A dup(13)(q31.2-qter) without abnormalities of hands or feet

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Abstract

We present a patient with a deletion of portion 5pter→p15.33 and a duplication of portion 13q31.2→qter. The male infant proband, the first child of healthy and unrelated parents, was born after a 41-week gestation. The proband had a birth weight of 2,015 g, a length of 42.2 cm and a head circumference of 32.0 cm. He had micrognathia, anteverted nostrils, low-set ears, cleft palate, sacral dimple, right retentio testis, shawl scrotum, and tetralogy of Fallot with severe pulmonary stenosis. There were no overlapping fingers, polydactylia or rocker-bottom feet. The maternal karyotype was normal. The paternal karyotype was not available. His karyotype was revealed as 46,XY,der(5)t(5;13)(p15.33;q31.2) by G-banded karyotype, SKY method and FISH analysis. The importance of this case suggests a critical region of trisomy 13 syndrome, especially of polydactyly.

Key words : chromosome 13, partial trisomy 13q, polydactyly, critical region

Introduction

A large number of cases involving partial trisomy for 13q have been reported in the literature[1]. However, a clear phenotype-karyotype correlation has not been established[2]. Many instances result from parental translocations, and such trisomies are derivatives involving other chromosomes. Alternatively, it may be mainly due to the extent of the segment involved or to different breakpoints. Depending on the point of breakage there can be widely variable clinical manifestations[1]. We present a patient with a partial trisomy 13q, and discuss about a critical region of trisomy 13 syndrome, especially of polydactyly.

Clinical and cytogenetic findings

The male infant proband, the first child of healthy and unrelated parents, was born after a 41-week gestation. The father was 36 and the mother 27 years of age at the time of birth. The mother had not experienced any spontaneous abortions or still births prior to the proband's birth and she denied having any infections, drinking alcohol, taking drugs, or exposing herself to known teratogenic agents.

The proband had a birth weight of 2,015 g, a length of 42.2 cm and a head circumference of 32.0 cm. Because of tachypnea soon after his birth, he was referred to the near hospital. There was a suspicion that he had a ductal dependent congenital heart disease. An artificial respirator was used and alprostadil was administered by an intravenous drip infusion. He was referred to the Department of Pediatrics, Miyazaki Medical College on the 2nd day after birth because the level of arterial oxygen saturation by pulse oximeter did not rise. At that time, generalized cyanosis existed but there was no

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audible heart murmur. Physical findings included the following: micrognathia, anteverted nostrils, low-set ears, cleft palate, sacral dimple, right retentio testis, and shawl scrotum. A dermatoglyphic study revealed bilateral single palmar creases, and 5 whorls and 5 urnal loops on the finger tips. The atd angles were 80° (right) and 90° (left). There were no overlapping fingers, polydactylia or rocker-bottom feet. An echocardiograph study revealed tetralogy of Fallot with severe pulmonary stenosis. He received therapy by artificial respirator, intravenous drip infusion of alprostadil, and tube feeding for one month. At 4 months he could control his head, smile, chase things by his eyes and measured; height, 56.8 cm (-3.7 SD); weight, 4,075 g (-4.3 SD) and head circumference, 38.5 cm (-3.0 SD) (Fig. 1). Polymolphonuclear projections on segmented neutrophils were observed in a Giemsa stained peripheral blood smear.

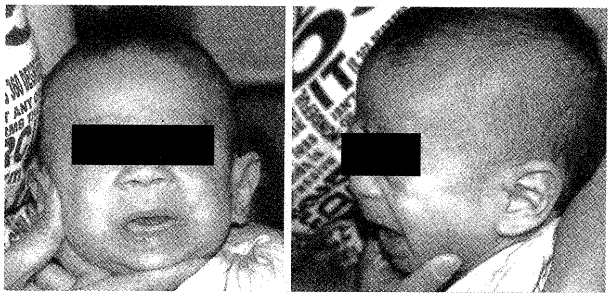

Fig.1

The patient's chromosomes were analyzed on cultured lymphocytes: G-banded karyotype revealed a derivative chromosome 5 that had an excessive portion on the short arm. Both the excessive portion and chromosomes 13 were stained the same color by the spectral karyotyping (SKY) method (data not shown). FISH (fluorescence *in situ* hybridization) analysis using RP11-122N18 clone that locates on 13q22.3 showed no signal, but FISH analysis using RP11-80P22 clone (13q31.2) and RP11-79A16 clone (13q32.1) showed a signal on a derivative chromosome 5 (data not shown). FISH using a probe to detect a region of 5p15.2 (D5S23) which is responsible for cri du chat syndrome revealed a signal on both the derivative and normal chromosome 5 (data not shown). Accordingly, he was determined to have a small deletion of portion 5pter→p15.33 and a duplication of portion 13q31.2→qter (Fig. 2). The maternal karyotype was normal. The paternal karyotype was not available because of a homecoming delivery.

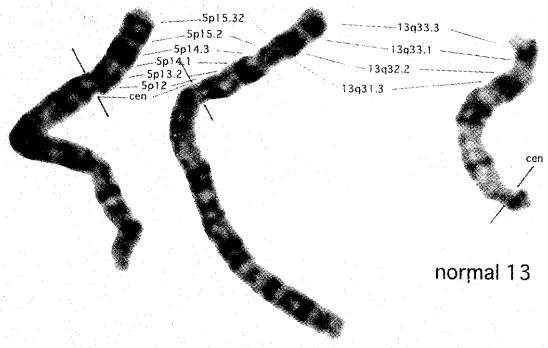

Fig.2

Discussion

Our patient had a simultaneous partial deletion for 5p. Since the portion was very small, our patient, in comparison with most patients with trisomy 13q, is presented as a phenotypically pure description. Even if this small deletion for 5p has some effect on the phenotype, the phenotype of our patient never becomes milder. Helali et al. reviewed the reported cases of partial trisomy 13q and classified patients into 4 groups by karyotypes; trisomies for 13q14→qter, 13pter→q22, 13q22→qter, and 13q32→qter. Microcephaly, cleft palate, raised fetal hemoglobin, and increased polymorphonuclear (PMN) projections on the segmented neutrophils are more represented in the proximal duplications 13pter→ q22. High arched palate, polydactyly, hernias, hemangiomas, and urogenital abnormalities are more represented in the distal duplications 13q14→qter. These phenotypic features are similar to those of complete trisomy 13. Their patient with dup 13q32→qter did not show the features classically seen in patients with duplications of 13q14→qter, and they concluded that the possible explanation for the lack of Patau syndrome in their patient could include restriction of the critical region for Patau syndrome to duplication 13q14→13q32 with variable expression[2]. Our patient with duplication of 13q31.2→qter has some features of trisomy 13, i.e. low birth weight, peculiar facial appearance, cleft palate, congenital heart disease, retentio testis, shawl scrotum, and increased PMN projections. It is possible that the features of trisomy 13 and duplication 13q14→qter are the result of genes that can now be restricted to the

segment between 13q14 and 13q31.2.

Band 13q32 has been defined as a critical region associated with thumb and/or big toe anomalies and major developmental abnormalities[3]; the trisomy of this band has been related to polydactyly[4] and the monosomy to absent thumbs[5]. Brown et al. hypothesized that band 13q32 contained genes critical for digit formation[3]. The patient with dup 13q32→qter reported by Helai et al.[2] and our patient with dup 13q31.2→qter have a duplication of band 13q32; however, neither have polydactyly. In a family with t(5;13)(p15;q22) reported by de Alba et al., when a partial trisomy of 13q22→qter is present, the fetuses have polydactyly in the four limbs, and when a fetuses is carrying a partial monosomy of this portion, an oligodactyly can be observed[1]. Accordingly, the genes for digit formation might be located in band 13q22.

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手足の異常を伴わない46,XY,dup(13)(q31.2-qter)の1例

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要　約

5pter→p15.33の部分欠失と13q31.2→qterの部分重複を併せ持つ症例を報告する。症例は、健康で血縁関係のない両親の第1子として生まれた男児である。在胎41週のときに体重2,015g、身長42.2cm、頭囲32.0cmで出生した。小下顎、上向き鼻孔、耳介低位を伴い、口蓋裂、仙骨部陥凹、右停留精巣、襟巻き状陰嚢、両側単一手掌横線、重度の肺動脈狭窄を伴うファロー四徴を有していた。多指や指の重なり、足の揺り椅子状変形はなかった。末梢血リンパ球を用いたGバンドによる染色体検査、SKY法、FISH法により患児の染色体核は46,XY,der(5)t(5;13)(p15.33;q31.2)と決定した。母親の染色体核型は正常であったが、父親については検査ができていない。この症例の重要性は13トリソミー症候群の危険領域、特に多指趾について、示唆することである。

キーワード：13番染色体長腕部分トリソミー、多指趾、危険領域