Korean Journal of Pediatrics Vol. 48, No. 12, 2005

□ Case Report □

A Case of Short Arm Deletion and Long Arm Duplication at Chromosome 3

Seung Hyun Kong, M.D., Jeong Il Seo, M.D., Jang Hui Kang, M.D.
So Young Jung, M.D.* and Ji Sun Mok, M.D.

Department of Pediatrics, Laboratory Medicine, Good Moonhwa Hospital, Busan, Korea*

The long arm duplication of chromosome 3 was reported for the first time in 1966 by Falek et al., and Hirschhorn et al. came to identify the duplication of 3q21→qter region in 1973. In most cases of duplication 3q syndrome patients, pure duplication of 3qter is believed to be rare and is often reported accompanied with deletion of another segment of the chromosome. Approximately 75 percent of parents of the patient in the meantime have been demonstrated to have unbalanced translocations or inversions of the chromosome. Partial deletion of the distal part of the short arm of chromosome 3 was first reported by Verjaal and De Nef in 1978 and terminal deletion of chromosome 3 (3p25-qter) has been observed in most cases. In karyotyping of chromosomes of immature infants showing the manifestations of flat occiputs, low set ears, hypertelorism, broad nasal roots, thin lips, web necks, hypotonia, hypertrichosis skin, cryptorchidism etc, we experienced a case diagnosed as 46,XY, rec(3)dup(3)(q21)del(3)(p25)inv(3)(p25q21). **(Korean J Pediatr 2005;48:1389-1393)**

Key Words : Chromosome 3, Unbalanced inversion

Introduction

Partial deletion of short arm at chromosome 3 had been reported for the first time by Verjaal and De Nef[1] in 1978 and more cases of 34 patients have been reported thereafter. In most cases, deletions have been observed at the region 25 short arm of chromosome 3. On occasion of short arm deletion at chromosome 3, the patient were accompanied with intrauterine and postnatal growth retardation, severe psychomotor retardation, craniofacial anomalies, serious congenital heart disease, urinary tract anomalies and renal anomalies and so forth, and died of cardiac disorder within the first 3 days after birth or aspiration pneumonia by 3 months thereafter. Nevertheless, most of surviving infants shall suffer disabilities of blindness or deafness.

Duplication of long arm at chromosome 3 had been reported for the first time in 1966 by Falek et al.[2] confused with Brachamann-de Lange syndrome and distinction of duplication of 3q21 (qter region from Brachamann-de Lange came to be made in 1973 by Hirschhorn et al.[3]. Long arm duplication of chromosome 3 is often accompanied with monosomy of short arm at chromosome 3 and accompanying clinical findings are craniofacial anomalies, intrauterine and postnatal growth retardation, severe mental retardation, limbs deficiency, cardiac defect, chest deformities, renal or urinary tract anomalies, genital anomalies, umbilical hernia and so on.

In the cases of mother being inversion carrier and an elder brother inversion carrier as well like his mother, we have encountered a case accompanied with short arm deletion and long arm duplication of chromosome 3 and would like to report the case together with inquiry into literature.

Case Report

A patient : ○○ Kim's baby, male

Chief complaint : Prematurity, congenital anomalies

Gestation and birth history : Estational age 34 weeks and 3 days, born at obstetrics of this hospital by cesarean section due to preterm labor. At the time of delivery, father was 31 years old, mother 31. He was second child and the lying-in woman had neither the history of specific

접수 : 2005년 7월 6일, 승인 : 2005년 9월 14일
책임저자 : 목지선, 좋은문화병원 소아과
Correspondence : Ji Sun Mok, M.D.
Tel : 051)630-0714 Fax : 051)633-8552
E-male : nicedoc@paran.com

disease during pregnancy nor past one of exposure to any teratogenic drug or substance. Apgar score recorded at 1 and 5 minute were 6 and 8. His birth weight was 2,750 g (50-75 percentile), head circumference 34 cm (90 percentile) and height 46 cm (50-75 percentile).

Physical examination : The patient had decreased activity and crying at birth, showed decreased muscle tone and perioral cyanosis. Head and neck findings were flat occiput, low set ears, hypertelorism, broad nasal root, thin lips and web neck etc. The muscle tone decreased, heart murmur was not heard, testis failed to descend, and skin had hypertrichosis (Fig. 1).

Laboratory findings : Peripheral blood test resulted in hemoglobin 21.1 g/dL, Hematocrit 64.1%, white blood cell 8,090/mm^3, platelets 146,000/mm^3 and electrolyte marked Na/K 136/3.8 mEq/L. Blood gas analysis showed PH 7.3, PCO_2 51 mmHg, PO_2 89 mmHg, HCO_3 21 mmol/L and biochemical test showed AST/ALT 42/5 IU/L, ALP 543 IU/L, total protein 4.3 g/dL, albumin 3.1 g/dL, BUN/Cr 8.8/0.8 mg/dL, triglyceride 39 mg/dL, C-reactive protein negative. Both TORCH and blood culture test resulted in negative.

Cytogenetic examination : The patient was diagnosed as duplication 3q and deletion 3p syndrome showing findings of 46,XY,rec(3)dup(3)(q21)del(3)(p25)inv(3)(p25q21)mat (Fig. 2). His parents and brother had examination at the same time, father showing 46,XY normal male pattern, mother and an elder brother 46,XX,inv(3)(p25q21) and 46, XY,inv(3)(p25q21) individually being diagnosed as pericentric inversion of chromosome 3.

Radiologic findings : Abnormalities of neither RDS finding of chest X-ray nor cardiomegaly have been found and

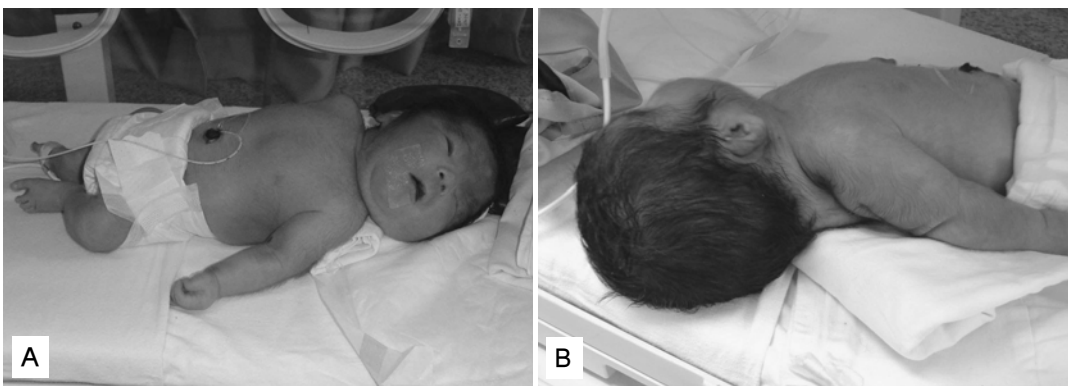

Fig. 1. The patient shows hypertelorism, broad nasal root, thin lips (A) and flat occiput, low set ears, web neck, hypertrichosis.

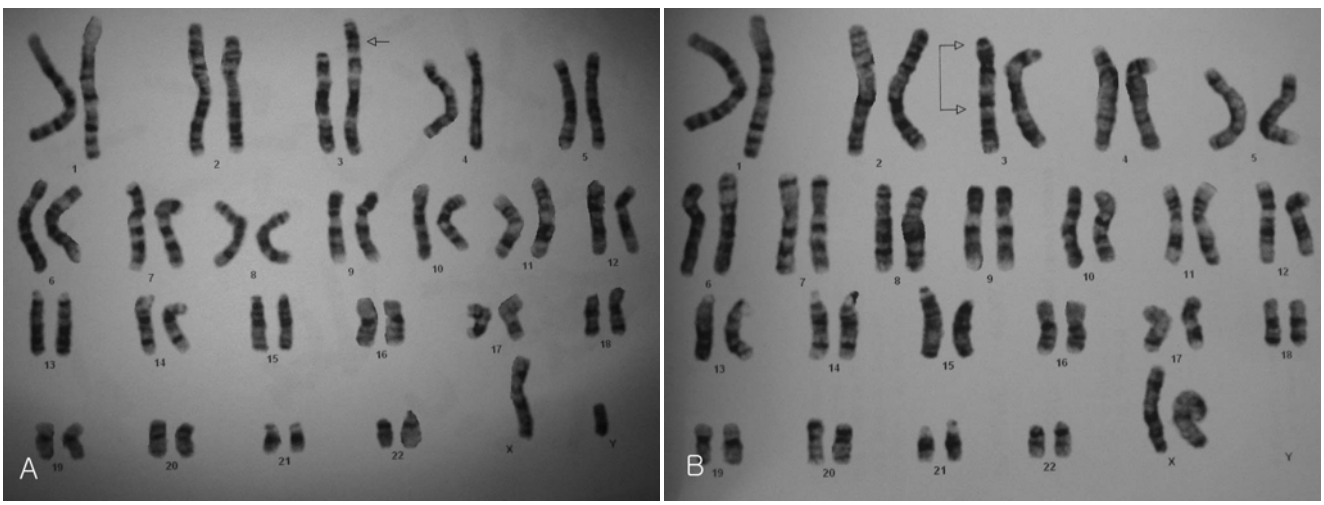

Fig. 2. Karyotype of patient is 46,XY,rec(3)dup(3)(q21)del(3)(p25)inv(3)(p25q21) **(A)** and karyotype of patient's mother is 46,XX, inv(3)(p25q21) **(B)**.

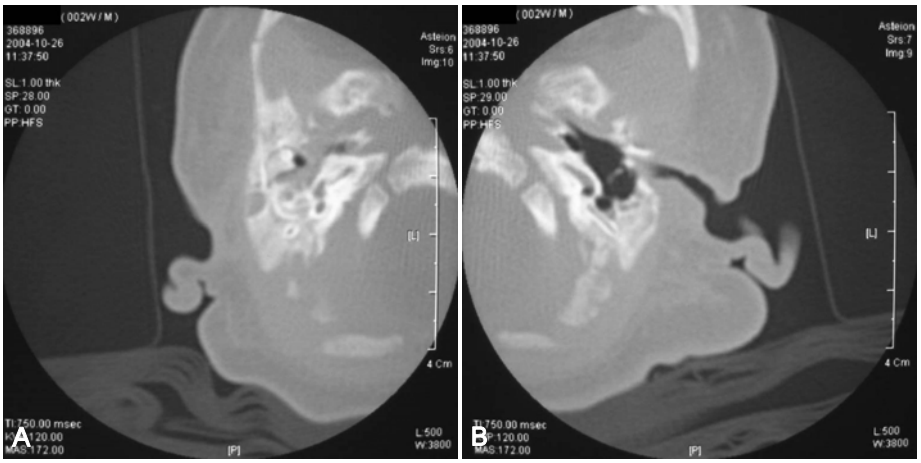

Fig. 3. Temporal CT shows Rt. ear congenital external auditory canal deformity and ossicle deformity **(A)** and normal Lt. ear **(B)**.

simple abdomen radiograph had no specific finding either.

Brain sonography : Vermis and cerebellar hemisphere had a little small size and both lateral ventricles looked a little bigger then usual.

Abdominal sonography : No specific findings

Echocardiography : Showed patent ductus arteriosis (PDA) manifestation in the range of 4-4.5 mm on the third day after birth, found mild tricuspid regurgitation (TR) and mild dysplastic tricuspid valve. PDA was closed on the seventh day after birth but two small perimembranous ventricular septal defect (VSD) of 1.5 mm and 3 mm size found. Findings of large perimembranous VSD (7 mm), mild TR, mild dysplastic tricuspid valve continued on the twenty-forth day after birth.

Brain MRI : Non specific findings.

Temporal CT : Congenital external auditory canal deformity and ossicle deformity of right ear (Fig. 3).

Treatment and progress : The patient showing PDA finding on the third day after birth, indomethacin prescribed. On the fifth day, patient showed respiratory failure and took ventilator care and thereafter from the ninth day on tried feeding, sucking power being weak and swallowing coordination not smooth, the baby mainly depended upon gavage feeding, on the twenty-forth day showing heart failure finding and large VSD at echocardiography he was treated with diuretics and digoxin and then condition grew worse, moved into third hospital on the twentyseventh day after birth but died of cardiac failure.

Discussion

Chromosome abnormalities take place in the frequency of approximately 0.4% of childbirth and are known as important cause of mental retardation, congenital anomaly and spontaneous abortion or stillbirth[4]. Chromosome abnormality is classified into numeric and structural one. The structural abnormality of chromosome can be divided into rearrangement within chromosome and inter-chromosome according to the position where the rearrangement occurs. Deletion, duplication, inversion and transversion can be listed by way of example of rearrangement within chromosome and translocation by way of inter chromosome[5].

Short arm partial deletion of chromosome 3 has been reported for the first time in 1978 by Verjaal and De Nef[1] and thereafter, 34 more cases have been reported. Clinical findings are characterized by intrauterine and postnatal growth retardation, severe psychomotor retardation, craniofacial anomalies, serious congenital heart disease, urinary tract anomalies and renal anomalies and so on.

Moderate to severe hearing loss can in the meantime be taken as particular clinical symptom of 3p syndrome but it is often difficult to detect it because of psychomotor retardation. So a great emphasis is placed on the requirement of various hearing test[6, 7].

Benneck et al.[8] defined 3p syndrome as characteristic clinical symptom and Schwyer et al.[9] took the case with specific clinical symptom and decided the first chromosome examination normal but diagnosed as terminal deletion of chromosome 3 (3p25-pter) at the second chromosome anal-

ysis. Consequently he put emphasis on the second chromosome analysis when clinical symptom is strongly doubtful even if the first examination is found normal.

Long arm duplication of chromosome 3 had been reported for the first time in 1966 by Falek et al.[2] confused with Brachamann de Lange syndrome and thereafter 40 more patients have been reported up to now. Making study of chromosome banding in 1973, Hirschhorn et al.[3] demonstrated duplication of 3q21-qter region and made distinction between two syndromes and then Wilson et al.[10] proved duplication of 3q21-qter region by cytogenetic test and described clinical symptoms including characteristic features of the patients. Clinical findings are characterized by craniofacial anomalies, intrauterine and postnatal growth retardation, severe mental retardation, limbs deficiency, cardiac defect, chest deformities, renal or urinary tract anomalies, genital anomalies, umbilical hernia etc. Wilson et al.[11] made distinction between the two syndromes by clinical criteria in 1978, making assertion that intrauterine growth retardation, prominent philtrum, proximally placed thumbs, oligodactyly and phocomelies are more frequent at Brachmann de Lange syndrome. On the other hand, craniosynostosis, cleft palate and urinary tract anomalies are more characteristic to duplication 3q syndrome. In this case report, flat occiput, low set ears, hypertelorism, broad nasal root, thin lips and web neck are inclusive to specific craniofacial anomalies findings and other clinical findings of hypotonia, skin hypertrichosis, cryptorchidism, congenital heart disease (PDA, VSD), external auditory canal deformity and ossicle deformity of right ear have been observed.

In most cases of duplication 3q syndrome patients, it is reported that pure duplication of 3qter is rare and often accompanied with deletion of another chromosome segment[12, 13]. Some 75% of the patients' parents in the meantime have been proved to have unbalanced translocation or inversion[14]. Inversion of chromosome 3 originated in a couple who got married in Newfoundland in early 1800 is one of a few cases from which information of evaluating separation of inversion chromosome at carrier's child can be obtained. Inv(3)(p25q21) has been reported at North American Center and giving chase to the ancestors resulted in coast district of Canada. It had been proved that the carriers who had chromosome inv(3) was normal but some of their children had chromosome 3 duplication q21-qter, deletion p25-qter syndrome, characteristic abnormal phenotype in association with recombinant chromosome 3[15]. In this case report we made an examination of chromosome held by the parents and a brother of the patient confirming that the mother and the brother were carriers who had inversion of chromosome 3. So this case report falls under an example of duplication 3q syndrome and we could learn that it resulted from chromosome abnormality recombinant from unbalanced inversion of the parents.

한 글 요 약

3번 염색체 단완 결실과 장완 중복을 동반한 1례

좋은문화병원 소아과, 진단검사의학과*

공승현 · 서정일 · 강장희 · 정소영* · 목지선

저자들은 출생 시 납작한 후두골, 낮은 변형 귀, 양안 격리증, 넓고 낮은 콧등, 얇은 입술, 넓고 짧은 목의 덧살, 저긴장증, 피부의 다모증, 잠복고환 등의 소견을 보이는 미숙아의 염색체 핵형 분석에서 부모의 불균형 전도로부터 재조합된 염색체 이상의 결과로 인해 46,XY,rec(3)dup(3)(q21)del(3)(p25)inv(3)(p25q21)로 진단된 증례를 경험하였기에 문헌 고찰과 함께 보고하는 바이다.

References

1) Verjaal M, De Nef MB. A patient with a partial deletion of the short arm of chromosome 3. Am J Dis Child 1978;132:43-5.
2) Falek A, Schmidt R, Jervis GA. Familial de Lange syndrome with chromosome abnormalities. Pediatrics 1966;37:92-101.
3) Hirschhorn K, Lucas M, Wallace I. Precise identification of various chromosomal abnormalities. Ann Hum Genet 1973;36:375-9.
4) Kang MN, Im IS, Kim BE, Chey MJ, Kim SW. A case of 4q deletion with partial agenesis of corpus callosum. J Korean Pediatr Soc 2002;45:273-7.
5) Kim HH. Basic medical genetics. 1st ed. Seoul : Jungmunkak Co, 1994:229-37.
6) Higginbottom MC, Mascarello JT, Hassin H, McCord WK. A second patient with partial deletion of the short arm of chromosome 3 : karyotype 46,XY,del(3)(p25). J Med Genet 1982;19:71-3.
7) Tolmie JL, Batstone P, Ruthven I, Gilmore DH. Partial deletion of the short arm of chromosome 3. Clin Genet 1986;29:538-40.
8) Beneck D, Suhrland MJ, Dicker R, Greco MA, Wolman SR. Deletion of the short arm of chromosome 3 : a case report with necropsy findings. J Med Genet 1984;21:307-10.
9) Schwyzer U, Binkert F, Caflisch U, Baumgartner B, Schinzel A. Terminal deletion of the short arm of chromosome

3, del(3pter-p25) : a recognizable syndrome. Helv Paediatr Acta 1987;42:309-15.
10) Wilson GN, Dasouki M, Barr M Jr. Further delineation of the dup(3q) syndrome. Am J Med Genet 1985;22:117-23.
11) Wilson GN, Hieber VC, Schmickel RD. The association of chromosome 3 duplication and the Cornelia de Lange syndrome. J Pediatr 1978; 93:783-8.
12) Rosenfeld W, Verma RS, Jhaveri RC, Estrada R, Evans H, Dosik H. Duplication 3q : severe manifestations in an infant with duplication of a short segment of 3q. Am J Med Genet 1981;10:187-92.
13) van Essen AJ, Kok K, van den Berg A, de Jong B, Stellink F, Bos AF, et al. Partial 3q duplication syndrome and assignment of D3S5 to 3q25-3q28. Hum Genet 1991;87:151-4.
14) Allderdice PW, Browne N, Murphy DP. Chromosome 3 duplication q21 leads to qter deletion p25 leads to pter syndrome in children of carriers of a pericentric inversion inv(3)(p25q21). Am J Hum Genet 1975;27:699-718.
15) Nussbaum, Robert L. Thompson & Thompson Genetics in Medicine. 6th ed. Philadelphia : WB saunders Co, 2002;149-50.