1]. Duplications of 17p accounted for only 4.5%. This may be attributed to the fact that duplications are not as easily diagnosed as deletions in karyotype [4,5]. 17p duplication is a diverse entity where copy number changes are present on the short arm of chromosome 17. It can either be inherited from parents or can occur *de novo* [4,5]. The clinical spectrum depends on the size and location of the duplication and thus on the genes that have been duplicated [4]. Few of the clinical features include hypotonia and feeding problems, dysmorphic facial features, cardiac and renal anomalies, digital abnormalities, and developmental delay, intellectual and behavioral abnormalities. Long term prognosis/outcome of these conditions also depends on the segment of the chromosome that is involved [4,5].

Case Presentation

This is a case of a neonate born second in order to healthy non-consanguineous couple by cesarean delivery with birth weight of 2 kg. The previous pregnancy of the couple resulted in missed abortion. There were no other co-morbidities or teratogenic exposure during pregnancy. Past medical and family history was unremarkable. NT scan and serum screen were normal. TIFFA scan revealed right hydronephrosis with PUJ obstruction. Follow up scans showed progressive hydronephrosis with fetal growth restriction. The APGAR scores were 8/8/9 at 1, 5, 10 minutes with no resuscitation being required. Arterial cord pH was 7.27 and Base Excess (BE) was 5.4. Baby was admitted in NICU in view of respiratory distress since birth and was started on oxygen delivered through nasal prongs. Feeding, activity, bladder and bowel habits were normal. Oxygen was gradually weaned off by day 10 of life with saturations maintaining at 98% on room air and the Respiratory Rate (RR) at 60 to 70 per min. On examination, weight of the baby was 2.07 kg (-2SD), length was 44 cm (-4.5SD), occipital-frontal-circumference was 30.5 cm (-4SD). Facial dysmorphism was noted in the form of small posteriorly rotated ears with over folded upper pinna, bulbous nasal tip with flared nostrils, a high arched palate and mild retrognathia. Neck and spine were normal. Chest was slightly narrow. There were increased Mongolian spots over the back and limbs. There was clinodactyly of bilateral fifth fingers, brachydactyly of toes, preaxial polydactyly of right hand. Parents did not give consent for photography. Examination of cardiovascular and respiratory systems was normal. Abdomen was soft with no obvious organomegaly. Baby was conscious with the tone and reflexes being normal.

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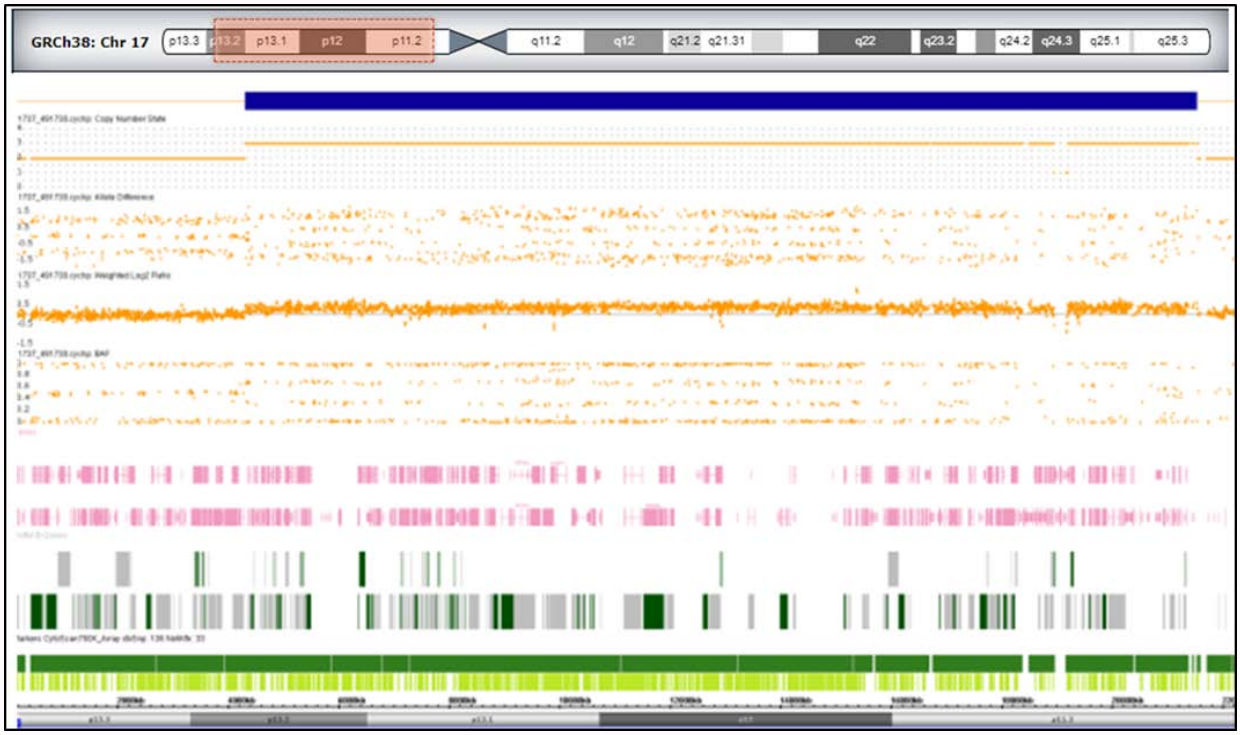

Figure 1: 17.2 Mb pathogenic duplication of 17p11.2p13.2.

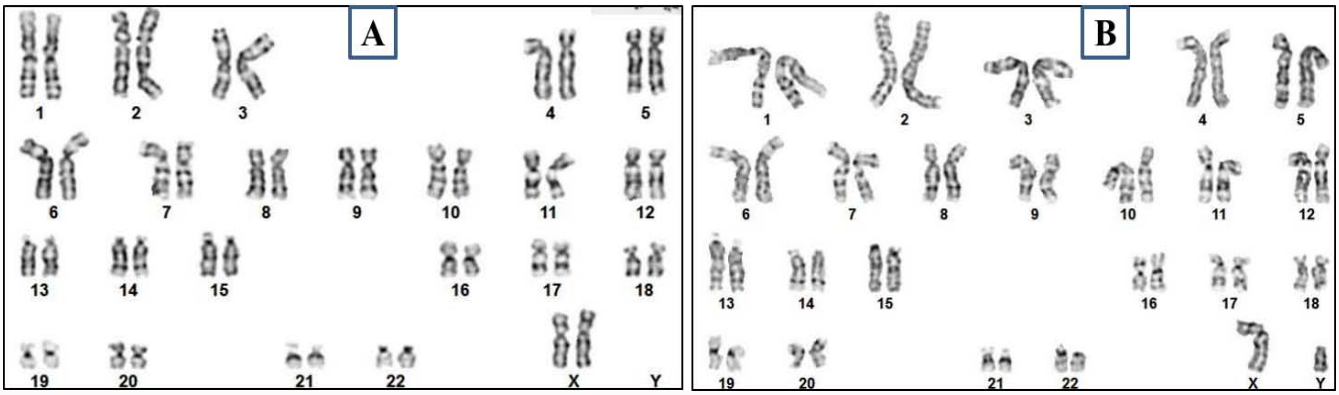

Figure 2: Karyotype of the parents.

Asymptomatic hypoglycemia was noted on day 1 of life was corrected with feeds and IV fluids and neonatal jaundice on day 3 of life (max TSB was 11.2 mg/dl), was treated with phototherapy. CBP and serum calcium levels were normal. Neurosonogram was normal. Post-natal USG abdomen also revealed gross right hydronephrosis (AP diameter - 30 mm). Chest X-ray revealed 11 pairs of ribs. 2D ECHO showed a moderate Patent Ductus Arteriosus (PDA) and Pulmonary Arterial Hypertension (PAH). PDA was treated with paracetamol for 1 week and a repeat ECHO on day 12 showed persistently high neonatal PVR along with moderate PDA for which baby was put on furosemide and sildenafil. Sepsis was suspected. Blood culture showed Serratia sepsis, urine culture demonstrated *Klebsiella* on day 3 of life. CSF analysis was suggestive of biochemical meningitis for which the baby was kept on antibiotics. In view of FGR, facial dysmorphism, hydronephrosis and preaxial polydactyly there was possibility of either chromosomal abnormality or Pallister-Hall syndrome. Chromosomal microarray has been sent. The child was discharged on the day.

Results

Chromosomal microarray has revealed a pathogenic duplication of 17.2 Mb containing 213 OMIM genes (Figure 1). Karyotype of both parents was normal (Figure 2). It is *de novo* duplication in the child. The couple was counseled. Implications of the syndrome and the recurrence risk of not more than 1% in subsequent conceptions have been discussed.

Discussion

17p duplication can occur in any segment of the short arm of chromosome 17. Non-Allelic Homologous Recombination (NAHR) between region-specific Low-Copy Repeats (LCRs) is a major cause of rearrangements associated with deletions and duplications in chromosomes [6-8]. Proximal short arm of chromosome 17 is rich in LCRs and is therefore an important locus for deletion/duplications

leading to genetic disorders. Duplication of 17p11.2 in Potocki-Lupski Syndrome, 17p11.2 to 17p12 in Charcot-Marie-Tooth disease type 1A, 17p13 in 17p13 microduplication syndrome, complete extra copy (Trisomy 17p) or almost complete extra copy of p arm (partial trisomy 17p) and several larger duplications that include 17p11.2 and additional segments of p arm with different breakpoints including 17p complex chromosomal rearrangements are reported in literature [9-15]. Children with 17p duplication are often healthy but all those so far reported with 17p duplication had some degree of developmental delay with learning difficulties. The present case had a 17.2 Mb long 17p duplication involving the segment between p11.2 and p13.2. To the best of our knowledge till now this *de novo* 17p duplication involving this large segment of p arm with p11.2 and p13.2 as the breakpoints has not been reported. 17p11.2 and p13.1 as the breakpoints has been reported. Clinical phenotypes of 17p duplication follow a fairly distinctive and recognizable pattern owing to the genes that are involved. 17p duplications resulting from unbalanced chromosomal translocations and complex genetic interaction of multiple genes have also been reported [16-18]. Common features of 17p duplication disorder as reported in literature are as follows: Eighty to Ninety percent of cases have FGR, facial dysmorphism (microcephaly, low set ears, micrognathia), clinodactyly, hypotonia, developmental delay, intellectual disability and short stature. Thirty to eighty percent show other dysmorphic features (hypertelorism, ptosis, Malar hypoplasia, narrow mouth, high arched palate). In addition, short neck, flexion contractures, generalized hypertrichosis, renal abnormalities like hydronephrosis and polycystic kidney, genitourinary abnormalities are reported. Less common features include CNS anomalies, cleft palate, macroglossia, cardiac anomalies [4,19-23]. To the best of our knowledge till now 5 cases of 17p11.2p13.1 duplication have been reported. The present case had FGR, facial dysmorphism, cardiac and renal defects, and limb abnormalities which were comparable to the features described in literature. Limb abnormalities reported in previous case reports are clinodactyly, tapering fingers and talipes. Additional findings like 11 pairs of ribs, excessive Mongolian spots, brachydactyly, preaxial polydactyly are not described in previous case reports of 17p duplication. In addition, there was no hypotonia or feeding difficulty in this case. Occurrence of this combination of the known and new findings in this case could in fact be a hallmark of this novel duplication of a large segment of the 17p. Chromosomal microarray is the test of choice in cases whose clinical phenotype does not correlate completely with a specific chromosomal abnormality [24,25]. Comprehensive management of these cases includes general care and prompt symptomatic management.

Conclusion

To the best of our knowledge, a *de novo* 17p duplication involving p11.2-p13.2 segment with atypical features of 11 pairs of ribs, excessive Mongolian spots and preaxial polydactyly not been reported in literature so far. This case is being reported for its novelty and rarity. There is a relative lack of literature regarding the spectrum of presentations falling under the umbrella of 17p duplication syndrome. Further studies are needed to understand and elucidate the complexities underlying this condition.

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