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Case Series

Radiology Section

Pituitary Stalk Interruption Syndrome: A Case Series Highlighting the Diagnostic Utility of MRI

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ABSTRACT

Pituitary Stalk Interruption Syndrome (PSIS) is a rare congenital anomaly characterised by an interrupted or thin pituitary stalk, hypoplasia of the anterior pituitary and an absent or Ectopic Posterior Pituitary (EPP). Clinically, this condition manifests as pituitary gland dysfunction, which may include Growth Hormone Deficiency (GHD), global pituitary insufficiency and developmental delay. Early diagnosis is crucial, as delayed recognition can result in suboptimal growth outcomes. Magnetic Resonance Imaging (MRI) of the brain plays a pivotal role in identifying pituitary gland abnormalities associated with PSIS. The present case series describes five patients (3 males, 2 females) and highlights the importance of brain MRI in diagnosing PSIS, emphasising the significance of early intervention to optimise patient outcomes. Early diagnosis and initiation of hormone replacement therapy are essential in improving clinical outcomes.

Keywords: Anterior pituitary, Developmental delay, Growth hormone, Hypoplasia, Magnetic resonance imaging, Pituitary gland dysfunction

INTRODUCTION

Pituitary Stalk Interruption Syndrome (PSIS) is a rare congenital anomaly of the pituitary gland. It is characterised by a classic MRI triad that includes an interrupted or thin pituitary stalk, hypoplasia of the anterior pituitary and an ectopic or absent posterior pituitary gland [1]. This syndrome is an important cause of hypopituitarism and can result in growth failure, delayed puberty, infertility, adrenal insufficiency and hypothyroidism [2,3].

The PSIS is one of the causes of Growth Hormone Deficiency (GHD), which may occur in isolation or as part of a broader spectrum of hypopituitarism. Early clinical diagnosis of GHD is often challenging. In such cases, MRI serves as a crucial imaging modality, enabling detailed evaluation of abnormalities in the hypothalamic–pituitary axis. It is particularly valuable in differentiating isolated GHD from Multiple Pituitary Hormone Deficiency (MPHD), as imaging features such as an interrupted or absent pituitary stalk and the presence of an EPP are associated with a higher risk of MPHD [3,4].

It has been reported that a visible but thin or truncated stalk often corresponds to isolated GHD, whereas complete absence of the stalk is strongly associated with MPHD. Additionally, the presence of an EPP in the infundibular recess supports the diagnosis of PSIS and correlates with the severity of hormonal deficits [5]. Delayed diagnosis and treatment can adversely affect growth and gonadal development and may lead to metabolic complications such as dyslipidaemia and non alcoholic steatohepatitis [6].

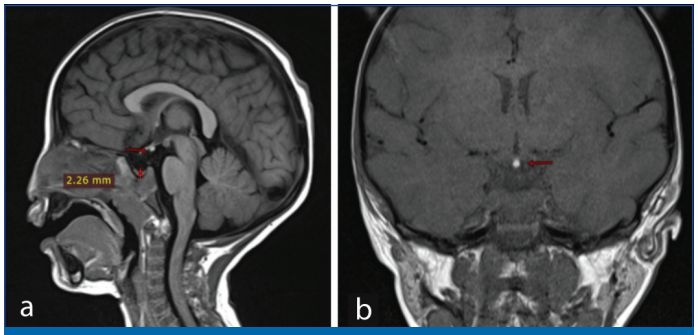
CASE SERIES

Case 1

A three-year-old boy presented with two episodes of generalised seizures over the previous year. There was no relevant family history and the child was appropriately immunised. The birth history was unremarkable, with a full-term vaginal delivery, a birth weight of 2.75 kg, immediate crying at birth and no admission to the Neonatal Intensive Care Unit (NICU). Developmental milestones were appropriate for age.

Clinical evaluation revealed severe growth retardation, with weight below 4 Standard Deviations (SD) and height below 6 SD. Micropenis was also noted. A subsequent seizure episode was associated with hypoglycaemia. Hormonal assessment demonstrated reduced levels of Growth Hormone (GH) (5 ng/mL), cortisol (84.2 nmol/L) and Thyroid-Stimulating Hormone (TSH) (14 mIU/L), consistent with multiple pituitary hormone deficiency.

The MRI of the sella turcica using a pituitary protocol revealed classic features of PSIS, including a hypoplastic anterior pituitary measuring 2.2 mm in height [Table/Fig-1a], an absent pituitary stalk [Table/Fig-1a] and an ectopic posterior pituitary located at the median eminence of the hypothalamus [Table/Fig-1a,b].



[Table/Fig-1]: a) MRI brain in sagittal T1 section reveals hypoplastic anterior pituitary (measuring 2.2 mm) with absent stalk. b) Bright spot of posterior pituitary is ectopic as indicated by rad arrow in sagittal (1a) and coronal (1b) section of brain on T1 image.

Following the diagnosis of PSIS, hormone replacement therapy was initiated with thyroxine (75 µg), hydrocortisone (14 mg daily) and recombinant GH (0.19 mg/kg/week). The patient currently demonstrates a growth velocity of 8.3 cm/year, with a mid-parental height of 168 cm and is responding well to therapy.

Based on these findings, the patient was diagnosed with PSIS associated with MPHD.

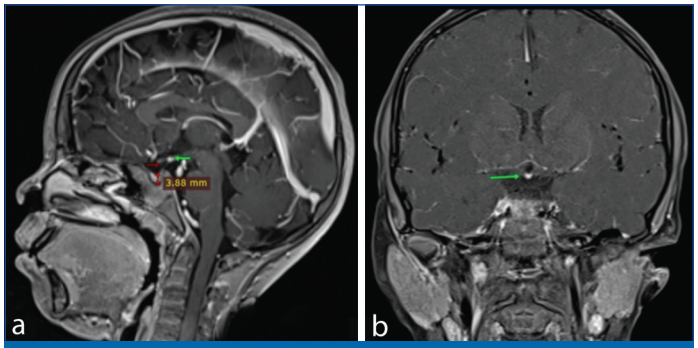
Case 2

A ten year old girl with progressive failure to gain height over the past three years. She was born preterm via lower segment caesarean section and required NICU admission for perinatal asphyxia. She was noted to be small for gestational age.

Physical examination revealed a bone age of 5.5 years, with height age corresponding to five years, indicating significant growth delay. The

upper-to-lower segment ratio was 0.91 and weight was 21 kg (-3 SD). Hormonal evaluation showed low GH levels on clonidine stimulation testing and serum insulin-like growth factor 1 (IGF-1) was 40.8 ng/mL (reference range: 125-541 ng/mL). She also had hypothyroidism (TSH 7 mIU/L) with negative antithyroid peroxidase antibodies.

Contrast-enhanced (CE) MRI of the brain demonstrated findings consistent with PSIS, including an absent pituitary stalk, hypoplastic anterior pituitary [Table/Fig-2a] and ectopic posterior pituitary [Table/Fig-2b]. She was started on recombinant GH therapy (0.25 mg/kg/week) and levothyroxine (75 µg). Subsequently, she showed an accelerated growth response, with height age improving to 7.8 years within six months.



[Table/Fig-2]: a) CE-MRI brain reveals hypoplastic anterior pituitary (measuring 3.8 mm), thin infundibular stalk as marked by red arrow in CE-T1 sagittal image. b) Bright spot of posterior pituitary is ectopic and is located in the infundibular recess near tuber cinereum, as indicated by green arrows in both sagittal (2a) and coronal (2b) sections.

Case 3

A 44-year-old woman with a known diagnosis of Pituitary Stalk Interruption Syndrome (PSIS) presented to the emergency department with acute onset of non projectile vomiting, fever, diffuse dull aching abdominal pain and hypotension for three days. Laboratory investigations revealed hyponatraemia (133 mmol/L). Her medical history was significant for primary amenorrhoea and hypothyroidism (TSH 10.2 mIU/L), for which she had been taking thyroxine 50 µg daily. Previous MRI findings had confirmed PSIS. There was no relevant family history.

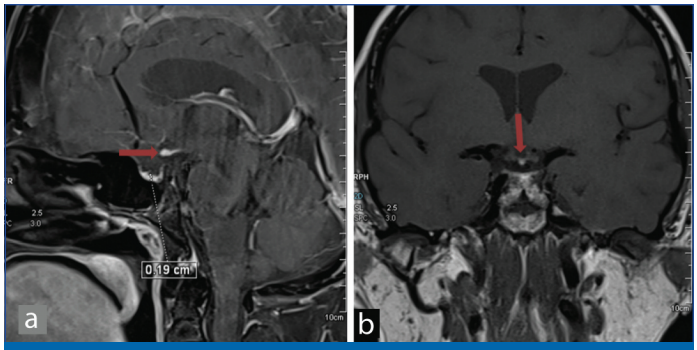
On examination, she appeared dehydrated and hypotensive, consistent with an adrenal crisis. Biochemical evaluation showed low free thyroxine (T4 7.98 pmol/L), suppressed Follicle-Stimulating Hormone (FSH 0.3 IU/L) and Luteinising Hormone (LH 0.06 IU/L) and markedly elevated prolactin (40 µg/L). These findings supported secondary adrenal insufficiency.

She responded well to intravenous hydrocortisone (100 mg/m²/day divided every six hours for four days, then tapered to 50 mg/m²/day every eight hours for the following seven days and subsequently to 15 mg/m²/day over the next two weeks). Hypertonic saline (3%) was administered for symptomatic hyponatraemia.

Contrast-enhanced MRI confirmed PSIS features, including an absent pituitary stalk [Table/Fig-3a], hypoplastic anterior pituitary (measuring 1.9 mm) and an ectopic posterior pituitary located at the median eminence [Table/Fig-3b]. The combination of imaging findings and hormonal abnormalities-central hypothyroidism, hypogonadotropic hypogonadism, adrenal insufficiency and hyperprolactinaemia-supported a diagnosis of Pickardt's syndrome, a PSIS variant associated with hyperprolactinaemia.

Case 4

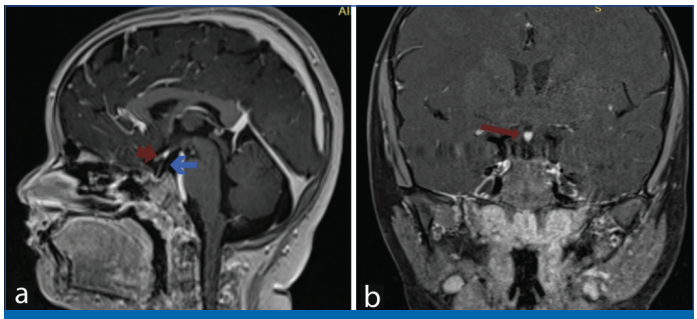
A 10-year-old boy was referred to the paediatric endocrinology clinic for evaluation of poor linear growth over the previous five years. His parents also reported reduced penile length. There was no history suggestive of chronic systemic illness. He was the first-born child of a non consanguineous couple, delivered at term via normal vaginal delivery. The neonatal period was complicated by a 10-day intensive care unit admission. Developmental milestones were appropriate for age.



[Table/Fig-3]: a) T1 weighted post contrast image shows hypoplastic anterior pituitary (measuring 1.9 mm) with ectopic posterior pituitary (red arrow). b) T1 coronal section reveals ectopic posterior pituitary (red arrow) with no stalk visualised in between anterior hypoplastic pituitary and ectopic posterior pituitary.

On examination, his height was 128 cm (–2 SD) and weight was 28 kg (–1 SD). Genital examination revealed a micropenis and hypopigmented scrotum, with bilaterally descended testes.

Biochemical evaluation showed a serum testosterone level of 1.7 ng/mL, which was low for age. Serum cortisol and thyroid function tests were within normal limits. In view of significant short stature and suspected growth hormone deficiency, contrast-enhanced MRI of the brain was performed. Imaging demonstrated an ectopic posterior pituitary [Table/Fig-4a,b], a mildly hypoplastic anterior pituitary [Table/Fig-4a] and a non visualised pituitary stalk, consistent with PSIS.



[Table/Fig-4]: a) CE-T1 weighted image of sagittal section shows hypoplastic anterior pituitary (red arrow) and thin stalk (blue arrow). b) CE-T1 coronal section reveals ectopic posterior pituitary (red arrow) with thin stalk.

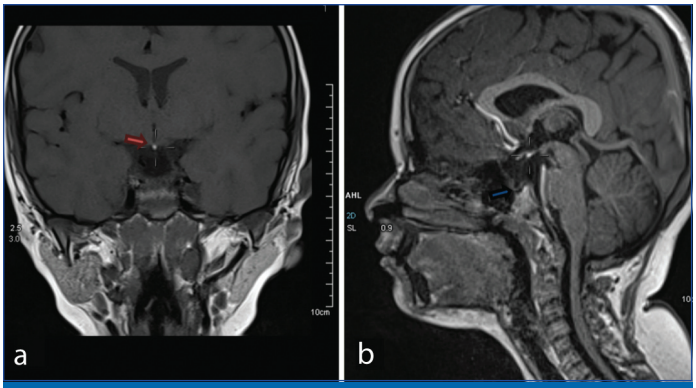
The patient was started on subcutaneous recombinant GH therapy (0.17 mg/kg/week). Over one year of follow-up, he exhibited an excellent growth response, with a growth velocity of 12 cm/year (approximately 1 cm/month). The mid-parental height was calculated as 175 cm, suggesting favourable long-term growth potential.

Case 5

A nine-year-old boy was referred for evaluation of short stature. His height was significantly below the expected range for age, corresponding to a Z-score of -3.5. On genital examination, penile length measured 6.5 cm, which was within the normal range for age (cut-off for concern <3.5 cm), thereby excluding micropenis. There were no dysmorphic features or Cushingoid characteristics and the child was clinically euthyroid.

Skeletal assessment revealed delayed bone age relative to chronological age. Biochemical evaluation showed reduced serum IGF-1 levels (3 nmol/L; reference range for age: 12.5-73 nmol/L). Growth hormone stimulation testing demonstrated subnormal GH secretion (6 ng/mL), confirming growth hormone deficiency.

Contrast-enhanced MRI of the brain revealed an ectopic posterior pituitary bright spot at the median eminence [Table/Fig-5a] and a hypoplastic anterior pituitary with an absent pituitary stalk [Table/Fig-5b], consistent with PSIS. The patient was commenced on recombinant GH therapy (0.20 mg/kg/week). A summary of all cases is presented in [Table/Fig-6].



[Table/Fig-5]: a) T1 weighted coronal image shows ectopic pituitaryin median eminence (red arrow). b) Hypoplastic/absent anterior pituitary (blue arrow) with no visible stalk on CE-T1 sagittal images.

In PSIS, the ectopic posterior pituitary is most commonly located in the infundibular recess or hypothalamus, distinguishing it from normal anatomy in which the posterior pituitary resides within the sella turcica. Previous studies report ectopic posterior pituitary in up to 91.2% of PSIS cases, most frequently within the infundibular remnant (60.4%) [11].

A recent study by Zhang Q et al., reported short stature in 85.5% of patients, with a mean bone age delay of 7.26±5.37 years [12]. Similarly, all patients in the present series presented with short stature and several exhibited delayed pubertal development, with MRI revealing characteristic PSIS features.

Pituitary height in the present cases was measured using Elster's rule, from the superior to inferior margins of the gland [13]. For pituitary stalk measurements, reference was made to Satogami N et al., who reported normal stalk diameters at the pituitary insertion as anteroposterior (AP) 2.32±0.39 mm and transverse 2.16±0.37 mm and at the optic chiasm level as AP 3.25±0.43 mm and transverse 3.35±0.44 mm [14].

Case	Age/Sex	Hormonal deficiency	Radiological features	Treatment given	Response to treatment
1	Three-year-old boy	Multiple (GH, cortisol, TSH)	Absent stalk, hypoplastic anterior pituitary (2.6 mm), Ectopic Posterior Pituitary (EPP) at median eminence	Thyroxine (75 microgram), hydrocortisone (14 mg daily then tapered), Recombinant growth hormone (0.19 mg/Kg/week)	Good growth response (8.3 cm/year); improving towards mid-parental height (168 cm)
2	10-year-old girl	Multiple (GH, TSH)	Absent stalk, hypoplastic anterior pituitary, Ectopic Posterior Pituitary (EPP)	Recombinant growth hormone (0.25 mg/Kg/week), levothyroxine (75 microgram)	Accelerated growth response
3	44-year-old female	Multiple (T3, cortisol, FSH, LH; ↑ prolactin) → Pickardt's syndrome	Absent stalk, hypoplastic anterior pituitary (1.9 mm), Ectopic Posterior Pituitary (EPP)	i.v. hydrocortisone (100 mg/m2/day in divided doses 6 hourly for 4 days), thyroxine (50 microgram), hypertonic saline	Clinical improvement post-adrenal crisis; stable on replacement therapy
4	10-year-old boy	Isolated GH deficiency	Absent stalk, Ectopic Posterior Pituitary (EPP), mildly hypoplastic anterior pituitary	Recombinant growth hormone (0.17 mg/Kg/week)	Excellent growth response (12 cm/year).
5	Nine-year-old boy	Isolated GH deficiency	Pituitary stalk not visualised, suggestive of PSIS	Recombinant growth hormone (0.20 mg/Kg/week)	Initiated; early stage of therapy

[Table/Fig-6]: Summary table of all the cases.

DISCUSSION

The PSIS is believed to result from genetic mutations involved in pituitary embryogenesis or perinatal asphyxia, with a reported Pituitary Stalk Interruption Syndrome (PSIS) is believed to result from genetic mutations affecting pituitary embryogenesis or from perinatal asphyxia, with a reported incidence of approximately 0.5 per 100,000 births [7].

The PSIS presents a unique diagnostic challenge due to its variable clinical manifestations and imaging findings, which may mimic conditions such as isolated Growth Hormone Deficiency (GHD) or combined pituitary hormone deficiency. The reported male-to-female ratio ranges from 2.3:1 to 6.9:1, suggesting a possible X-linked inheritance pattern [8]. In the present case series, three of the five patients were male. The mean age at diagnosis is reported to be approximately 9.4±11.6 years and associations have been suggested with neonatal distress and breech delivery, which may influence the age of presentation [8].

The pathogenesis of PSIS remains incompletely understood, though several mechanisms have been proposed. One hypothesis suggests defective migration of the pituitary gland during foetal development, possibly due to ischemic injury, resulting in malformation of the pituitary stalk and ectopic positioning of the posterior pituitary. Genetic mutations involving the HESX1, LHX4, OTX2, PROKR2, TGIF and SOX3 genes have been implicated in familial cases, although these account for only a small proportion of PSIS cases. Disruption of the hypothalamic–pituitary axis commonly leads to multiple hormonal deficiencies, including growth hormone, gonadotropins, corticotropin and thyrotropin deficiencies [8-10].

Recent studies have reported growth hormone deficiency in nearly 100% of patients with PSIS, with gonadotropin deficiency being the second most frequent, followed by corticotropin and thyrotropin deficiencies [8]. Consistent with these findings, all patients in the present case series exhibited growth hormone deficiency.

The PSIS has been associated with midline anomalies such as cleft lip, optic nerve hypoplasia and other cerebral malformations; however, none of the patients in this series demonstrated such abnormalities. These associations support a possible genetic basis linking PSIS with other congenital anomalies, though clinical presentations remain heterogeneous and additional anomalies are not universally present [15].

The differential diagnosis of PSIS includes congenital hypopituitarism due to other structural abnormalities of the hypothalamic-pituitary axis, septo-optic dysplasia and acquired conditions such as perinatal injury, traumatic brain injury, tumours (e.g., germinoma, craniopharyngioma) and infiltrative disorders including Langerhans cell histiocytosis. Nevertheless, the classical MRI triad of PSIS remains highly characteristic and aids in accurate diagnosis [8].

CONCLUSION(S)

The present case series highlights the importance of early recognition and intervention in Pituitary Stalk Interruption Syndrome. Prompt diagnosis using MRI and timely initiation of hormone replacement therapy can significantly improve growth outcomes and positively influence the long-term developmental trajectory of affected patients.

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