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A Case of Multiple Congenital Anomalies, Imperforate Anus and Penoscrotal Transposition with del(13)(q22)

D.L. Lakhakar*, Sunil Mhaske, S.A. Nemane***, S.M. Bhagat****, S.R. Shinde****, K.J. Athawale****, P.V. Deochake******

Abstract

13q- syndrome is known to have widely variable manifestation of brain and heart, anal atresia, and anomalies of face and limbs. Here we describe a case with penoscrotal inversion, hypospadias, imperforate anus and a subtelomeric deletion of chromosome 13q. In addition, he had unilateral renal agenesis. We propose that these patients represent a clinically recognizable, novel chromosomal microdeletion syndrome. The findings indicate the presence of a major gene(s) on chromosome 13q22 that regulate(s) the migration and development of ano-reno-genital cells and organs. We speculate that mutations of this developmental gene(s) may also result in more frequent congenital malformations (isolated hypospadias, uterus bicornis, unilateral renal agenesis).

Keywords: Chromosome 13; Imperforate anus; Penoscrotal transposition.

Introduction

Various phenotypic abnormalities have been associated with deletions of long arm of chromosome 13. The most common clinical features of this 13 q deletion syndrome are mental and growth retardation, facial abnormalities, limb and digital abnormalities, retinoblastoma, microcephaly and intestinal atresia.[1] Here we report a case of del(13)(q22) with multiple major congenital anomalies.

Case Report

The male infant was born after 37 weeks of gestation by normal delivery. There was no e/o mother being exposed to teratogens during the pregnancy. Birth weight was 2200 g. On the 2nd day of life the infant was transferred to our hospital for the evaluation of the multiple congenital anomalies.

On physical examination he had imperforate anus and bifid scrotum with cephalad transposition of small penis relative to the position of scrotum and hypospadias with club foot deformity (Figure 1 & 2).

Figure 1: Showing Imperforated Anus and Penoscrotal Transposition

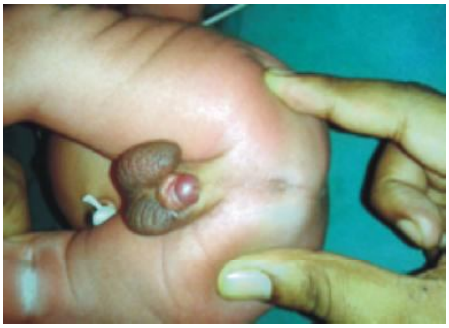
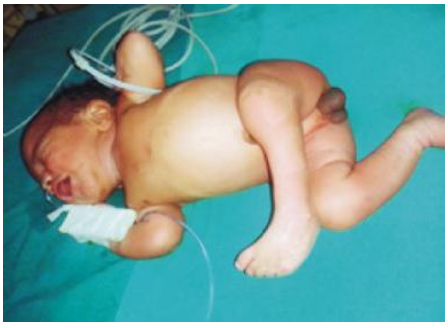


Figure 2: Showing Club Foot Deformity

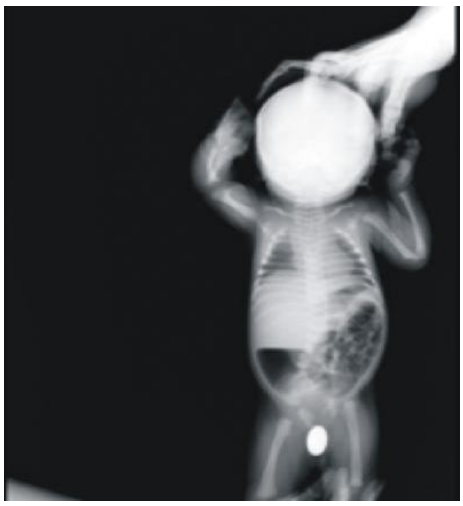


Author's Affiliation:*Professor and Head Radiology, **Professor and Head Paediatrics,***Senior Resident,****Assistant Professor, Dept. of Paediatrics, Padmashree Dr. Vithalrao Vikhe Patil medical College, Ahmednagar-414111, Maharashtra.

Corresponding Author: Dr. Sunil Mhaske, Professor and Head Paediatrics, Dept. of Paediatrics, Padmashree Dr. Vithalrao Vikhe Patil medical College, Ahmednagar-414111, Maharashtra.

E-mail: sunilmhaske1970@gmail.com

Figure 3: Showing Proximal Focal Femoral Deficiency and Hypoplastic Right Upper Limb



Abdominal ultrasound shows absent left sided kidney.

Topogram:

The topogram revealed focal femoral deficiency of right femur with cubits varus deformity and Hypoplastic upper limb.

There are seen multiple neural tube defect involving lower lumbar vertebrae (Figure 3 & 4).

USG Scrotum

Cephalad postion of scrotum. Both testis are

Figure 5: Ultrasound of Pelvic Region showing Stenosed Anal Canal (ac) and Proximal Dilation of Rectum(r)

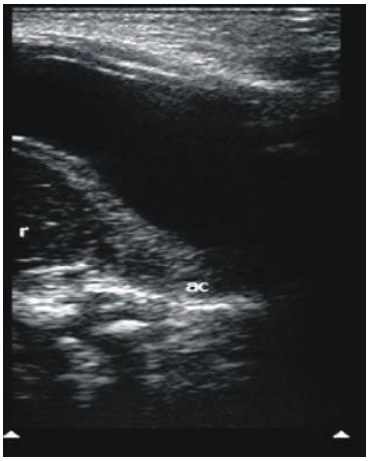
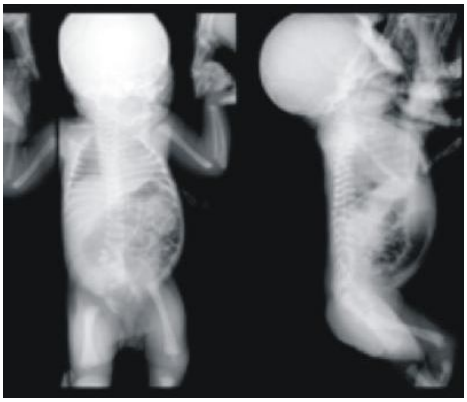


Figure 4: Showing Spina Bifida at L4 and L5 Vertebra



well developed and normally deseneded in to scrotal sac. The penis is Hypoplastic but internal anatomy (two cavernosa and one spongiosa are well seen). The left kidney is not seen (Figure 7).

Discussion

13q syndrome is caused by the absence of a portion of the long arm of chromosome 13, as first reported by Allderdice *et al.*[2] The majority of cases have ring chromosome formation, terminal and interstitial deletions are less common. Specific diagnostic criteria are difficult to define because they are widely variable menifestations in 13q deletion patients. Common clinical finding have included

Figure 6: Ultrasound Left Hypochondriac Region showing Empty Left Renal Fossa. S- Spleen

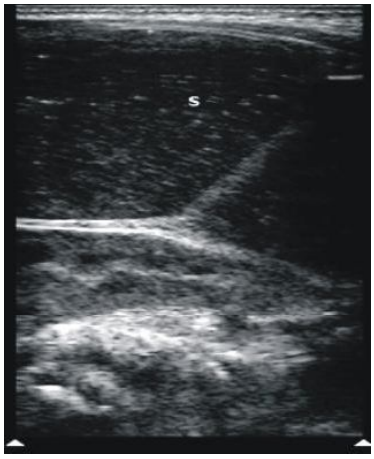
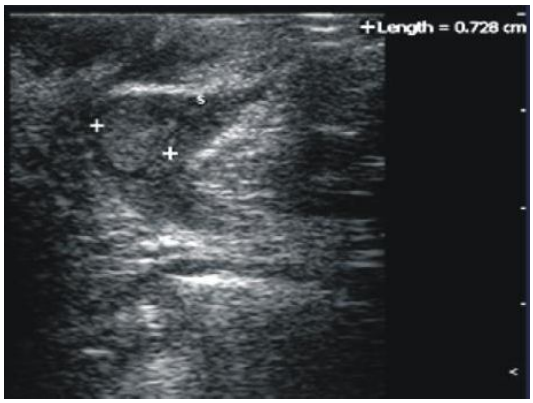


Figure 7: Ultrasound Scrotum showing Normal Testicle, Hypoplastic Penis.



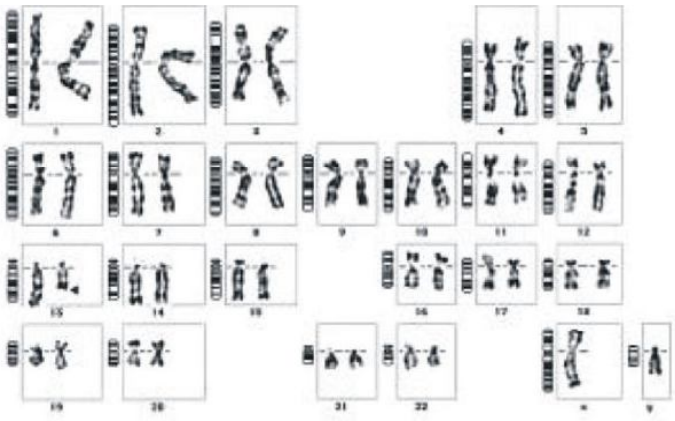
retinoblastoma, mental retardation, brain malformations, renal malformations,heart malformations, anal atresia and other gastrointestinal malformations.[1-3] With the advent of chromosomal banding techniques, several attempts have been made to correlate the region of deletion with phenotype.[1,3-6] It is sometimes associated with skeletal abnormalities like neural tube defect.

Niebuhr proposed four categories associated with deletions of different portions of chromosome 13.[3] Category 1 patients with monosomy of the distal long arm, most often having a ring chromosome with a break point at q33 or q34. Frequently observed features were microcephaly, tigonocephaly, hypertelorism, epicanthic folds, large ears and protruding maxilla. Category 2 included patients with a deletion involving the segment distal to 13q22. In addition to category 1 features, most of these patients had absent or fused metacarpals, absent or fused toes, and many showed intrauterine growth retardation and early death. Category 3 included patients with a deletion encompassing q14, the main distinguishing feature of which was retinoblastoma. According to factor of host resistance and degree of carcinogenic potential of deletion of 13q, it was calculated that some 13 % to 20 % of de novo deletion 13q14 cases remain unaffected with retinoblastoma. Category 4 was tentatively associated with the deletion of q21. Although these patients were defined primarily by the absence of thumb defects and retinoblastoma, they also shared a group of abnormalities, including microcephaly, hypertelorism, large ears, abnormal dermatoglyphics and cardiac defects. In summary Nieubuhr observed that those patients with distal deletions of 13q were the most severely affected, and that those with more proximal deletions tended to have fewer major anomalies except for retinoblastoma.

Another approach to 13q deletion is described in the report of Brown *et al.* They proposed that 13 q deletion patients fall into three separate groups. According to this scheme group 1 I comprised of those with proximal deletion, usually not extendeing into q32 and with mild or moderate mental retardation, variable dysmorphic feature and growth retardation. Depending on the deleted segment, retinoblastoma may or may not be present.

Group 2 is comprised of those with more

Figure 8: Karyotype of Patient showing 46,XY,del(13)(q22), by Giemsa Banding



distal deletion, including at least a part of q 32, and one or more major malformations. These are most frequently severe microcephaly and brain malformations such as holoprosencephaly, absent thumbs or other distal limb abnormalities, eye malformations and genitourinary and gastrointestinal tract malformations.

Group 3 is comprised of those with more distal deletions, involving q33 -q34, with severe mental retardations but without major malformations and usually without growth retardation.

According to brown's classifications our case would fall into group 2.

Brown *et al* also postulated that there is critical region in 13q32 where deletion leads to a syndrome of severe major malformations including digital and brain anomalies.[6]

This patient showed complete penoscrotal transposition with bifid scrotum and hypospadia. This is explained by an embryological hypothesis. At four month gestation there is a caudal shift of scrotal swellings with fusion to form a definitive scrotal sac posterior to the penis. A failure of this shift produces the aforementioned anatomic arrangement.[7] It has been also associated with mosaic trisomy 18 karyotype and other chromosomal abnormalities.[8,9]

In conclusion this case gives additional information about the deletion of chromosome 13. Its manifestations are so variable that further studies, such as the high resolution banding technique, fluroscent banding in-situ hybridization (FISH), and molecular mapping may be needed to clarify the correlation between 13q deletion and clinical features.

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