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An Unusual Combination of Trisomy 21 and Partial Trisomy 5q

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The authors describe a male newborn with multiple congenital anomalies; craniofacial dysmorphism, bilateral cleft palate and lip, ambiguous external genitalia with absence of phallus, ventricular septal defect, agenesis of olfactory bulbs, and presence of small round cells simulating migration defect in the cerebellar white matter. Cytogenetic study demonstrated a chromosomal constitution of 47,XY, + 21, + 5q. Its pathological significance compared with Down's syndrome and hitherto reported partial trisomy 5q is discussed.

Key Words: *Trisomy 21, Partial trisomy 5q, Multiple congenital anomalies.*

INTRODUCTION

Although trisomy 21, known as Down's syndrome, is among the more frequent chromosomal disorders, partial trisomy 5q is a relatively rare chromosomal aberration. So far, about 20 cases of partial trisomy 5q with different break points have been reported, but the presence of syndromic stigmata in this chromosomal aberration is still obscure, and the association of trisomy 21 and partial trisomy 5q has not been reported in the literature as yet (Curry et al., 1979; Jones et al., 1979; Rodewald et al., 1980; Martin et al., 1985; Kumar et al., 1987).

We experienced an autopsy case of a male newborn with multiple congenital anomalies. Abnormal association of trisomy 21 and partial elongation of 5q was also demonstrated in this case. Considering the unusual combination of chromosomal aberrations, we believe that the case may give us valuable information on the phenotypic correlation of each chromosomal aberration. Its significance is discussed with detailed pathological descriptions.

CASE REPORT

The proband was born on May 7, 1989, to a 25-year-old mother at Cha Women's Hospital as her first baby. The gestational age was 38 weeks and a vacuum delivery was performed due to a spontaneous rupture of the membrane. Apgar scores were 7 and 8 at 1 and 5 minutes, respectively. The birth weight was 2,900 gm and multiple external anomalies were found with signs of respiratory distress such as intercostal retraction. He died a day later and an autopsy was conducted at the Department of Pathology, Seoul National University Children's Hospital, which demonstrated multiple systemic anomalies; craniofacial dysmorphism, complete bilateral cleft palate and lip, low set dysplastic ears, prominent nasal bridge (Fig. 1), lobster claw deformity of the left hand (Fig. 2A), flexion deformity of the right wrist, and ambiguous exenal genialia with absence of phallus were the external anomalies (Fig. 2B). The internal anomalies included ventricular septal defect, persistent left superior vena cava in the cardiovascular system; agenesis of the olfactory bulbs, and multiple nests of primitive small round cells simulating migration defect, in the cerebellar white matter, abnormal cerebellar, folia, foreshortening of the cerebral anteroposterior diameter in the central nervous system; and bilateral cystic renal dysplasia, bilateral cryptoorchidism and cystic change of the epididymis in the genitourinary system. Other anomalies were persistent omphalomesenteric duct, agenesis of the phalangeal bone in the left fifth finger, intrapancreatic splenic heterotopia, and medial displacement of adrenals. Severe meconium aspiration pneumonia was present and this was thought to be

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the direct cause of death. All the pathological findings are summarized and are compared with those of previously reported cases of partial trisomy 5q in Table 1.

A cytogenetic analysis from 30 peripheral blood lymphocytes, performed before death at the Department of Medical Genetics, Han Yang University, College of Medicine, revealed a peculiar mixed chromosomal aberration in G banded chromosomes of all cells; trisomy 21 and partial trisomy for the long arm of chromosom 5 (Fig. 3). The partial idiogram of Giemsa banded karyotype is shown in figure 4. The extra segment of 5q seemed to be duplicated at the region of 5q14-33.

DISCUSSION

In the present case, a relatively large extra segment was clearly visible in the long arm of chromosome 5 as well as trisomy 21. The partial trisomy 5q per se is a very rare occurrence and this combination of trisomy 21 an partial trisomy 5q has not been reported as yet (Kumar et al., 1987; Choi et al., 1990).

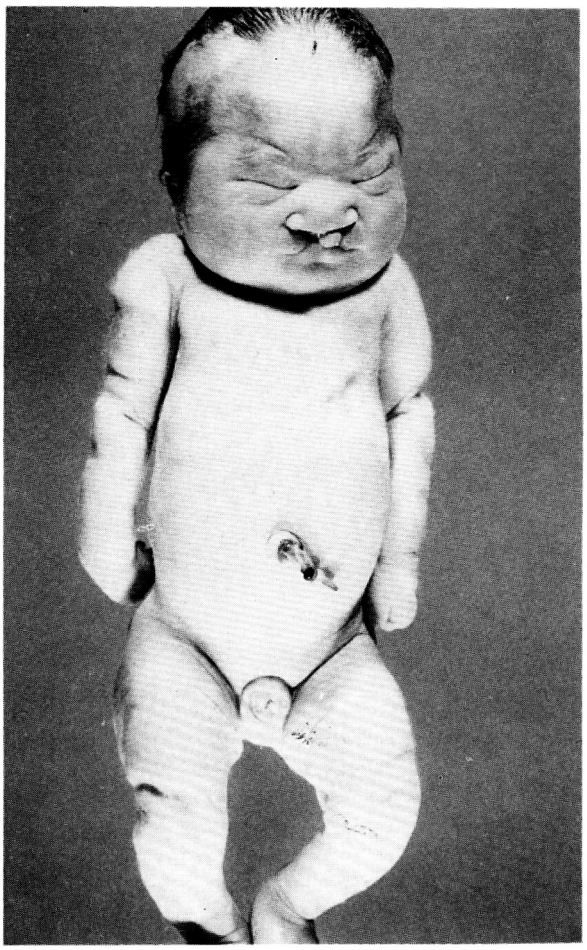

Fig. 1. The proband has craniofacial dysmorphism, bilateral cleft palate and lip, flexion deformity of right wrist and low set ears.

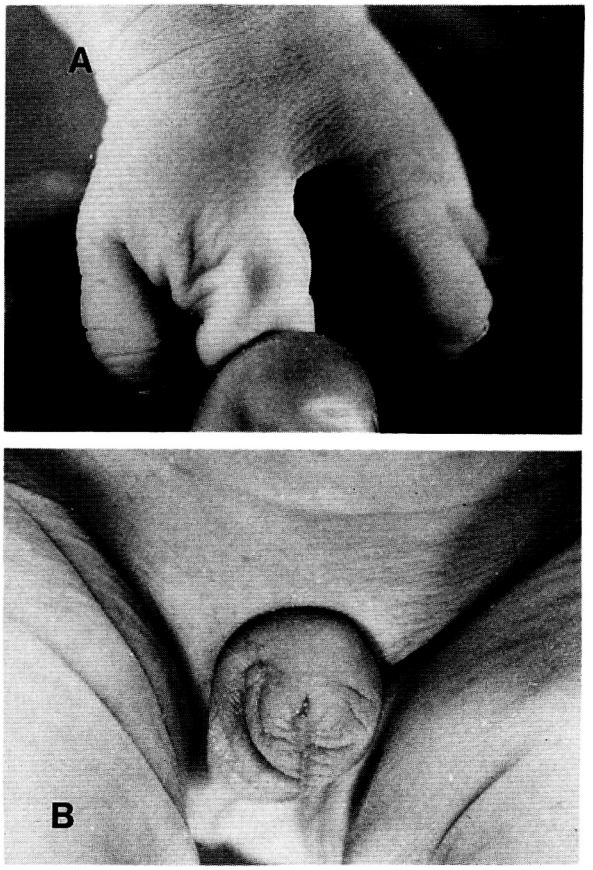

Fig. 2. Features of (A) lobster claw deformity of the left hand, and (B) ambiguous external genitalia without phallus.

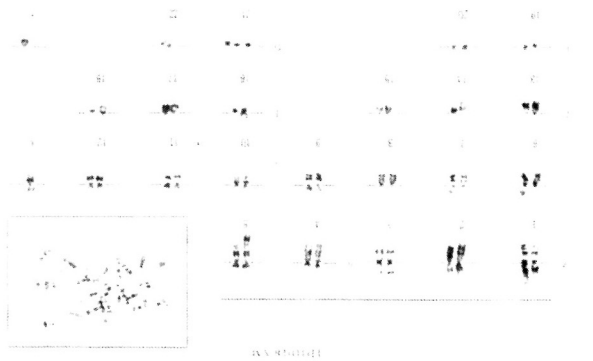

Fig. 3. The idiogram showing trisomy 21 and clearly visible partially duplicated 5q.

Although syndromic anomaly complex is well established in trisomy 21 Down's syndrome, the presence of syndromic stigmata in partial trisomy 5q is still under debate due largely to the lack of accumulated cases, but growth and mental retardation, craniofacial dysmorphism, microcephaly, antimongoloid slant, strabismus, prominent nasal bridge, low set dysplastic ears, brachydactyly or clinodactyly, and congenital heart defect are rather frequently described anomalies in previous cases of partial trisomy 5q (Zabel e al., 1978; Kumar et al., 1987). Among the complex systemic anomalies of the present case, prominent features, which have not been described in the previous reports of Down's syndrome or partial trisomy 5q, include shortening of the cerebral anteroposterior diameter, olfactory bulb agenesis, presence of small round cells simulating migration defect in the cerebellar white matter, abnormal cere-

Table 1. Summary and comparison of pathological findings of the present case with those of previously described partial duplication of the long arm of chromosome 5.

Anomalies	Previous reports	Present case
Growth and mental retardation	+	?
Craniofacial dysmorphism	+	+
Microcephaly	+	+
Short receding forehead	+/−	−
Antimongoloid slant	+/−	−
Epicanthus	+/−	−
Strabismus	+/−	?
Hypertelorism	+/−	−
Prominent nasal bridge	+/−	+
Upper lip: large/thin	+/−	−
Low set dysplastic ears	+	+
Microstomia	+/−	−
Muscle hypotrophy	+/−	−
Hypotonia	+/−	−
Brachydactyly/Clinodactyly	+/−	−
Hernias	+/−	−
Congenital heart defect	+	+
Cleft palate and lip	−	+
Cystic renal dysplasia	−	+
Amhiguous external genitalia	−	+
Cystic dilatation of epididymis	−	+
Cryptoorchidism	−	+
Lobster claw deformity of hand	−	+
Absence of phallangeal bone in the fifth finger	−	+
Flexion deformity of wrist	−	+
Olfactory bulb agenesis	−	+
Islands of primitive cells in the cerebellar white matter	−	+
Abnormal cerebellar folia	−	+
Persistent omphalomesenteric duct	+	−
Intrapancreatic splenic heterotopia	−	+

* The findings of previous reports were quoted from the summary table of clinical finding in the study of Kumar et al. (1987): (+) designates rather constant findings while (+/−) does equivocal or occasional findings.

** The findings under the interrupted line are the unique findings in the present case and may be additional features of partially duplicated 5q.

bellar folia, ambiguous external genitalia with absence of phallus, cystic renal dysplasia, and lobster claw deformity of hand, which are all mainly of the central nervous system and genitourinary tract. The combination of two separate chromosomal aberrations makes adequate evaluation of karyotype vs phenotype correlation more complicated and nonspecific, but there is a possibility that the aforementioned features may be a new spectrum of anomalies in partial trisomy 5q.

Because the parental karyotypes were normal, the partial trisomy 5q and trisomy 21 seem to be a result of de novo chromosomal rearrangement due to nondisjunction and unequal crossing over during meiotic division of maternal or paternal gametogenesis rather than a result of other mechanisms such as balanced translocation in the parents or balanced insertion (Zabel et al., 1978; Jalbert et al., 1975). Concomittant and unhappy chromosomal rearrangement of chromosome 21 and 5q should have resulted in lethal and complex systemic malformations and, previous cases of partial trisomy 5q alone were compatible with survival for at least a few months.

The major problem in the interpretation of the present case was to delineate the exact break point with conventional G-banding alone because high resolution banding was not performed. The duplicated segment seems to be consistent with 5q 14-33 and this type of duplication has not been described in previous partial trisomy 5q (Kumar et al., 1987). The combination of trisomy 21 and partial trisomy 5q along with some unique pathological features in this case may imply new aspects of phenotypic expression in partial trisomy 5q.

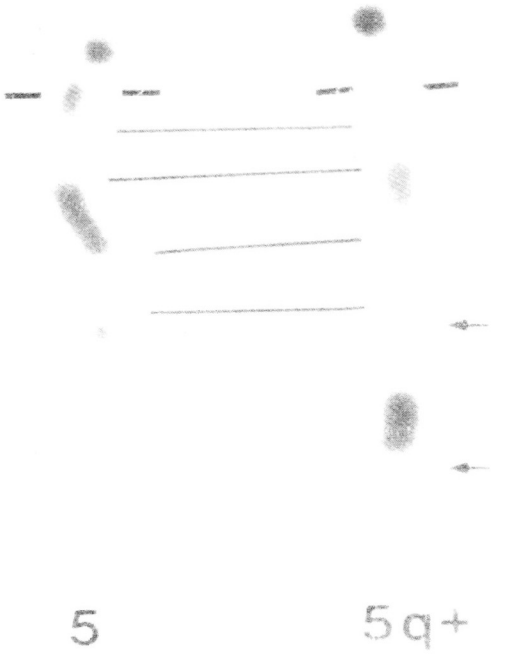

Fig. 4. The partial idiogram of chromosome 5 showing an extra segment (conventional G-banding) in the arm that is consistent with 5q 14-33.

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