

Case Report

VACTERL association-type anomalies in a male neonate with a Y-chromosome abnormality

Manish Bhagat*

Department of Paediatrics, K. J. Somaiya Medical College, Hospital and Research Centre, Mumbai, India

*Correspondence address. Department of Paediatrics, K. J. Somaiya Medical College and Hospital, Sion (E), Mumbai 400022, India. Tel: +918147597296; E-mail: drmvbhagat@gmail.com

Received 29 October 2014; revised 12 December 2014; accepted 17 December 2014

The acronym VACTERL describes the non-random co-occurrence of three of the following anomalies: vertebral (V), anal (A), cardiac (C), tracheoesophageal fistula with or without oesophageal atresia (TE), renal (R) and limb defects (L). Here, we report a newborn baby with VACTERL-type anomalies along with a single umbilical artery. The additional interesting findings include development dysplasia of the right hip, dislocation of the left knee and the left club foot. The karyotype revealed 46, X,i (Yp), i.e. deletion in the long arm, while duplication in the short arm of the Y chromosome (isochromosome Yp), which has never been previously reported in VACTERL association.

INTRODUCTION

The acronym 'VATER/VACTERL' association describes the combination of at least three of the following congenital anomalies: vertebral defects (V), anorectal malformations (A), cardiac defects (C), tracheoesophageal fistula with or without oesophageal atresia (TE), renal malformations (R) and limb defects (L) [1]. Various other anomalies, such as a single umbilical artery (SUA) and genital and/or urinary anomalies, have also been reported with VACTERL patients [2, 3]. Most of the cases of VACTERL association occur sporadically; however, chromosomal abnormalities have also been described in a few cases [4]. We report here a case of VACTERL anomalies in a male neonate with a Y chromosome abnormality.

CASE REPORT

A male baby was born at 35 weeks of gestation to a 23-year-old primigravida mother by caesarean section in view of foetal distress with breech presentation. The mother was healthy and did not receive any teratogenic medications and/or radiation. There was no family history of consanguinity or congenital malformations. The baby cried immediately after birth with an Apgar score of 9/10 and 10/10 at birth and 1 min, respectively. The weight of the baby was 2.2 kg (between 10th and 50th centiles); length (46 cm) and occipito-frontal circumference (32 cm) were both on 50th centiles. At

birth, SUA, imperforate anus and club foot with talipes equinovarus abnormality in the left lower limb were noted (Fig. 1). No craniofacial abnormality was seen. A nasogastric tube was inserted with ease. Systemic examination was unremarkable.

Plain X-ray abdomen showed dilation of the descending and rectosigmoid colon without the gas shadow in the distal rectum (Fig. 2). Invertogram confirmed the intermediate type of anorectal malformations. A Barlow–Ortolani test on the right hip was positive suggestive of reducible developmental dysplasia of the hip. The skeletal survey revealed hemivertebrae and block in the lumbar vertebrae, and also dislocation of the left knee joint (Fig. 2). Ultrasonography of the abdomen showed left renal agenesis. The right kidney was normal. Based on the presence of vertebral segmentation defect, imperforate anus, unilateral renal agenesis and absence of features, suggestive of alternative diagnosis infant, meet criteria for VACTERL association.

The karyotype in the peripheral blood revealed Y chromosomal abnormality, i.e. deletion in the long arm (Yq), while duplication in the short arm of the Y chromosome (Yp) [46, X,i (Yp): isochromosome Yp] (Fig. 3). Fluorescence in situ hybridization (FISH) analysis demonstrated the presence of two orange signals for SRY (sex determining region on the Y chromosome) gene locus in the interphase and metaphase cells, indicating two copies of the SRY genes on the Y chromosome are present. The cytogenetic analysis of the parents was normal.

Complete blood count, thyroid profile, transthoracic echocardiogram, cranial ultrasonography and ophthalmological examination all were normal. The infant underwent colostomy within few hours after birth. Postoperative recovery was uneventful and he was subsequently discharged on Day 10 of life with full feeds. The infant was planned for anorectoplasty at 3 months of age. He was seen twice in the first- and second-month follow-up visits and was doing well.

DISCUSSION

Our patient presented with anal atresia, lumbar vertebrae defect (block and hemi-vertebrae) and left renal agenesis, suggestive of VACTERL association [1]. Interestingly, infant had



Figure 1: Newborn with imperforate anus.

additional defects in the form of SUA and lower limb anomalies, which included developmental dysplasia of the right hip, left knee dislocation and left club foot. While typically defined by the presence of radial anomalies (thumb aplasia/hypoplasia), other limb anomalies, such as distal tibial aplasia, clubfoot, hallucal deficiency and pre-axial polydactyly, have also been described to VACTERL association [1, 5]. Other abnormalities may include cleft lip and cleft palate, hypothyroidism, duodenal atresia or stenosis, abnormalities of genital and urinary system, and anomalies of the respiratory, intestinal, vascular and central nervous system [6]. Virtually, all the features of VACTERL association may occur in a patient with Fanconi anaemia (FA), but radial-ray defects, haematological (bone marrow failure) and pigmentation anomalies that are considered as distinct features are not seen in the present case. VACTERL-type anomalies have been increasingly described in proven cases of FA [7]. Hence, chromosomal breakage studies should be done in patients with the VACTERL phenotype, especially with radial anomalies and if there are features suggestive of FA [1, 7]. The overlapping of defects of VACTERL association has also been described with Pallister-Hall syndrome, Towne-Brocks syndrome, 22q11.2 deletion syndrome and MURCS association, which is characterized by the presence of Mullerian duct aplasia, renal aplasia and cervico-thoracic somite dysplasia [1].

The combination of VACTERL abnormalities may present with some known chromosomal abnormalities, including trisomy 13, 18, 21 and 5p syndrome. Most of the VACTERL patients have sporadic occurrence; however, reports of familial cases are increasingly being reported [4, 8]. Chromosomal aberrations, in particular, 6q, 8q, 10q, 17q, and 22q with recurring or *de novo* copy number variations (DNA gains or losses)

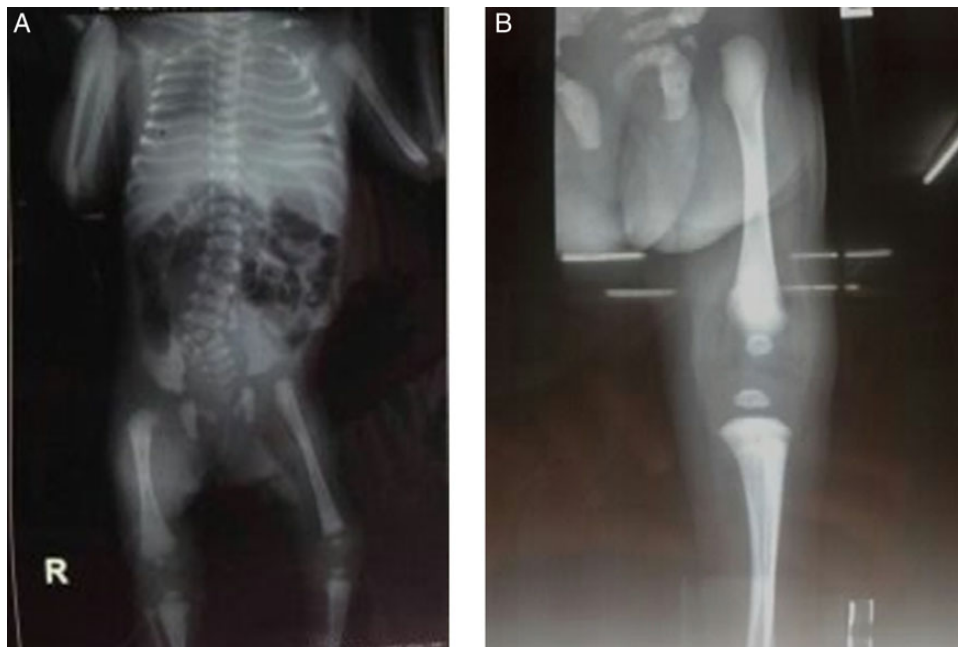


Figure 2: X-ray images of the patient (A) showing a dilated descending and rectosigmoid colon without the gas shadow in the distal rectum, and (B) dislocation of the left knee.

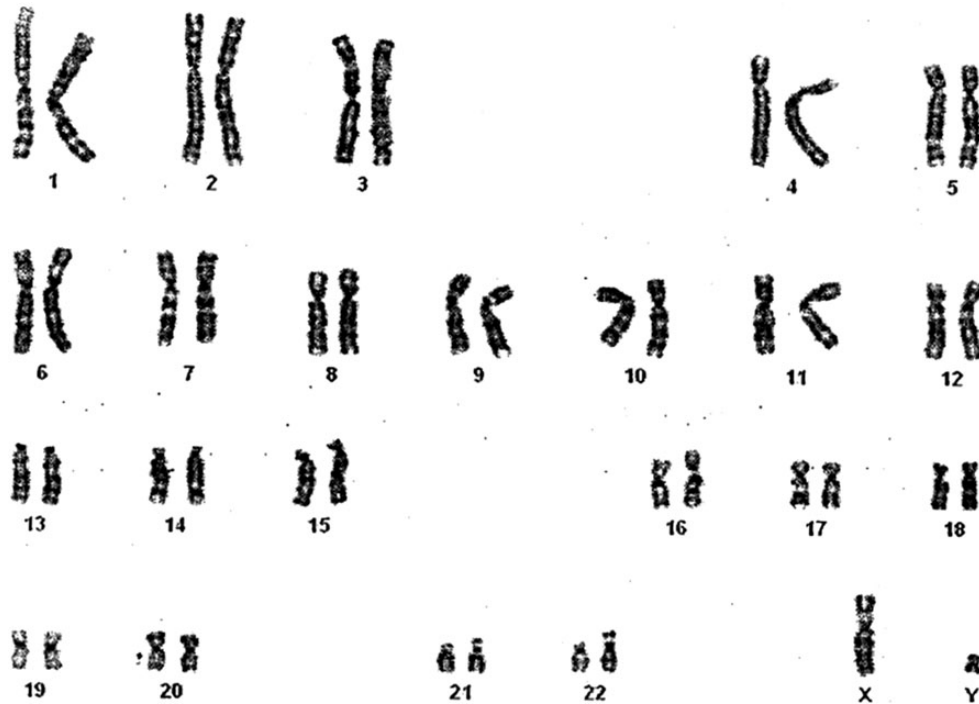


Figure 3: Karyotype of the patient showing 46, X,i(Yp): isochromosome Yp.

were noted in affected VACTERL patients [4]. Recently, Brosens *et al.* [4] reported a duplication involving X chromosome and gain in Xp22.3 in VACTERL patients. In the present case, deletion in Yq and duplication in Yp were seen, and FISH revealed the presence of two copies of the SRY gene in the Y chromosome, which is a novel finding not yet reported.

VACTERL has been defined as a multiple polytopic developmental field defect [1]. A disruption in differentiating mesoderm in the first 4–5 weeks may lead to the different malformations of the VACTERL spectrum, including the presence of an SUA. Other aetiological factors include diabetic mother, infertility treatment and exposure to oestrogen and/or progesterone-containing compounds, such as lead, anticonvulsants, folic acid antagonists, alcohol during the period of embryogenesis and mutations in the genes (ZIC3, HOXD13 and FOXF1) and/or mitochondrial mutations leading to disturbances in the development of different anatomical structures [1, 9].

In addition to classically defined features, a patient with VACTERL association may have other wide spectrum of anomalies. Due to overlapping features, this condition should be differentiated from other closely related conditions such as FA. Cytogenetic analysis should be done in a VACTERL patient to detect chromosomal anomalies, which will offer an insight into the aetiology of VACTERL association.

AUTHORS' CONTRIBUTION

M.B. managed the patient, reviewed the literature, analysed the data and wrote the manuscript.

CONFLICT OF INTEREST STATEMENT

None declared.

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