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Case report

PITUITARY STALK INTERRUPTION SYNDROME PRESENTING WITH NEONATAL HYPOGLYCEMIA AND MICROPENIS: A CASE REPORT

Article History:

Name of Author:
Dr. Naga dakshata malepati[1], Dr. Meenakshi BR[2], Dr. Shreya patted[3].

Affiliation: [1]Junior Resident & Post Graduate, ,Dept of paediatrics
Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital & Medical Research Center,Belagavi.
[2]Assistant Professor and division of paediatric endocrinology,
Dept of paediatrics
Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital & Medical Research Center, Belagavi.
[3]Senior resident ,Dept of paediatrics
Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital & Medical Research Center,
Belagavi.

Corresponding Author:
Dr. Naga dakshata malepati

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Abstract:
Background: Pituitary Stalk Interruption Syndrome (PSIS) is a rare congenital anomaly of the hypothalamic–pituitary axis characterized by the classic radiological triad of an absent or hypoplastic anterior pituitary gland, interrupted or thin pituitary stalk, and an ectopic posterior pituitary. It commonly presents with varying degrees of pituitary hormone deficiencies and may manifest during the neonatal period with severe metabolic and endocrine disturbances. ***Case Presentation****:* A case of a full-term male neonate born to a non-consanguineous couple who presented on the second day of life with vomiting and severe hypoglycemia. Critical sampling during hypoglycemia revealed low serum cortisol and growth hormone levels with undetectable insulin. On clinical examination, the infant was noted to have micropenis and bilateral undescended testes. Further endocrine evaluation demonstrated low free thyroxine with inappropriately low thyroid-stimulating hormone, suggesting combined pituitary hormone deficiency. Magnetic resonance imaging of the brain revealed absence of the anterior pituitary gland and pituitary stalk with an ectopic posterior pituitary, confirming the diagnosis of Pituitary Stalk Interruption Syndrome. The infant was initiated on glucocorticoid and levothyroxine replacement therapy. During the physiological minipuberty period, gonadotropin therapy with purified follicle-stimulating hormone and human chorionic gonadotropin was administered, resulting in descent of both testes and improvement in penile length. The patient is currently under regular endocrinological follow-up with plans for testosterone and growth hormone therapy. **Conclusion:** Early recognition of neonatal hypoglycemia associated with genital abnormalities is essential for timely diagnosis of PSIS. Prompt hormone replacement therapy can significantly improve outcomes and prevent life-threatening complications associated with combined pituitary hormone deficiency.

Keywords: Pituitary Stalk Interruption Syndrome; Congenital Hypopituitarism; Combined Pituitary Hormone Deficiency; Neonatal Hypoglycemia; Micropenis; Cryptorchidism; Ectopic Posterior Pituitary; Magnetic Resonance Imaging; Hormone Replacement Therapy; Neonatal Endocrine Disorders.

INTRODUCTION

Pituitary stalk interruption syndrome (PSIS) is a rare congenital abnormality of the hypothalamic–pituitary axis characterized by structural defects of the pituitary gland and its connecting stalk. The condition is classically defined by a radiological triad consisting of an absent or ectopic posterior pituitary lobe, a thin or interrupted pituitary stalk, and a hypoplastic or aplastic anterior pituitary gland (1). These anatomical abnormalities result in varying degrees of pituitary hormone deficiencies, most commonly presenting as combined pituitary hormone deficiency (CPHD). Magnetic resonance imaging (MRI) is the imaging modality of choice for confirming the diagnosis, as it allows clear visualization of pituitary anatomy and associated midline brain abnormalities (2).

PSIS is considered an uncommon disorder, with an estimated incidence of approximately 0.5 per 100,000 live births. The condition predominantly affects males and may present at different stages of life depending on the severity and number of hormonal deficiencies (3). In many cases, the clinical manifestations appear gradually, which may delay diagnosis until childhood or adolescence when growth failure becomes evident. However, in some neonates and infants, PSIS may present early with life-threatening endocrine abnormalities such as recurrent hypoglycemia or adrenal insufficiency (4).

The clinical manifestations of PSIS are largely determined by the deficiency of hormones secreted by the anterior pituitary gland. Growth hormone deficiency is the most common hormonal abnormality and may lead to growth retardation, poor weight gain, and failure to thrive during infancy and childhood (5). Deficiencies of other pituitary hormones such as adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) may also occur, resulting in secondary adrenal insufficiency, central hypothyroidism, and hypogonadotropic hypogonadism respectively (6). In male neonates, gonadotropin deficiency may present as micropenis and cryptorchidism due to impaired testosterone production during fetal life and early infancy (7).

Neonatal hypoglycemia is one of the most important early clinical indicators of congenital hypopituitarism and may be the first sign of PSIS. Hypoglycemia occurs primarily due to growth hormone and cortisol deficiency, both of which play crucial roles in maintaining glucose homeostasis (8). Additional neonatal manifestations may include prolonged jaundice, poor feeding, lethargy, and temperature instability. Because these symptoms are often nonspecific, early diagnosis may be challenging, and the condition may remain unrecognized unless detailed endocrine evaluation is performed (9).

The exact etiology of PSIS remains incompletely understood. Several hypotheses have been proposed, including genetic mutations affecting pituitary development as well as perinatal insults that disrupt the hypothalamic–pituitary axis. Mutations in transcription factors such as LHX4, PROP1, and POU1F1 have been identified in a subset of patients with congenital hypopituitarism (10). These genes play an important role in the embryological development and differentiation of pituitary cells. In addition to genetic factors, environmental or perinatal events such as birth trauma, perinatal hypoxia, breech delivery, and maternal diabetes have also been implicated as possible contributing factors (11).

Early recognition and prompt initiation of hormone replacement therapy are crucial for preventing serious complications associated with PSIS (12). Lifelong endocrine management is typically required and may include glucocorticoid replacement for adrenal insufficiency, levothyroxine for central hypothyroidism, growth hormone therapy for growth failure, and sex hormone replacement during puberty. With timely diagnosis and appropriate treatment, many patients can achieve near-normal growth, development, and quality of life (13).

Given the rarity of the condition and its variable clinical presentation, awareness among clinicians is essential to facilitate early diagnosis. Reporting such cases contributes to a better understanding of the clinical spectrum of PSIS and highlights the importance of considering congenital hypopituitarism in neonates presenting with unexplained hypoglycemia and genital abnormalities (14).

CLINICAL DESCRIPTION

CASE PRESENTATION

Patient Information

A full-term male neonate was born to a non-consanguineous couple following an uncomplicated pregnancy and delivery. The antenatal period was uneventful with no history of maternal illness, drug intake, gestational diabetes, or exposure to teratogens. The baby was delivered at term by normal vaginal delivery and cried immediately after birth. Birth weight and other anthropometric measurements were appropriate for gestational age. The immediate postnatal adaptation was normal and the infant was initially stable during the first 24 hours of life.

Early Clinical Presentation

On the second day of life, the neonate developed repeated episodes of vomiting associated with lethargy and poor feeding. Bedside blood glucose monitoring revealed severe hypoglycemia with a blood glucose level of 24 mg/dL. In view of symptomatic hypoglycemia, the infant was immediately managed with intravenous glucose infusion and admitted to the Neonatal Intensive Care Unit (NICU) for further evaluation and monitoring.

Given the severity and persistence of hypoglycemia, a critical blood sample was obtained during the

hypoglycemic episode to evaluate the underlying etiology. Laboratory investigations revealed markedly low serum cortisol and growth hormone levels, with undetectable insulin levels, indicating that the hypoglycemia was not due to hyperinsulinism. These findings raised suspicion of an underlying endocrine disorder involving the hypothalamic–pituitary axis.

Physical Examination

A detailed clinical examination was performed to identify possible congenital anomalies or endocrine manifestations. On focused examination of the external genitalia, the neonate was noted to have micropenis and bilateral undescended testes (Fig 1). These findings suggested possible gonadotropin deficiency. No dysmorphic facial features, craniofacial abnormalities, midline defects, or skeletal anomalies were observed. Examination of the cardiovascular, respiratory, abdominal, and neurological systems did not reveal any abnormalities. The presence of recurrent hypoglycemia together with genital abnormalities raised the possibility of congenital hypopituitarism or combined pituitary hormone deficiency.

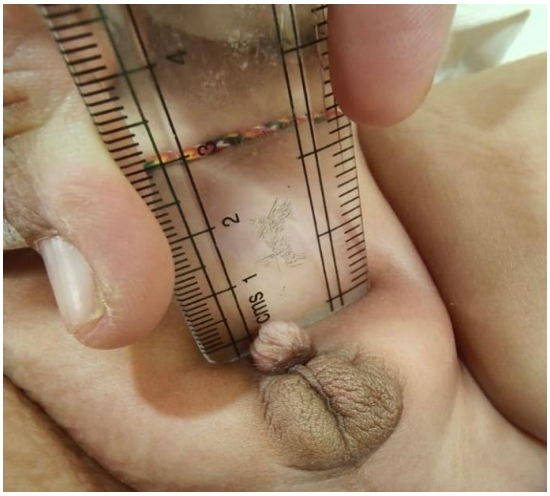

Figure 1: Clinical Photograph Showing Micropenis in a Neonate

Endocrine Evaluation

Further hormonal investigations were performed to evaluate pituitary function comprehensively. Thyroid function testing demonstrated low free thyroxine (FT4) levels with inappropriately low thyroid-stimulating hormone (TSH), consistent with central hypothyroidism. The coexistence of cortisol deficiency, growth hormone deficiency, and central hypothyroidism strongly suggested combined pituitary hormone deficiency (CPHD).

Given the biochemical evidence of multiple pituitary hormone deficiencies, structural abnormalities of the hypothalamic–pituitary axis were suspected.

Neuroimaging Findings

Magnetic resonance imaging (MRI) of the brain with a dedicated pituitary protocol was performed to evaluate the pituitary gland and surrounding structures. MRI revealed absence of the anterior pituitary gland along with absence of the pituitary stalk (infundibulum). In addition, an ectopic posterior pituitary bright spot was identified along the median eminence. These radiological findings are characteristic of Pituitary Stalk Interruption Syndrome (PSIS), confirming the structural basis for the patient's endocrine abnormalities (Fig 2).

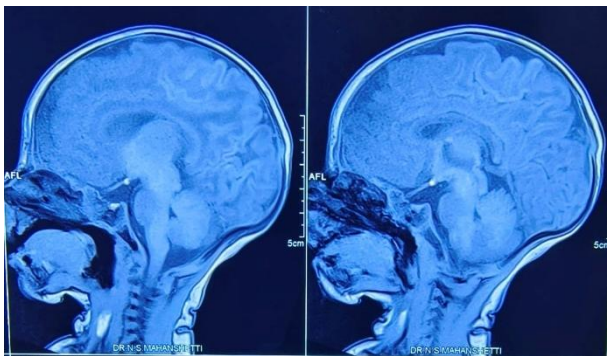

Figure 2: Sagittal MRI of the Brain Demonstrating Pituitary Stalk Interruption Syndrome with Ectopic Posterior Pituitary and Absent Pituitary Stalk

Management and Outcome

Initial Hormonal Replacement

Following confirmation of the diagnosis, prompt hormone replacement therapy was initiated to correct the underlying endocrine deficiencies and prevent potential life-threatening complications. Glucocorticoid replacement therapy was started first using hydrocortisone at a dose of 10 mcg/m²/day to manage secondary adrenal insufficiency and reduce the risk of adrenal crisis. Initiation of steroid therapy prior to thyroid hormone replacement was essential to avoid precipitating an adrenal crisis.

After stabilization and initiation of glucocorticoid therapy, levothyroxine replacement was commenced at a dose of 50 mcg/m²/day to treat central hypothyroidism. The dosage was gradually titrated based on regular monitoring of thyroid hormone levels and clinical response.

Evaluation During Minipuberty

At the age of three months, the infant was reassessed during the physiological "minipuberty" period of infancy, a phase characterized by transient activation of the hypothalamic–pituitary–gonadal axis. Hormonal evaluation during this period confirmed hypogonadotropic hypogonadism. To stimulate

testicular development and improve genital growth, the child was started on minipuberty replacement therapy using purified follicle-stimulating hormone (FSH) and human chorionic gonadotropin (hCG).

Clinical Response to Therapy

Following hormonal therapy, significant clinical improvement was observed. Both testes descended into the scrotal sacs, indicating effective stimulation of gonadal function. Testicular volume increased to 0.4 cm^3 on the right side and 0.39 cm^3 on the left side. In addition, penile length increased to 1.8 cm, reflecting a positive response to gonadotropin therapy.
The infant continued to tolerate hormone replacement therapy well, with no major complications reported during follow-up.

Long-Term Management Plan

The child remains under regular follow-up with the pediatric endocrinology team for ongoing monitoring and management. The future treatment plan includes administration of testosterone enanthate to further improve penile growth and genital development. Growth hormone therapy will be initiated at a later stage to support normal linear growth and optimize developmental outcomes.
Early recognition of the condition and timely initiation of appropriate hormone replacement therapy have played a crucial role in stabilizing the patient and improving the overall prognosis. Continuous long-term endocrine follow-up will be essential for monitoring growth, development, and the emergence of additional hormone deficiencies that may occur over time in patients with Pituitary Stalk Interruption Syndrome.

DISCUSSION

Pituitary Stalk Interruption Syndrome (PSIS) is an uncommon congenital disorder of the hypothalamic–pituitary axis characterized by structural abnormalities of the pituitary gland and varying degrees of pituitary hormone deficiency. The classical radiological triad consists of an absent or hypoplastic anterior pituitary gland, a thin or absent pituitary stalk, and an ectopic posterior pituitary, which can be reliably identified on magnetic resonance imaging (MRI). Early diagnosis is essential because the disorder may present with life-threatening endocrine deficiencies in the neonatal period. The present case highlights the importance of recognizing neonatal hypoglycemia associated with genital abnormalities as an early indicator of congenital hypopituitarism.

Lichiardopol and Albulescu (2017) described PSIS as a rare congenital condition with highly variable clinical presentation depending on the number and severity of pituitary hormone deficiencies (1). Their report emphasized that most patients demonstrate combined pituitary hormone deficiency (CPHD), particularly involving growth hormone, adrenocorticotropic hormone, and thyroid-stimulating hormone. Similar endocrine abnormalities were observed in the present case, where biochemical evaluation revealed deficiency of cortisol, growth hormone, and thyroid hormones, supporting the diagnosis of CPHD.

The role of MRI in confirming the diagnosis of PSIS has been widely recognized. Sabsabee et al. (2025) highlighted that MRI with dedicated pituitary protocol is the imaging modality of choice for evaluating structural abnormalities of the hypothalamic–pituitary region in children presenting with endocrine dysfunction (2). The imaging findings in our patient, including absence of the anterior pituitary gland and pituitary stalk along with an ectopic posterior pituitary bright spot, correspond closely with the classical imaging features described in previous studies.

Several reports have documented that PSIS may present during infancy or childhood with growth failure; however, neonatal presentation with metabolic disturbances is less common. Prusty et al. (2025) described a case series in which the majority of patients were diagnosed later in childhood due to short stature and delayed puberty (3). In contrast, our patient presented early in the neonatal period with severe hypoglycemia, emphasizing that early manifestations may occur when deficiencies of cortisol and growth hormone are profound.

Neonatal hypoglycemia is a well-recognized manifestation of congenital hypopituitarism. Rosenfeld and Thornton (2023) reported that deficiencies of growth hormone and cortisol impair glucose homeostasis, leading to recurrent hypoglycemia in neonates and infants (8). In the present case, critical sampling during hypoglycemia demonstrated low cortisol and growth hormone levels with undetectable insulin, supporting a hormonal rather than hyperinsulinemic etiology.

Genital abnormalities such as micropenis and cryptorchidism are important clinical clues suggesting gonadotropin deficiency in male neonates. Rodprasert et al. (2020) explained that inadequate secretion of luteinizing hormone and follicle-stimulating hormone during fetal life may lead to impaired testosterone production and incomplete testicular descent (7). The presence of micropenis and bilateral undescended testes in our patient further supported the diagnosis of hypogonadotropic hypogonadism associated with PSIS.

The etiology of PSIS remains uncertain, with both

genetic and perinatal factors being implicated. Wang et al. (2024) reported that mutations in genes involved in pituitary development may contribute to the pathogenesis of the disorder (10). Additionally, perinatal insults such as hypoxia have been proposed as possible contributing factors affecting hypothalamic–pituitary development (11). However, in the present case, no history of perinatal complications was identified.

Early initiation of hormone replacement therapy is essential to prevent life-threatening complications. Gounden et al. (2023) emphasized that glucocorticoid replacement should be started before thyroid hormone therapy in patients with hypopituitarism to avoid precipitating adrenal crisis (6). In our patient, hydrocortisone therapy was initiated prior to levothyroxine, which resulted in stabilization of metabolic status.

Recent studies have also highlighted the importance of early endocrine management in newborns with PSIS. Winkler et al. (2025) reported that prompt hormone replacement therapy significantly improves survival and long-term outcomes (14). Similarly, Salvat and Sevilla (2024) described successful management of PSIS presenting with panhypopituitarism following early hormonal treatment (12).

Overall, the present case reinforces the importance of considering congenital hypopituitarism in neonates presenting with unexplained hypoglycemia, particularly when associated with genital abnormalities. Early diagnosis using hormonal evaluation and MRI, followed by timely initiation of hormone replacement therapy, plays a crucial role in improving clinical outcomes and preventing serious complications associated with PSIS.

CONCLUSION

Pituitary Stalk Interruption Syndrome is a rare congenital disorder of the hypothalamic–pituitary axis that can lead to multiple pituitary hormone deficiencies. Early clinical manifestations during the neonatal period may include persistent hypoglycemia, micropenis, cryptorchidism, prolonged jaundice, and feeding difficulties. Recognition of these early warning signs is essential, as delayed diagnosis may result in life-threatening complications such as adrenal crisis, recurrent hypoglycemia, and impaired growth and neurodevelopment. Magnetic resonance imaging plays a crucial role in confirming the diagnosis by demonstrating the classical triad of absent or hypoplastic anterior pituitary gland, interrupted pituitary stalk, and ectopic posterior pituitary. Prompt endocrine evaluation and early initiation of hormone replacement therapy significantly improve clinical outcomes and long-term prognosis. Lifelong follow-up with regular endocrine monitoring is essential to manage evolving hormonal deficiencies. Early identification and timely treatment can ensure optimal growth, development, and quality of life in affected children.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given consent for images and other clinical information to be reported in the journal. The guardian understands that name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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