□ Case Report □

Sprengel's deformity associated with a de novo balanced translocation involving chromosome 3 and 17

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This is the first case of a de novo balanced translocation 46, XY, t(3;17)(p12.2;q25) associated with multiple musculoskeletal abnormalities, including Sprengel's deformity (congenital undescended scapula to be reported). This translocation has not been described previously with this congenital anomaly in Korea. **(Korean J Pediatr 2007;50:311-314)**

Key Words : Balanced translocation, Musculoskeletal abnormalities

Introduction

Of all the structural chromosome rearrangements, translocations are the most clinically significant. These abnormalities in chromosome structure follow a chromosome break and reunion of the different segments of the chromosome during the repair process. Following repair, if there is no net gain or loss of chromosomal material, the rearrangement is referred to as balanced; additional family studies are then needed to determine whether the rearrangement is inherited. If no other family member has the translocation, the rearrangement is called de novo; if a neonate is found to have a de novo translocation, there is a 6-10% empiric risk of having an anomaly associated with it[1].

Sprengel's deformity is an uncommon congenital anomaly characterized by elevation and medial rotation of the inferior scapulae; it is associated with congenital anomalies of other organ systems such as congenital scoliosis, fusion of the cervical vertebrae such as in the Klippel-Feil syndrome (KFS), hemivertebrae as well as congenital heart diseases[2].

We report a de novo balanced translocation involving chromosome 3 and 17 in a newborn. Physical examination of the baby born at term revealed multiple skeletal anomalies, including Sprengel's deformity. Association of this translocation and Sprengel's deformity has not been reported previously.

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Case Report

A male infant was admitted to the neonatal intensive care unit due to multiple anomalies and tachypnea. He was delivered vaginally at 37 weeks to a 30 year-old mother with a history of previous stillbirth. The Apgar scores were 7 and 8 at 1 and 5 minutes, respectively. He was the second baby born to his parents. The mother denied taking medications as well as illness during the pregnancy. There was no history of inherited diseases in the family.

On admission, the vital signs were: temperature was 36.2℃; pulse rate of 120/minutes; respiration rate of 70/minutes. The body weight was 3,020 gm (50-75 percentile), height 49 cm (50-75 percentile), and head circumference 37 cm (>90 percentile). The baby had a round face, hypertelorism, broad nasal bridge, micrognathia, posteriorly angulated ears, palatal anomalies and webbed neck (Fig. 1A, B). The Breath sounds were coarse with mild chest retraction. Examination of the limbs showed proximally located thumbs (Fig. 1C), rocker bottom deformity of the feet, pes varus, adduction of the both halluces and asymmetric calves (Fig. 1D). Neurologically, the infant was hypotonic with a decreased Moro and grasp reflex.

Laboratory analysis of the blood revealed a hemoglobin of 14.3 g/dL, white blood cell count of 15,370/mm^3 and platelet count of 288,000/mm^3. The chest radiograph showed subtle peribronchial infiltration in the both central lung and elevation of both scapulae (Sprengel's deformity) (Fig. 2A). The spine AP and lateral films showed mild thoracic scoliosis and hypoplastic vertebral bodies of C3-6 (Fig.

2B). The hip AP films showed dislocation at the left hip joints (Fig. 3). Echocardiogram demonstrated an atrial septal defect. Brain magnetic resonance imaging revealed a small subdural effusion. Computed tomogram of the thigh demonstrated lymphedema of the right lower extremity (Fig. 4). Auditory evoked potential studies revealed bilateral moderate sensorineural hearing loss. Cytogenetic study of the baby showed an apparently balanced translocation involving chromosomes 3 and 17; 46, XY, t(3;17)(p12.2;q25). Both parents had a normal karyotype and phenotype (Fig. 5).

The baby received oxygen therapy via nasal cannula for two days and required tube feedings due to a poor suck. At the time of discharge, at 26 days of age, the baby exhibited slightly improved oral intake with a body weight of 3,340 g. The follow-up spine films showed the additional findings of apparent hypoplastic vertebral bodies at C5-6; C-spine magnetic resonance imaging performed at five months of age showed a decreased vertebral height at C5-6 and intervertebral disc space at C6-7 with kyphotic angulation deformity and spinal stenosis. Followed up at hospital's outpatient department after discharge was carried out where the baby received manual lymphatic drainage to decrease limb volume. The pvlik harness was used for six months of age to hold the hips in place.

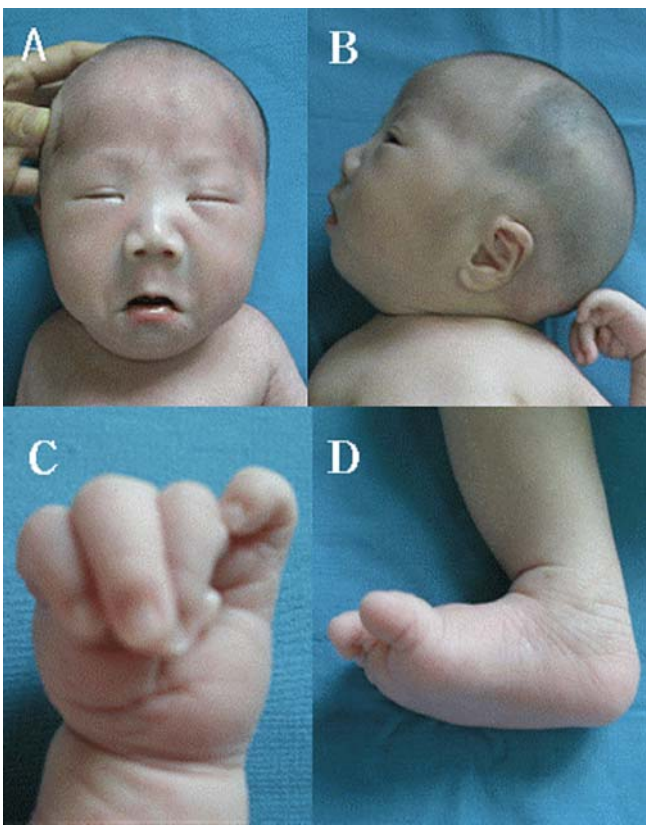

Fig. 1. (A) (B) Clinical features include a dysmorphic face, (C) proximally located thumb, (D) rocker bottom deformity, pes varus and adduction of the hallux.

Discussion

Translocation happens when DNA is transferred from one non-homologous chromosome to another. The types of translocation include: reciprocal translocations, Robertsonian translocations and insertional translocations. Translocations can be balanced or unbalanced; in the unbalanced state, chromosome material is unequal, resulting in duplicated or deleted genes. Balanced reciprocal translocations as a whole are thought to occur at a rate of about 1 in 500 in the general population and are not clinically significant[1]. However, there are rare exceptions where anomalies are reported in association with apparently balanced translocations. Evaluation

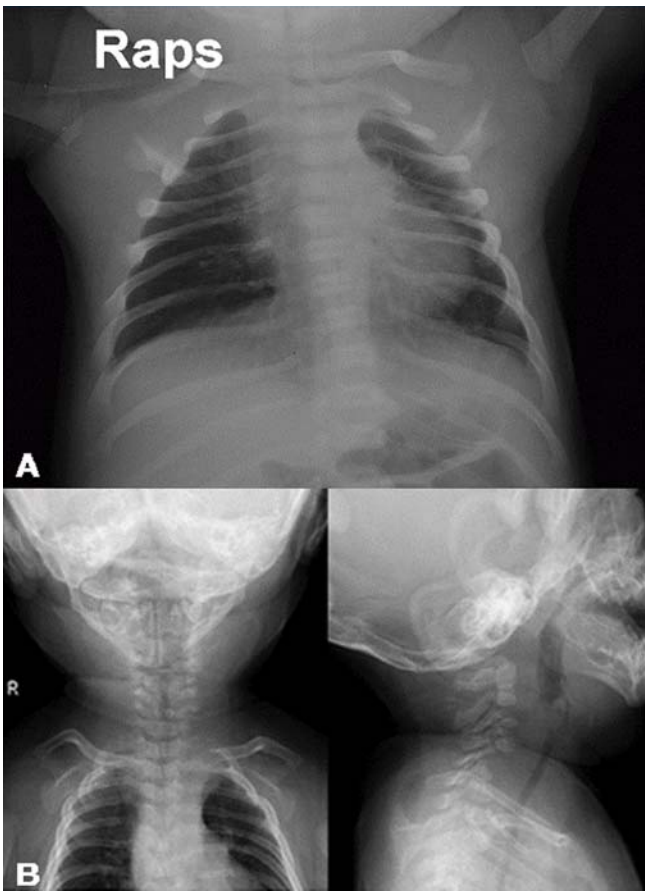

Fig. 2. (A) Chest AP shows elevation of both scapulae (Sprengel's deformity) and scoliosis of thoracic vertebrae. (B) C-spine AP and lateral views show hypoplasia of C3-6 and kyphotic deformity of C5-6.

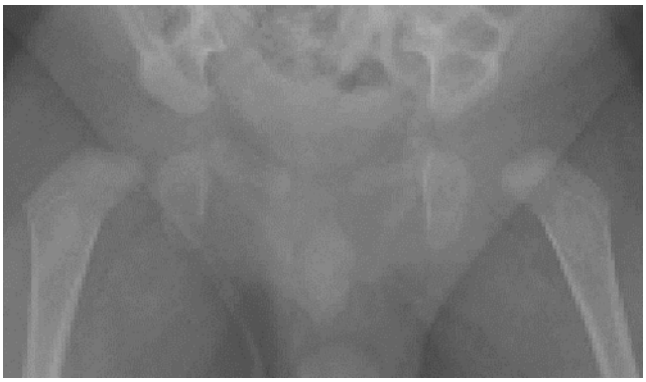

Fig. 3. Hip AP film shows dislocation of the left hip joint.

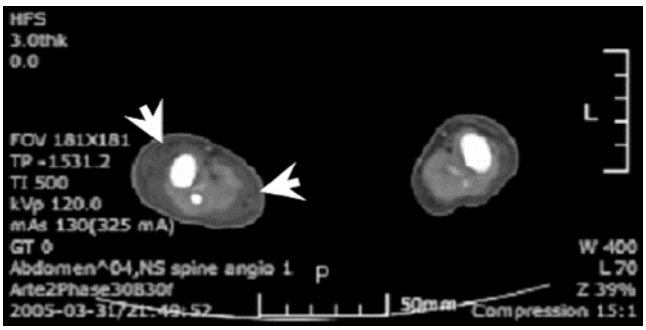

Fig. 4. Thigh CT shows lymphedema (arrows) of the right lower extremity.

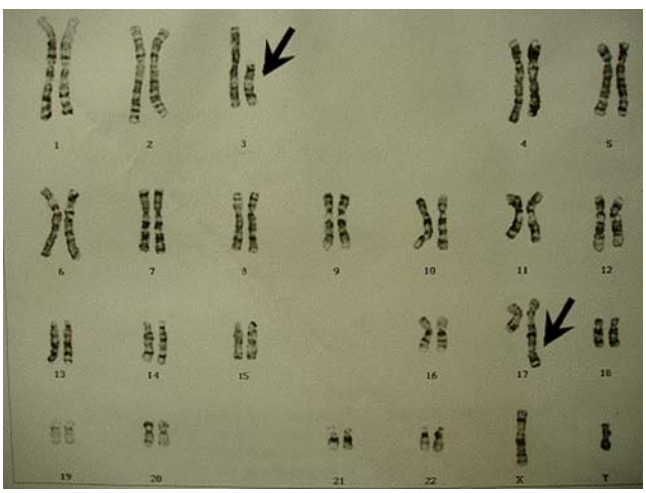

Fig. 5. The karyotype (arrows) of the patient shows 46, XY, t(3;17)(p12.2;q25) by GTC banding.

of a symptomatic newborn with a balanced translocation includes chromosome studies of both parents. If the parents are asymptomatic and are not translocation carriers, the fetus or newborn with the balanced translocation has a 6-10% empiric risk of having anomalies[1]. Jamshidi et al[3] propose that reciprocal translocation may disrupt a putative gene or a regulatory element at one or both translocation breakpoints.

This reported infant had craniofacial variations such as round face, hypertelorism, broad nasal bridge, micrognathia, and palatal defects as well as skeletal deformities including: proximally located thumbs, rocker-bottom feet, pes varus and adduction of the both halluces. This phenotype resembled the clinical manifestations of a deletion involving the long arm of chromosome 17[4-8]. Salamenca et al[8] described cytogenetic findings in a spontaneously aborted fetus with chromosome 17 deletion. Dallapiccola et al[4] and Park et al[5] reported on affected cases consisting of 46, XY, del(17)(q21.3q23) associated with characteristic facial features, developmental delay and visual or auditory defect. Bridge et al[7] reported a patient with microcephaly, hypertelorism, epicanthical folds, micrognathia, arachnodactyly with proximal thumbs and coxa vara. Deletions involving long arm of chromosome 17 are relatively rare and have been presumed to be incompatible with life.

Review of the articles reported on a balanced translocation involving chromosome 17 included the following reports. Young et al[9] presented a female fetus with campomelic dysplasia and a rearrangement involving the long arm of chromosome 17; indicating that this chromosome region may harbor the genetic locus for campomelic dysplasia. Savarirayan et al[10] reported a severely affected infant with the acampomelic form of campomelic dysplasia, who died at 11 days and was found to have a de novo reciprocal translocation, 46, XX, t(5;17)(q15;q25.1). Ireland et al[11] described a female infant with Cornelia de Lange syndrome and severe limb reduction defects. Chromosome analysis showed a de novo translocation with breakpoints at 3q26.3 and 17q23.1.

For the case reported here, congenital elevation of scapulae, more commonly referred to as Sprengel's deformity was identified. This abnormality occurs when the scapula does not descend to its normal position in the thoracic wall during 9th to 12th week of fetal development. The inferior pole of the scapula is adducted and the superior angle is prominent in the web of the neck. The superior border of the undescended scapula can be as high as the fourth cervical vertebra. A variety of congenital anomalies have been associated with Sprengel's deformity and include: congenital scoliosis, anomalies of cervical vertebrae such as KFS, cervical ribs, hemivertebrae, kidney abnormalities, anal stenosis and cleft palate[2].

Clinical manifestations of KFS include short neck, low posterior hairline and motion restriction of the neck due to fusion of the cervical vertebrae. The typical radiological findings in KFS include thin and broad vertebrae, fusion of cervical spine, and narrow intervertebral space. The vertebral fusion is most apparent after normal spinal ossification is completed in the young child[12-15]. In addition, KFS has been associated with skeletal, urogenital, cardiac, neurological, auditory, ocular, craniofacial, limb and digital anomalies in varying degrees. It is too early to diagnose the patient reported here with KFS. However, the progressive vertebral hypoplasia and associated anomalies such as Sprengel's deformity, scoliosis, atrial septal defect and sensorineural hearing impairment may lead to KFS as the final diagnosis.

한 글 요 약

선천성 고위 견갑골을 동반한 3번과 17번 염색체의 균형전좌 1례

가톨릭대학교 의과대학 소아과학교실

정 온 · 이정현 · 전정식

선천성 고위 견갑골과 두개안면기형, 심기형, 척추기형이 동반된 신생아에서 3번과 17번 염색체의 균형전좌를 확인하였으며 이는 국내 첫 번째 사례로 문헌 고찰과 함께 보고하는 바이다.

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