We report on the clinical, cytogenetic, and imaging findings in a patient with a 7q terminal deletion. The 11-year-old girl had mental retardation, microcephaly, a distinctive face, relatively small hands and feet, and sacral dysgenesis. High resolution GTG banding (550–850 bands) showed a 7q terminal deletion. A detailed evaluation of associated malformations and the overall clinical picture should be taken into account when identifying the underlying diagnosis in cases of sacral dysgenesis with mental retardation.

1. Introduction

The phenotypic spectrum of de novo 7q terminal deletion syndrome comprises short stature, microcephaly, facial anomalies, and mental retardation. Deletions range in size from 7q32–qter to 7q36–qter. In most cases, the deletion involves the 7q32–qter region. To date, only ten patients with a de novo 7q36–qter deletion have been reported. In several patients, the 7q36, terminal deletion was associated with sacral agenesis. It has recently been demonstrated that the homeobox gene, HLXB9, located at 7q36, is involved in the development of sacral agenesis. We present an additional patient with sacral dysgenesis and a de novo 7q36 deletion.

2. Case Report

An 11-year-old girl was the second child born to non-consanguineous Taiwanese parents. Her elder sister was normal. At the time of birth, her mother was 29 years old and her father was 30 years old. She was born at 40 weeks’ gestation, after an uneventful pregnancy. Her birth weight was 2,650 g (10–25th centile), body length was 49 cm (50th centile), and occipitofrontal circumference (OFC) was 30 cm (<3rd centile). After birth, she exhibited muscular hypotonia, feeding problems, failure to thrive, and early developmental delay. The patient first sat at 12 months and began walking at 3 years. She was able to use a few words at 38 months. At 38 months, she had a body height of 88 cm (<3rd centile), weight of 9.7 kg (<3rd centile), OFC of 42 cm (<3rd centile), down-slanting palpebral fissures and hyperkinesis. An examination at 7 years and 9 months old, showed a body height of 112 cm (<3rd centile), and weight of 20 kg (10–25th centile). As an 8-year-old, she underwent tonsillectomy and adenoidectomy, due to tonsillar and adenoid hypertrophy.

She was first examined at our genetics clinic at 10 years and 8 months old because of discomfort...
due to menarche. At that time, she presented with a height of 134 cm (10–25th centile) and weight of 28 kg (25th centile), bilateral ptosis, down-slanting palpebral fissures, high arched eyebrows, and depressed nasal bridge (Figure 1). She had normal teeth, including normal maxillary incisors. Relatively small hands and feet were noted. Magnetic resonance imaging (MRI) of the brain was completely normal. Endocrine tests revealed elevated basal estradiol levels, and peak luteinizing hormone levels during a gonadotropin-releasing hormone test were 109 IU/L. Bone age was appropriate for her age. An anteroposterior radiograph demonstrated agenesis of the lower segments of the sacrum (Figure 2). MRI revealed a fibrolipoma of the filum terminale (Figure 3A) with tethered cord, hydromyelia, hypogenesis and deformity of the sacrococcygeal spine (Figure 3B) and arcuate uterus (Figure 4).

We performed high resolution GTG banding (550–850 bands) in our laboratory. Chromosome analysis showed a 46, XX, del(7)(q36–qter) karyotype (Figure 5). The karyotypes of the parents and elder sister were normal. This represents a de novo case of 7q36 terminal deletion.

At 10 years and 9 months of life, a neuropsychological evaluation was performed using the Wechsler Intelligence Scale for children (WISC-III). Her verbal IQ was 46, and her full scale IQ was 40.

3. Discussion

We report the clinical, cytogenetic and imaging findings of a patient with a 7q36 deletion. The phenotypes of this patient show the typical sacral agenesis associated with the terminal 7q deletion syndrome, but without holoprosencephaly. Lynch et al suggested that the genes for holoprosencephaly and sacral agenesis were allelic, and involvement of different functional domains of the gene could explain the occurrence of one or more phenotypes. The phenotypic features of holoprosencephaly and sacral agenesis are variable; the features of holoprosencephaly range from midface hypoplasia to cyclopia, and those of sacral agenesis range from partial agenesis of the coccyx to complete absence of the sacral and lumbar vertebrae. Lynch et al also suggested that the 7q terminal region contained genes that “play a critical

![Figure 1](image1.png) Frontal view at 10 years and 8 months showing ptosis, down-slanting palpebral fissures, highly arched eyebrows, and depressed nasal bridge.

![Figure 2](image2.png) Radiograph of the lumbosacral spine showing malformation of the sacrum. The dysplastic sacrum is formed from only two segments.
role in differentiation of midline mesoderm at both ends of the developing notochord.

In our case, the arcuate uterus detected by abdominal MRI resulted from abnormal differentiation of the midline mesoderm. This variable phenotype, together with fibrolipoma of the filum terminale, tethered cord, hydromyelia, hypogenesis/deformity of the sacrococcygeal spine and arcuate uterus, which also arose from a blastogenetic midline developmental field, could be indicative of a midline defect in patients with 7q36 deletion.

In a previous report, a patient underwent a spinal de-tethering operation with excision of the mass. The histological features were characteristic of fibrofatty tissue. In our case, MRI demonstrated that the caudal end of the spinal cord was low (L2/L3; normal, L1), and ended in a lipomatous mass in the sacral canal. It also revealed the tethering cord. This pattern of sacral dysgenesis differs from the classical “hemisacrum” characteristic of the Currarino triad, which is associated with a presacral mass (anterior meningocele, enteric cyst and/or presacral teratoma) and anorectal stenosis. The underlying gene defect causing Currarino syndrome is also localized on chromosome 7q36, and mutations in the homeobox gene, HLXB9, have been identified in several affected patients. Because Currarino syndrome has variable expressivity and many heterozygotes are asymptomatic, we carefully evaluated our case using MRI to identify hemisacrum, presacral mass and anorectal malformations.

Our case highlights the value of phenotypic details in aiding diagnosis of sacral dysgenesis-related
disorders. We suggest that the application of advanced imaging techniques and high resolution chromosome analysis in selected patients with retardation and caudal regression might result in the identification of additional cases of chromosome 7q deletion.

References