Currarino triad with a terminal deletion 7q35→qter

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Abstract

We describe a *de novo* terminal deletion of the long arm of chromosome 7 in a 5 year old girl with the Currarino triad, characterised by congenital anorectal stenosis, a sacral defect, and a presacral mass. Recently, this autosomal dominant trait has been shown to be linked to 7q36, the same region as holoprosencephaly (HPE3). The cytogenetic findings in the present patient with the Currarino triad provided further evidence that a gene(s) for the Currarino triad is located in the 7q terminal segment.

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Key words: Currarino triad; terminal deletion; 7q.

Barium enema examination confirmed severe caudal rectal stenosis. Lower sacral agenesis was diagnosed radiologically. Magnetic resonance imaging of the spine and pelvis showed sacral deformity and intraspinal lipoma with cord tethering extending to the presacral region. The presacral tumour was made up of fat and water and was considered to be an anterior lipomeningocele or teratoma. Intravenous pyelography and voiding cystography showed no abnormalities. Computed tomography of the brain was normal without overt holoprosencephaly. Findings of serum chemistry, complete blood counts, and urine were normal.

Through a sacral approach, laminotomy of L5 and S1 was performed at 3 years 5 months. The lamina ended abruptly below S2 and a presacral mass was found. The right nerve root of S2 was located together with that of S1 in the vertebral canal. The anterior sacral mass (5 × 3 cm) was excised with release of a thickened tethered filum terminale. The histological features were those of a mature teratoma which consisted of fibroadipose tissue containing neuroglial elements and skin with adnexae. After operation the patient was managed by rectal dilatation. She walked alone at 3 years 11 months and spoke meaningful words at 4 years 6 months.

CYTOGENETIC FINDINGS

Chromosome analysis was carried out on peripheral lymphocyte cultures. The karyotype of the proband by GTG high resolution banding was 46,XX,del(7)(q35) (fig 1). Both parents had normal chromosomes. An EBV transformed lymphoblastoid cell line (KCMC-267) from the patient is available from Dr M Masuno.

Discussion

Recently, a gene for autosomal dominant sacral agenesis including the Currarino triad has

The Currarino triad (MIM No *176450) is an autosomal dominant trait characterised by congenital anorectal stenosis, a sacral defect, and a presacral mass.¹ Recently, this trait has been shown to be linked to 7q36,² the same region as holoprosencephaly (HPE3).^{3,4} Here we report a patient with the Currarino triad associated with a *de novo* terminal deletion of the long arm of chromosome 7.

Case report

The female proband was the second child of healthy, non-consanguineous Japanese parents. The mother and father were 37 years old at the time of her birth and had had a healthy son. The mother had no history of abortions or stillbirths. The proband was born at 37 weeks of gestation after an uneventful pregnancy. At birth, her weight was 2125 g, length 44.5 cm, and occipitofrontal circumference (OFC) 29.0 cm. Apgar score was 10 at one minute. She had had intractable constipation since birth. She had suffered from recurrent urinary tract infections up to 4 months of age.

She was first evaluated by us at 3 years 2 months of age because of marked abdominal distension owing to constipation. At that time, her height was 79.2 cm (-3.9 SD), weight 8.9 kg (-3.1 SD), and OFC 41.0 cm (-4.6 SD). Physical examination detected severe stenosis of the anus and distal rectum. The main clinical manifestations were frontal bossing, flattened occiput, deep set eyes, telecanthus, short palpebral fissures, esotropia, low nasal bridge, short nose with anteverted nostrils, depressed nasal tip, hypoplastic columella, large ears, protuberant upper lip, downturned corners of the mouth, submucosal cleft palate, absent uvula, and overriding second toes. The development quotient was 32.

Figure 1 Two pairs of chromosome 7 of the proband showing the terminal deletion of the long arm. Arrows show the breakpoint at 7q35.

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been mapped to 7q36,² the same region containing a gene for holoprosencephaly (HPE3).^{3,4} The cytogenetic findings in the present patient provided further evidence that a gene for the Currarino triad is located in the 7q terminal segment.

Holoprosencephaly and sacral agenesis,^{5,6} as well as holoprosencephaly and urological abnormalities, including hydronephrosis or hydroureter,^{5,7} have been occasionally observed in patients with 7q terminal deletions. Previously, we described two unrelated patients with a single maxillary central incisor, which is a mild form of holoprosencephaly, and urological abnormalities with terminal deletions at the same breakpoint of 7q36.1. In addition, case 1 had a defect of the lower sacrum and severe constipation requiring colostomy in another institution. Case 2 had spina bifida occulta of the sacrum.⁸ Thus, case 1 showed that holoprosencephaly sequence, sacral agenesis, anorectal abnormalities, and urological abnormalities are attributable to 7q terminal deletion. Therefore, the terminal segment of 7q contains genes responsible for sacral agenesis including the Currarino triad, holoprosencephaly, and urological abnormalities.

Nagai *et al*⁹ described a patient with the Currarino triad and partial trisomy of chromosome 13q and 20p. Thus, the Currarino triad seems to be a genetically heterogeneous trait.

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