17. A Rare Case of Klippel-Feil Syndrome Presenting with Multisystemic Involvement and Progressive Short Stature

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BACKGROUND: Klippel–Feil syndrome is a rare congenital anomaly characterised by a clinical triad consisting of a low posterior hairline, a short neck, and restricted cervical mobility [1]. Although the hallmark feature of this disorder is congenital fusion of the cervical vertebrae, it may also present with extraskeletal manifestations and additional spinal abnormalities [2]. **THE CASE:** A 5-year-10-month-old girl was referred to pediatric endocrinologists for evaluation of short stature and developmental delay. From the medical history, girl was born at 37 weeks of gestation (length of 42 cm and weight of 2230 g) via vaginal delivery in breech presentation. Congenital clubfoot and developmental dysplasia of the hips were diagnosed. A spinal MRI performed in the same year revealed Klippel–Feil syndrome, kyphotic deformity at the Th8–Th12 levels, vertebrae Th9 and Th10 resembling hemivertebrae, and spina bifida in the sacral region; neurosurgical intervention was performed. Genetic testing demonstrated a 46, XX karyotype without major chromosomal abnormalities. At 6 years old, during evaluation by a pediatric endocrinologist, her height was 94 cm (12 cm below the 3rd percentile), and weight was 13.7 kg. Body mass index (BMI) was 15.4 (50th percentile). The patient had a proportional body build. No abnormalities were observed in other systems. Radiography of the left hand demonstrated a bone age of 6 years 9 months (chronological age 5 years 10 months), adult height of 125 cm was predicted. A growth hormone stimulation test with glucagon showed an adequate response (peak GH 101.4 mU/L), thereby excluding GH deficiency. Further follow-up was recommended due to suspected primary IGF-1 deficiency. At age 8, repeated genetic consultation identified a duplication of uncertain clinical significance, 638 kb in size, located on the long arm of chromosome 9 arr[GRCh37]9q31.1(103338012_103976442) x3. There was insufficient evidence for a chromosomal disorder. At age 10, the patient was re-examined by a pediatric endocrinologist for the same complaints. At that time, her height was 113 cm and weight 20 kg, with a BMI of 15.66. The patient wears a brace due to scoliosis. No abnormalities were detected in other systems. Serum IGF-1 concentration was 19.9 nmol/L (reference range 24.6–67.3). Therefore, the prognosis for final height was considered poor due to underlying skeletal deformities and the primary syndrome. **CONCLUSION:** This case highlights a rare manifestation of Klippel-Feil syndrome in which persistent short stature developed despite normal growth hormone secretion. Genetic testing revealed a chromosomal duplication of uncertain significance, expanding the spectrum of possible genotype-phenotype correlations in this syndrome. Early detection of skeletal and spinal anomalies allowed timely structural interventions, but the long-term multisystemic impact, including orthopedic deformities, neurological sequelae, and growth concerns, required ongoing multidisciplinary management to optimize functional outcomes and quality of life. Recently observed low IGF 1 level warrant ongoing monitoring and may indicate evolving endocrine involvement. While current treatment strategies remain primarily supportive, targeted endocrine therapies such as recombinant IGF 1 replacement have shown benefit in select primary IGF 1 deficiency conditions and could represent a potential avenue for future investigation, although evidence specific to Klippel-Feil syndrome is currently lacking.

Key Words: Klippel-Feil syndrome, Short stature, IGF-1, Deformity, Chromosomal duplication.

References:

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Figure 1: Growth trajectory plotted on the CDC Girls 2-20 years stature-for-age weight-for-age percentile chart. Background growth chart adapted from the Centers for Disease Control and Prevention (CDC) Growth Charts.