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Case Report

Secondary Hypopituitarism Due to a Pituitary Stalk Interruption: A Case Report

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Abstract

Pituitary stalk interruption syndrome is a rare malformation characterized by a triad of aplasia or hypoplasia of the anterior pituitary, a thin or absent pituitary stalk, and ectopic posterior pituitary observed on magnetic resonance imaging. It is a major cause of hypopituitarism, particularly growth hormone deficiency leading to growth retardation. The insidious progression of the disease explains why the diagnosis is often made in the late phase. We present the case of an 11-year-old child presenting with growth retardation, whose hormonal assessment revealed complete hypopituitarism. Magnetic resonance imaging showed interruption of the pituitary stalk with ectopic posterior pituitary and hypoplastic anterior pituitary. Through this case, we describe the clinical, biological presentation, and MRI findings of pituitary stalk interruption syndrome. We emphasize the need for early diagnosis of growth retardation and timely hormonal replacement therapy to improve prognosis.

Keywords: *Pituitary Stalk Interruption Syndrome (PSIS); Hypopituitarism; Growth Retardation; Ectopic Posterior Pituitary*

Introduction

Pituitary stalk interruption syndrome (PSIS) is a rare condition characterized by the presence of a thin or absent pituitary stalk, associated with hypoplasia or aplasia anterior pituitary and ectopic posterior pituitary (EPP) on magnetic resonance imaging (MRI) [1]. This can be associated with midline abnormalities and various pituitary endocrine deficiencies, ranging from isolated growth hormone deficiency to combined pituitary hormone deficiency [2]. The endocrine outcome appears to be a gradual onset of hormonal deficits leading to panhypopituitarism, but posterior pituitary function is usually preserved, though it may sometimes be disrupted depending on the position of the posterior pituitary [3]. During the neonatal period and early childhood, signs and symptoms of PSIS are often not evident, thus diagnosis is delayed. Early detection of hormonal deficiency and initiation of treatment can impact both the quality of life and prognosis of patients with PSIS. Therefore, diagnosis and management of this condition need improvement to help patients achieve a better quality of life and prevent reproductive health issues. Here, we evaluate the etiologies, genetic characteristics, clinical manifestations, diagnosis, and treatment of PSIS. Through this case, we emphasize the importance of enhancing diagnosis and initiating treatment promptly.

Case Report

An 11-year-old boy presented for evaluation of his short stature. History revealed no fetal distress, no neonatal incidents, no head trauma, or similar cases in the family. Clinical examination revealed a well-appearing child with stunted growth and delayed puberty: height at 102 cm (-3SD), weight at 18 kg (-3SD), with no signs of puberty, specifically Tanner stage I. There were no malformative syndromes.

Initial laboratory investigations showed no signs of malabsorption or parasitic infection. Hand X-ray revealed a bone age of 7 years. Hormonal analysis showed low follicle-stimulating hormone (FSH): 0.46 mU/ml (N = 1 - 10 mIU/ml) and luteinizing hormone (LH): 0.10 mIU/ml (N = 2 - 8 mIU/ml), elevated prolactin: 48.6 ng/dl (N = 2 - 15 ng/dl), undetectable testosterone: < 0.45 nmol/L (N = 10 - 35 nmol/L), growth hormone (GH) stimulation test (insulin): < 0.05 ng/ml (> 10 ng/ml), low morning cortisol: 2.4 µg/dl (N = 5 - 25 µg/dl), low thyroid-stimulating hormone (TSH): 0.04 µIU/ml (N = 0.4 - 5.0 µIU/ml), and low free thyroxine (FT4): 3.06 µg/dl (N = 5 - 12 µg/dl). This constituted a complete hypopituitarism. Hypothalamic-pituitary MRI (Figure 1) in frontal and sagittal sections showed a hypoplasia anterior pituitary gland with an absent pituitary stalk. The posterior pituitary was ectopically located high within the infundibulum, with a normal signal on MRI. This triad of symptoms was indicative of PSIS. Substitutive hormone therapy with hydrocortisone, thyroxine, and growth hormone (GH) was initiated, followed by androgen replacement therapy. The patient will be regularly monitored for clinical and biochemical evaluation.

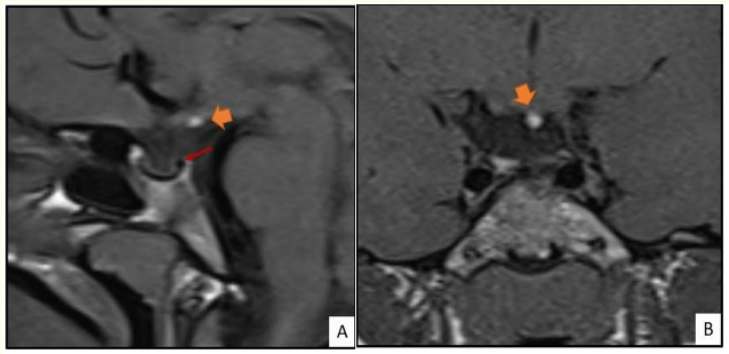

Figure 1: *Sagittal (A) and coronal (B) sections of a hypothalamic-pituitary MRI in T1-weighted sequence showing an ectopic posterior pituitary at the level of the infundibulum (Orange arrow), a non-visualized pituitary stalk, and a hypoplasia anterior pituitary (Red arrow).*

Discussion and Conclusion

Pituitary stalk interruption syndrome was first described in 1987 by Fujisawa., *et al*. [4], with an incidence of 0.5 per 100,000 births [5]. It is a rare congenital anatomical anomaly of the pituitary gland, characterized by a triad visualized on MRI including a thin or non-visible pituitary stalk, anterior pituitary hypoplasia, and ectopic posterior pituitary [4]. Diagnosis is confirmed by clinical features, results of endocrine evaluation, and contrast-enhanced MRI findings, which is the technique used to assess the shape, size, and microstructure of the pituitary gland in PSIS patients [6]. PSIS shows a male predominance, suggesting X-linked inheritance. The average age at diagnosis is 9.4 ± 11.6 years with no effect of neonatal distress and breech delivery on the age of presentation [3].

The etiology of PSIS is not well understood. The proposed pathophysiological mechanism of PSIS is a mutation in genes encoding transcription factors involved in anterior pituitary ontogenesis, with the most commonly implicated genes being PROP1 [7], POU1F1, HESX1 [8], LHX3, and LHX4. Additionally, the presentation of breech position during delivery and perinatal asphyxia can damage the pituitary stalk [9].

However, typical characteristics include permanent deficiencies in anterior pituitary hormones during childhood, which gradually manifest and evolve into panhypopituitarism in adulthood. In a large Chinese study involving 55 patients, short stature was observed in 85.5% of patients with a delayed bone age of 7.26 ± 5.37 years. The prevalence of different hormonal deficiencies was 100% for growth

hormone (GH), 95.8% for gonadotropins, 81.8% for adrenocorticotropic hormone (ACTH), and 76.3% for thyroid-stimulating hormone (TSH). Hyperprolactinemia was found in 36.4% of cases. More than two deficiencies in anterior pituitary hormones were observed in 92.7% of cases [10].

The anterior pituitary's ability to respond to stimulation tests using hypothalamic releasing hormones depends on the cause of PSIS, pituitary volume, and age at presentation [3]. Neonatal diagnosis is often established in cases of severe hypoglycemia, with or without a malformative syndrome [11]. In older children, the presentation is either a slowing of growth velocity or, more rarely, diabetes insipidus. The insidious and well-tolerated clinical picture with progressive endocrine involvement necessitates regular monitoring, especially considering that over time, the deficits become severe and multiple. In our patient, a long diagnostic delay led to severe statural retardation. This delay was exacerbated by poor socio-economic and cultural conditions and the absence of acute symptoms.

MRI of the pituitary gland is key to diagnosis. It involves thin sagittal and coronal slices (≤ 3 mm), centered on the hypothalamic-pituitary axis in T1-weighted sequences, supplemented by a T2-weighted sequence and gadolinium injection [12]. In Yang's study [13], magnetic resonance imaging (MRI) revealed the triad of the absent pituitary stalk (98.3%), hypoplasia anterior pituitary (98.3%), and ectopic posterior pituitary (91.4%). Ectopic neurohypophysis was frequently observed in the infundibular recess (60.4%) and the hypothalamus (18.9%). The localization of the ectopic posterior pituitary has functional prognostic significance, with a greater number of deficiencies in anterior pituitary hormones when the posterior pituitary is located at the median eminence or hypothalamic region [14]. The entire brain should be explored to rule out associated malformations such as Chiari I malformation or basipharyngeal canal.

Treatment relied on hormone replacement therapy with lifelong polyhormonal replacement therapy. Early detection of hormonal deficiency and initiation of treatment impact both the quality of life and prognosis of patients with PSIS [15,16]. The patient lacked adrenaline, thyroxine, gonadal steroids, and growth hormone. Glucocorticoid replacement was the initial treatment, followed by Euthyrox, androgens, and human chorionic gonadotropin. Calcium tablets, calcitriol, and alendronate sodium were used to treat osteoporosis.

In conclusion, pituitary stalk interruption syndrome is a rare disease with poorly understood etiology. It represents a cause of hypopituitarism, particularly affecting growth hormone secretion, which plays a crucial role during the growth period. However, various other hormones can also impact growth.

The insidious progression of the disease and the good tolerance of its manifestations explain the cases that are diagnosed late, often associated with a more severe prognosis. Therefore, understanding PSIS in clinical practice, especially through diagnosis via MRI, and prompt treatment in newborns or children, should be improved. This way, negative effects on long-term growth and development can be avoided.

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