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Case Report

Evolving pituitary abnormalities in a child with newly diagnosed ROHHAD syndrome

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ABSTRACT

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation and autonomic dysregulation (ROHHAD) is a rare pediatric disease with a high rate of morbidity and mortality. Most reported cases of ROHHAD demonstrate normal magnetic resonance imaging (MRI) findings despite hypothalamic-pituitary abnormalities; only a few describe interval structural changes. We describe a 17-month-old female with rapid-onset obesity, central hypothyroidism, and developmental delay who presented with polyuria and irritability. Laboratory evaluation confirmed central diabetes insipidus, and repeat MRI revealed loss of the posterior pituitary bright spot compared to a normal study five months earlier. She was treated with desmopressin and did not demonstrate any additional pituitary dysfunction. This case supports the need for close monitoring and follow up in children with suspicion of ROHHAD, as the clinical course has the potential to evolve quickly. Repeat imaging and hormonal evaluation are key in the early detection and management of disease progression. The evolving pituitary findings also suggest a possible autoimmune etiology of ROHHAD warranting further research into its pathogenesis and the need for biomarkers to assess disease progression.

Keywords: ROHHAD, Rapid-onset obesity, Hypothalamic dysfunction, Pituitary bright spot loss, Diabetes insipidus, Central hypothyroidism, Central sleep apnea

INTRODUCTION

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) in children consistently shows a core phenotype of previously healthy children, typically between 2 and 7 years of age, who develop rapid-onset obesity as the earliest and most consistent feature.[1] This is followed sequentially by hypothalamic dysfunction, including hyperprolactinemia, central hypothyroidism, diabetes insipidus, and other pituitary hormone deficiencies, followed by central hypoventilation, and finally autonomic dysregulation. Mortality in ROHHAD is high, underscoring the need for consistent surveillance and a multidisciplinary approach.[1] Despite significant hypothalamic involvement, most reported cases of ROHHAD demonstrate normal brain imaging throughout their disease course.[1] Anterior pituitary dysfunction has been well documented; whereas diabetes insipidus has been less consistently observed and typically occurs without structural pituitary abnormalities on magnetic resonance imaging (MRI).[2,3] Rare cases with rapid progression to encephalitis have been reported, including one with additional anti-ZSCAN1 antibodies.[4] However, evolving pituitary abnormalities are rarely described. We report a 17-month-old child with newly diagnosed ROHHAD who developed central hypothyroidism, diabetes insipidus, and loss of the posterior pituitary bright spot within 5 months of a normal baseline MRI, highlighting the importance of repeat imaging, endocrine surveillance, and consideration of autoimmune mechanisms.

CASE REPORT

The patient is a 17-month-old female who was born prematurely at 32 weeks. Her past medical history includes intrauterine cocaine and alcohol exposure, congenital syphilis, macrocephaly, macroglossia, lateralized overgrowth, central hypothyroidism, and developmental delay. At two months of age, the patient weighed less than the first percentile. She rapidly gained weight, reaching above the 90th percentile by 6 months. Presently, she is above the 99th percentile (26.4 kg at 17 months, length 86 cm, body mass index (BMI) corresponding with 184% of the 95th percentile). The patient was found to have elevated IGF-1, a normal sleep study (5/2025), and a normal MRI brain (4/2025). The patient was suspected to have Beckwith-Widemann syndrome; however, methylation studies were negative. Prader-Willi and Angelman syndrome were also ruled out.

On admission, the patient was nonverbal, had noisy breathing, and notable macrocephaly and macroglossia. The patient was able to sit without support and had normal female genitalia. Initial serum sodium was 154 mmol/l and serum osmolality was 314 mOsm/kg. Once admitted, the patient was placed on IV fluids and urine osmolality (166 mOsm/kg) and urine sodium (44 mEq/l) were obtained, prompting a water deprivation test. Water was held for four hours, and serum sodium rose from 153 mmol/l to 157 mmol/l with significant urine output, confirming diagnosis of diabetes insipidus. TSH was 0.09 (mIU/l) and free T4 was 0.91 ng/dl. We started levothyroxine 50 mcg daily, around 2 mcg/kg/day. During the hospitalization, an MRI of the pituitary was obtained that showed no bright spot present. A second sleep study was also obtained which supported a diagnosis of central sleep apnea with an overall AHI of 5.6 events/hour, 24 central apneas, and 1 obstructive apnea. Transcutaneous CO_2 ranged from 36-57 mmHg and exceeded 50 mmHg for 34.6% of her sleep time, and oxygen saturation remained stable SpO_2 ≥93%.

Given the patient's obesity, hypothalamic dysfunction, central hypoventilation, and autonomic changes, the patient met criteria for ROHHAD syndrome and was discharged with close outpatient follow up.

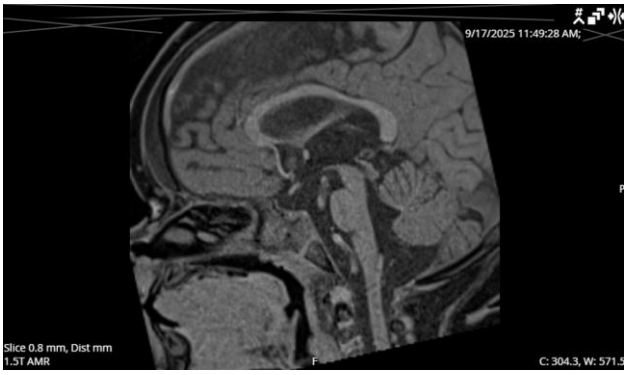

Figure 1: MRI from 17 September 2025 with absent posterior pituitary bright spot.

DISCUSSION

ROHHAD remains a challenging disorder to study and manage due to its rarity, phenotypic heterogeneity and the absence of definitive diagnostic markers. Despite wide variability, this syndrome most often presents in early childhood, beginning with rapid weight gain and followed by central hypoventilation, autonomic disturbances, and hypothalamic dysfunction. While neuroimaging findings are typically unremarkable, the present case illustrates loss of the posterior pituitary bright spot alongside central hypothyroidism and diabetes insipidus. These findings raise the possibility that structural pituitary changes may evolve dynamically in a subset of patients. Moreover, although most children are diagnosed between two and seven years of age (median four years), our case serves as an example that the full clinical phenotype may emerge earlier, emphasizing the importance of finding meaningful biomarkers to distinguish this disease.

To date, genetic studies have not identified germline or recurrent pathogenic variants, reinforcing the hypothesis that ROHHAD may follow a non-genetic, possibly autoimmune, pathogenesis.[5,6] Evidence supporting this includes reports of anti-hypothalamus, anti-pituitary, and anti-ZSCAN1 autoantibodies in affected patients, each associated with variable clinical presentations. Anti-ZSCAN1 has been linked particularly to patients with concurrent neuroblastic tumors, while anti-hypothalamus and anti-pituitary antibodies have been identified in patients with hypothalamic-pituitary dysfunction, suggesting that immune-mediated injury may contribute to evolving abnormalities such as those seen in this patient.[7] While these antibodies have been described, their role remains uncertain, and they have not yet been incorporated into clinical practice.[8,9]

Given the risk of rapid progression to life-threatening hypoventilation and cardiorespiratory arrest, longitudinal assessment including sleep studies and monitoring for signs and symptoms of pituitary dysfunction, is critical. Because diagnosis remains clinical, a high index of suspicion and a multi-disciplinary approach are essential. This case underscores that ROHHAD may present earlier and with evolving hypothalamic-pituitary abnormalities, challenging the traditional view that neuroimaging is unremarkable. Recognition of these changes highlights the importance of early suspicion, repeat imaging when indicated, and multidisciplinary management to improve outcomes in this high-risk population.

CONCLUSION

This case demonstrates that evolving pituitary abnormalities in ROHHAD may reflect an underlying autoimmune process, underscoring the importance of considering immune-mediated mechanisms and monitoring for treatable pituitary dysfunction in affected children. This case supports serial MRI imaging and proactive endocrine hormone screening in patients with

suspected ROHHAD. Further research is needed to clarify the mechanisms behind pituitary structural changes and their potential role in ROHHAD.

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