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Case Report

Pituitary Stalk Interruption Syndrome- A Rare Case Report

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Introduction

Pituitary stalk interruption syndrome (PSIS) is a rare, congenital pituitary anatomical defect with varying clinical and radiographic presentations. It is defined by the triad of thin or interrupted pituitary stalk, hypoplastic or aplastic anterior lobe and absent or ectopic posterior lobe [1].

PSIS is characterized by a spectrum of clinical manifestations resulting from deficiencies in one or more anterior pituitary hormones. The most frequently observed features include growth retardation and hypogonadism, although additional endocrine abnormalities such as central hypothyroidism may be present, depending on the nature and severity of the hormonal deficits [4].

There are no reported cases with PSIP in Sri Lanka which were diagnosed in adulthood. We present a 38-year-old male who presented with clinical features of multiple anterior pituitary hormone deficiencies and was later diagnosed to have PSIS via Magnetic Resonance Imaging (MRI) of the brain and the pituitary.

Case History

A 38-year-old male presented with generalized body weakness, lethargy and dizziness with worsening symptoms over 2 months. He also complained of cold intolerance and dry skin.

He was born to non-consanguineous parents at term. He was diagnosed with neonatal meningitis soon after birth and managed with antibiotics for 2 weeks. He was further followed up at a tertiary care center due to growth faltering and a seizure disorder but lost the follow up after 2 years. At the age of 16, he was evaluated for delayed puberty and was found to have testosterone deficiency. However, he declined hormone replacement therapy and was subsequently lost to follow-up.

In the current presentation, his blood pressure was 90/60 with a significant postural drop. On general examination his height and weight were 163cm (mid parental height-160.5cm) and 45kg, respectively. BMI was 16.93kg/m^2. The body upper to lower segment ratio was 0.78. There was a lack of secondary sexual characteristics (Tanner stage 1) with empty scrotal sac suggestive of undescended testes. The skin was thin and dry. There was no hyper pigmentation. Cardiovascular, Respiratory and neurology examinations were normal. There was no visual field defect. There was no polyuria or polydipsia.

Biochemical investigations (Table 1) revealed all four anterior pituitary axes deficiencies with normal prolactin levels.

Ultrasound scan of the scrotum showed bilaterally atrophic cord testes. Subsequently, MRI of the pituitary confirmed the diagnosis of Pituitary Stalk Interruption syndrome. (Figure 1).

Table 1: Summary of Laboratory Test Results

Laboratory Parameters (Serum)	Results	Reference Range
Follicular Stimulating Hormone	●.9 mIU/mL	1.6-9.7 mIU/mL
Luteinizing Hormone	●.2 IU/L	1.8-8.6 IU/L
9amTestosterone	●.26 nmol/L	4.6-28.● nmol/L
9am Cortisol	19.7 nmol/L	2●0-6●0 nmol/L
Insulin like Growth Factor-1	4●.52 ng/mL	6●-35● ng/mL
Thyroid stimulating Hormone	3.577 micro-IU/mL	●.38●-4.31 µIU/mL
Free T4	●.58 ng/dL	●.82-1.63 ng/dL
Prolactin	357 microgram/L	<425 µgram/L
Sodium	136 mmol/L	136-145 mmol/L
Potassium	4.2 mmol/L	3.5-5.2 mmol/L
Corrected calcium level	1●.1mg/dL	(8.5-1●.2mg/dL)

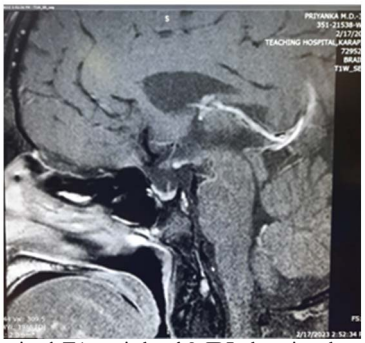

Figure 1: Sagittal T1-weighted MRI showing hypoplastic pituitary stalk, ectopic posterior pituitary bright spot at the median eminence, and hypoplastic anterior pituitary in the Sella.

Upon the diagnosis, the patient promptly started on hormone replacement therapy, including hydrocortisone, levothyroxine, and testosterone, which resulted in marked clinical improvement. Additionally, he was referred to the surgical team for the removal of bilateral atrophic testes.

Discussion

PSIS was first reported by Fujisawa et al. in 1987[3]. The exact prevalence of PSIS is uncertain, and data is lacking in literature globally. In a retrospective study done in 2013 on 55 patients with PSIS who came from different parts of China in a 10-year period, accounted for 21.9% of hospitalized hypopituitary patients diagnosed in the center during the same period. The ratio of male to female was 6.9:1. The average age was 19.7±6.7 years (range, 9 to 43 years) [6]. The only case report available in Sri Lankan literature was of a 16-year-old girl who was evaluated for short stature, reported in 2015[2]. Uniquely, our patient presented at the age of 38, with delayed puberty noted earlier but not adequately followed up. This highlights the importance of early endocrine evaluation in cases of growth failure and delayed puberty to avoid missed or late diagnoses such as PSIS.

The etiology of Pituitary Stalk Interruption Syndrome (PSIS) remains incompletely understood, with genetic factors implicated in only a subset of cases. Emerging evidence points to a complex multigenic origin, as whole exome sequencing has identified pathogenic variants in several genes critical to pituitary development, including BMP4, GLI2, and HESX1 [4,10]. Additionally, mutations in ROBO1, a gene associated with axonal guidance and ocular anomalies, have also been reported in PSIS, suggesting a broader developmental disruption that may contribute to the syndrome's pathogenesis [11].

PSIS can present with anterior pituitary hormone deficiencies (growth hormone, 100%; gonadotropin, 97.2%; corticotropin, 88.2%; and thyrotropin, 70.3%); however, hyperprolactinemia (6.9%) due to lack of dopaminergic inhibition can be seen. Posterior pituitary function is usually considered normal. however, in rare cases some degree of posterior pituitary dysfunction may occur depending on degree of stalk interruption and location of ectopic posterior pituitary. The anterior pituitary hormone deficiencies can present as hypoglycemia, hypothyroidism, neonatal jaundice, short stature, cryptorchidism, delayed puberty and features of adrenal insufficiency [4]. In our patient, the main presenting complaint, generalized body weakness, lethargy, and dizziness, could be explained by both cortisol deficiency and central hypothyroidism, which was further confirmed biochemically. The appearance of these symptoms in the fourth decade of life shows the diversity of phenotypic presentation of this syndrome. Although IGF-1 levels were found to be low, dynamic testing with ITT or GST to confirm the integrity of the growth hormone axis was not pursued; it is noteworthy that cases of PSIS with normal height have been reported in the literature [9]. Poor development of the secondary sexual characteristics and cryptorchidism in our patient shows the congenital nature of the illness but also proves the diversity of different hormone deficiencies with this illness during the lifetime. Prolactin (PRL) levels have shown a considerable degree of heterogeneity. It can be deficient, or on the opposite hyperprolactinemia can be seen, from 17% to one-third of patients. It varies depending on the severity of dopaminergic pathway disconnection [5].

Early diagnosis of PSIS through imaging is crucial, in terms of timely intervention for improved patient outcomes; however, it is challenging due to its rare nature and nonspecific symptoms [7]. MRI variations in pituitary stalk interruption syndrome include absent or ectopic posterior pituitary, interrupted pituitary stalk, and anterior pituitary hypoplasia. Additional anomalies like ophthalmic disorders may also be present [8].

Prompt and appropriate hormone replacement is the cornerstone of treatment for PSIS. The management plan for our patient was decided in accordance with multi-disciplinary team decisions as well as the patient's wishes. The patient showed a dramatic response to multiple hormone replacement therapies in terms of functional improvement. The patient's Adult Growth Hormone Deficiency Assessment (AGHDA) score was 5 out of 25, indicating a low symptom burden and rendering him ineligible for growth hormone replacement therapy [12].

Conclusion

PSIS is a rare but significant cause of anterior pituitary hormones deficiency in adults. Timely diagnosis can be obtained with a high degree of suspicion for this illness. Hormone replacement following early diagnosis will gain significant favorable outcomes for the patients. Given the rarity of adult-onset PSIS and the lack of previous adult cases in Sri Lanka, this case serves as an important reminder for clinicians to maintain a high index of suspicion for this rare syndrome.

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