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Phelan-McDermid Syndrome with Concomitant Growth Hormone and Thyroid Hormone Deficiency: A Longitudinal Case Report

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BACKGROUND

Phelan-McDermid syndrome (PMS) is a neurodevelopmental disorder caused by terminal or interstitial deletions of chromosome 22q13, most commonly involving the SHANK3 gene. Haploinsufficiency leads to impaired synaptic plasticity, resulting in hypotonia, global developmental delay, and severe expressive language impairment. Recent studies have explored insulin-like growth factor-1 (IGF-1) and growth hormone (GH) therapy in PMS, based on their roles in synaptic maturation and neuroplasticity. However, clinical evidence remains limited, particularly in patients with concomitant structural brain injury

CASE REPORT

A 2-month-old male infant presented for early rehabilitation. Cardiomegaly had been identified at 32 weeks' gestation. He was born at 40 weeks (3.16 kg) via cesarean section. At birth, he developed respiratory distress syndrome unresponsive to surfactant therapy, and echocardiography revealed pulmonary hypertension. . He had experienced a massive left parieto-occipital intracranial hemorrhage after ECMO.

At 6 months of age, he showed poor visual fixation, impaired eye–hand coordination, and minimal voluntary movement. Array comparative genomic hybridization revealed a 4.1 Mb deletion at chromosome 22q13.31–q13.33, confirming PMS. Laboratory tests demonstrated subclinical hypothyroidism (T3 1.910 ng/mL, free T4 1.170 ng/dL, TSH 6.420 μIU/mL). Follow-up was temporarily interrupted. Growth parameters were initially within normal percentiles.

At 36 months, he was diagnosed with asymmetric spastic cerebral palsy (GMFCS level II; MACS level IV). He ambulated with bilateral articulated AFO but remained non-verbal.

At 4 years, evaluation for growth deceleration revealed growth hormone deficiency and central hypothyroidism. Hormone replacement therapy was initiated. Despite continuous speech therapy since 20 months of age, his language level had remained at approximately the 4–5-month developmental stage.

At 6 years, reassessment demonstrated improvement. On the Bayley Scales of Infant and Toddler Development, developmental levels were: cognitive 12 months; receptive language 4 months; expressive language 9 months; fine motor 16 months; and gross motor 16 months. On SELSI, receptive language improved to 10 months, expressive language to 8 months, and overall language to 9 months. Clinically, he began visually attending to the therapist's mouth, producing vowel sounds upon cue, and occasionally vocalizing sounds resembling familiar words—behaviors not observed before hormone therapy.

Figure 1. brain MRI T2WI

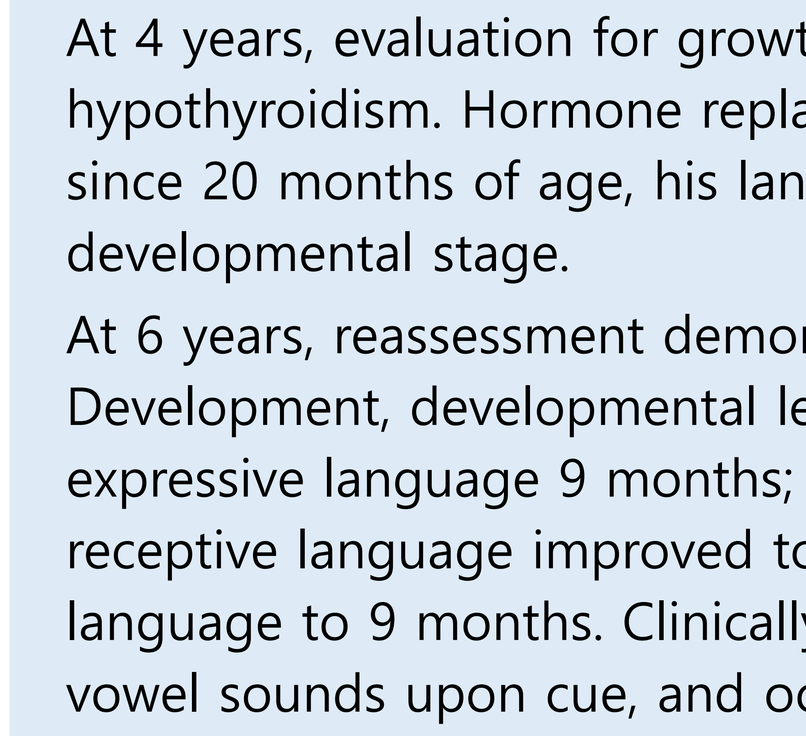
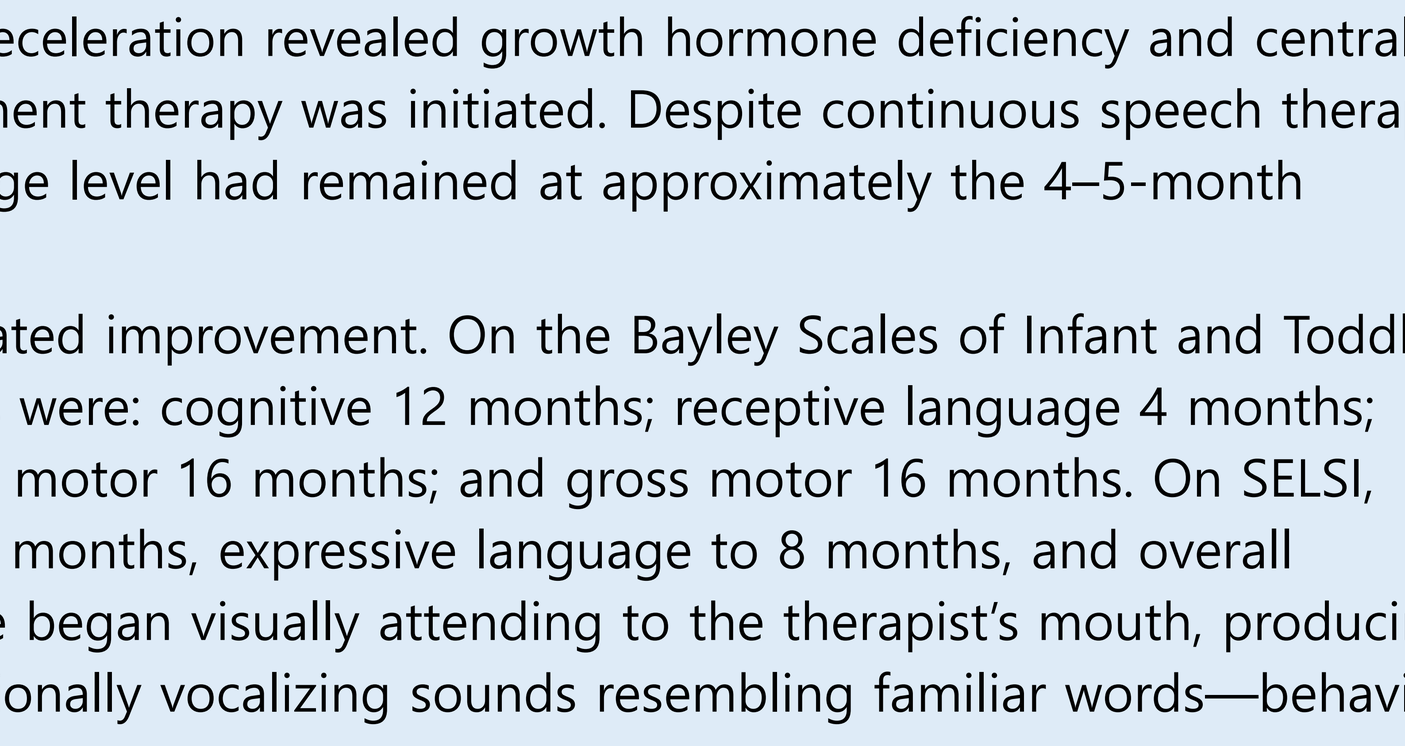


Figure 2. Chromosomal microarray



CONCLUSION

Although this is a single longitudinal observation and the improvement cannot be solely attributed to hormone therapy. Recently, growth hormone therapy has been explored in patients with PMS. In this patient, who had concomitant brain injury and required periodic endocrine evaluation, hormone deficiencies were identified and treated with continuous thyroid hormone and growth hormone replacement. Subsequent improvements in language developmental level were observed. We report this case to highlight the potential role of hormonal evaluation and replacement therapy in children with Phelan-McDermid syndrome and associated developmental delay.