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Case Reports

Two Siblings with Currarino Syndrome with 7q34 Deletion Due to Maternal t(7;14)(q34;p13)

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Abstract Currarino syndrome is a rare but well-described form of caudal regression syndrome characterised by anorectal malformations, sacral bony defects and a presacral mass. We present two siblings with Currarino triad due to pure 7q34 deletion but different phenotypes. They had the typical spectrum of sacral agenesis, pre-sacral tumor and anorectal malformations. Interestingly, they have the same genotype but different dysmorphic characteristics. Chromosomal analysis detected that the mother was carrier. To the best of our knowledge, this is the first reported 7q34-14p translocation.

Key words Currarino syndrome; Microcephaly; *MNX1*; Sacral dysgenesis

Introduction

Currarino syndrome (CS) first described in 1981 by Currarino et al[1] as a rare congenital complex of sacral bone defect, a congenital hindgut anomaly and a presacral tumour. It has broad inter- and intra-familial phenotypic variability.[2] It is thought to result from abnormal separation between neuroectoderm and endoderm.[1] Prevalence has been estimated as 1-9:100000 and presentation may be at any age.[3] It shows variable clinical spectrum, ranging from minor anomalies to complex malformations.[4]

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Mutations of *MNX1* gene, previously known as HLXB9, located on chromosome 7q36 cause the syndrome.[4] More than 70 mutations were defined.[4-6] Most of the Currarino syndrome cases reported in the literature are de novo 7q deletions but a few cases are unbalanced translocations involving 7q36.

We report cases of two siblings with features of CS combined with microcephaly, facial dysmorphism, growth retardation, mental retardation and chronic constipation with pure terminal 7q34 deletion due to novel maternal 7q34-14p13 terminal translocation.

Case Report

A pregnant woman was referred to us because she was anxious about her husband's two nephews who had mental retardation and multiple congenital anomalies. The children's mother and father were also relatives (first cousins). Firstly, chromosomal analyses with standard peripheral blood samples and GTG banding of the children (index cases) were done and deletion of 7q34-qter was detected. In the GTG banded chromosomal analysis of parents of the patients, the mother was detected to have balanced translocation. The chromosomal analyses of the pregnant woman and her husband (the patients' uncle) were normal. The pregnancy of the consultant resulted in a healthy child.

Features of our cases were as follows and are also presented in Table 1.

Case 1 is a 15-year-old male, operated on three times for chronic constipation. Cranial magnetic resonance imaging (MRI) was not performed because his parents did not accept radiodiagnostics.

Case 2 is a 13-year-old female patient. She had one operation for chronic constipation. Congenital sacral hypoplasia, tethered cord, neurogenic bladder and hydronephrosis were detected. Cranial MRI was normal.

Fluorescence In Situ Hybridization (FISH) analyses performed from metaphases and whole chromosome painting probes for 7 and 14 were used. Results were as follows:

Case 1: 46,XY,der(7)t(7;14)(q34;p13)mat.ish der(7)t(7;14)(q34;p13)(wcp7+,wcp14+)

Case 2: 46,XX,der(7)t(7;14)(q34;p13)mat.ish der(7)t(7;14)(q34;p13)(wcp7+,wcp14+)

These results confirmed that the very tiny chromatin added on satellite of 14 p ter originated from 7q. This is the first t(7;14)(q34;p13) translocation case in the literature.

Mother's karyotype was 46,XX,t(7;14)(q34;p13) (Figure 1). The mother's parents did not accept chromosome analysis.

Table 1 Features of cases

Features	**Our report**		**Masuna et al, 1990[7]**		**Rodriguez et al, 2002[8]**	**Pavone et al, 2010[9]**
	Case 1	**Case 2**	**Case 1**	**Case 2**		
Sex/age	Male/15 years	Female/13 years	Female/2.6 years	Male/7.2 years	Male/38 weeks	Female/3 years
Feeding difficulties	+	+	nm	nm	+	nm
Growth retardation	+	+	+	+	+	+
Mental retardation	+	+	nm	nm	nm	+
Hypotonia	+	+	–	–	–	+
Microcephaly	+	+	+	+	+	+
Hypotelorism	+	–	+	+	–	+
Epicanthus	+	+	nm	nm	–	+
Eye anomalies	+	–	nm	nm	–	+
Blepharoptosis	+	–	nm	nm	+	+
Downslanting palpebral fissures	–	+	nm	nm	–	nm
Small nose	–	+	nm	nm	–	nm
Broad nasal bridge	–	+	+	–	–	+
Bulbous nasal tip	+	+	nm	nm	–	nm
Choanal narrowing	+	–	nm	nm	–	nm
Small mouth	+	–	nm	nm	nm	+
Large mouth	–	+	nm	nm	nm	–
Ear anomalies	+	–	nm	nm	nm	–
Currarino triad						
Sacral agenesis	+	+	+	+	+	+
Pre-sacral tumour	+	+	–	–	+	+
Anorectal malformations	+	+	–	–	–	+
Cytogenetic/FISH	46,XY, der(7) t(7;14)(q34;pter)	46,XY, der(7) t(7;14)(q34;pter)	46,XX,del(7) (pter→q36.1)	46,XY,del(7) (pter→q36.1)	46,XY,del(7) (q36→qter)	46,XY,dup7 q34-q35 del7q36

nm: not mentioned; FISH: Fluorescence In Situ Hybridization

Discussion

The phenotypes of our patients with pure terminal 7q34 deletion included a number of non-specific features of the syndrome consisting of moderate mental retardation, growth deficiency, feeding problems, and microcephaly. Both cases have CS but interestingly they have different facial appearance; case 1 has thin and case 2 has thick upper lips, case 1 has blepharoptosis but case 2 does not. Case 2 does not have holoprosencephaly and case 1 could not be examined for holoprosencephaly (parents did not accept radiodiagnostics) but he has no signs, such as cleft lip or palate, premaxillary agenesis or single central incisor.

Holoprosencephaly and caudal deficiency was reported in 70% and 25% of terminal 7q deletion cases. But a lot of cases with Currarino syndrome were reported from pediatric surgery departments and did not have chromosome analysis performed. Our cases were operated at another university hospital but were not referred for chromosome analysis with caudal deficiency indication. Patients with clinical findings such as cleft lip or palate, premaxillary agenesis, single central incisor, or ptosis should be screened for holoprosencephaly.[10]

Of 94 cases of 7q terminal deletions reported in literature, 32 are 7q32, 30 are 7q36 and 19 are 7q34; 48% were de novo, 36% familial and 10% uncertain. Familial cases were due to different chromosomal translocations but our family is the first reported 7q34-14p translocation. The 7q34 region is highly prone to translocations. But translocation in our cases' mother was from 7q34 to 14p and this is the first such translocation reported in the literature. 14p is a satellite region of acrocentric chromosome and in this region there are ribosomal RNA genes as other acrocentrics, therefore terminal deletion is not effective on phenotype. Also translocation is one sided so there is no additional chromatin added to the 7th chromosome. So our cases' phenotype is

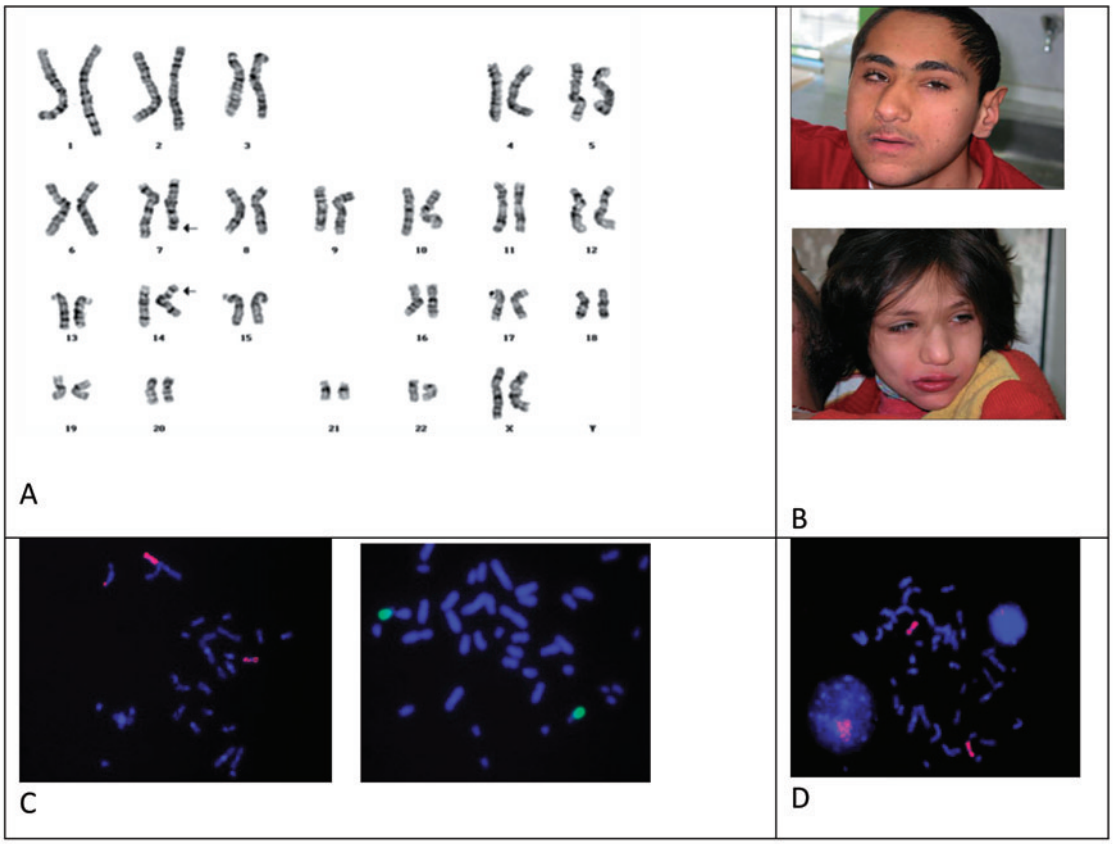

Figure 1 (A) Mother's karyotype 46,XX,t(7;14)(q34;p13); (B) Facial features of case 1 (above) and case 2 (below); (C) Mother's metaphase FISH WCP 7 (left) and mother's FISH WCP 14 (right); (D) Chromosome 7, FISH of case 1. (Consent has been obtained from the family to include their clinical photographs in this manuscript.)

pure 7q34 deletion. It is interesting that although they have same genotype they have different dysmorphic characteristics (Table 1).

Balanced translocation carriers have a risk of recurrence but they can also have chromosomally normal and balanced translocation carrier children. Both will have normal phenotypes. Prenatal or preimplantation genetic diagnosis is possible with FISH. Prenatal diagnosis is also possible with chromosome analysis but because the deleted region is very thin, FISH analysis is preferred.

Because of high recurrence risk in familial cases chromosome analysis of cases and parents are essential.

Declaration of Interest

To the best of our knowledge, no conflict of interest, financial or other, exists. The authors report no declarations of interest.

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