



PITUITARY STALK INTERRUPTION SYNDROME: CASE REPORT OF TWO CASES AND REVIEW OF LITERATURE

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ABSTRACT

Pituitary stalk interruption syndrome is a rare congenital disorder characterized by a triad of absent or hypoplastic anterior pituitary, ectopic posterior pituitary and a thin or absent pituitary stalk. Reported incidence of this condition is around 0.5 per 1,000,000 births. Age of presentation and clinical symptoms are heterogeneous, depending of the spectrum of hormone deficiencies. MRI is the cornerstone of diagnosis. We present two cases of PCIS spectrum in 6 year male and 15 year male patients who presented with short stature.

KEYWORDS : Pituitary Stalk Interruption, Pituitary Gland, Magnetic Resonance Imaging, Short Stature

INTRODUCTION

Pituitary stalk interruption syndrome (PSIS) is a rare congenital disorder characterized by a triad of absent of hypoplastic anterior pituitary, ectopic posterior pituitary and a thin or absent pituitary stalk.^[1] The exact incidence is unknown, however some studies describe an incidence of about 0.5 per 1,000,000 births.^[1,2,3] PSIS has a heterogeneous age of presentation, clinical features, biochemical and radiological findings.^[3] Magnetic resonance imaging (MRI) is useful in confirmation of diagnosis.^[3] Management is conservative, with lifelong hormone replacement and follow-up.^[1,3] Early diagnosis and initiation of growth hormone replacement is necessary to allow for normal growth of the patient before puberty.^[2] We present a case report of two cases of PSIS with a review of existing literature.

Case Report

Case 1

A 6 year old male child presented with complains of short stature and delayed growth. Antenatal and perinatal history was unremarkable. There was no history of premature delivery, low birth weight, delayed cry or history of intensive care unit (ICU) admission following birth. The family history was unremarkable. No other co morbidity or surgical history was present. Motor and language milestones were normal. On examination, the child had a height of 89 centimeters and weight of 9.3 kg. Upper body to lower body ratio was normal. The child was conscious and oriented with a normal systemic examination. No evidence of dysmorphic features was seen. Growth hormone stimulation test revealed a deficiency of growth hormone and parathyroid hormone. X ray of wrist revealed bone age lagging behind clinical age, with estimated bone age of less than 4 years. The child subsequently underwent a contrast enhanced dynamic MRI scan on a 3 Tesla MRI machine (Siemens Magnetom Skyra) to assess for any pituitary cause of short stature. Written informed consent was obtained from the parents prior to investigation. Intravenous gadolinium at a dose of 0.2 mmol/kg was administered via a pressure injector at the rate of 3 mL/s and thin section images of the sella were acquired (Table 1). MRI revealed a small sized sella tursica with the native pituitary gland measuring 1.6x2x2.5 mm in size. A round, ectopic soft tissue measuring 4.5x2.5x3.2 mm, appearing hyperintense on T1WI (relative to the native sellar tissue) with homogeneous post contrast enhancement was seen in adjacent to the proximal part of the pituitary stalk. The pituitary stalk was thin and midline and measured 0.6 mm in calibre. Of particular interest in this case was the fact that the native pituitary gland as well as proximal part of the infundibular stalk had hyperintense signal intensity on sagittal T1WI (similar to the ectopic pituitary gland) with homogenous post contrast enhancement. (Figure 1). A

possible explanation for the hyperintense signal within the native pituitary tissue and the infundibulum was partial volume averaging with the bony sella and the posterior pituitary bright spot. Based on the clinical, biochemical and radiological findings, a diagnosis of pituitary stalk interruption syndrome spectrum was made.

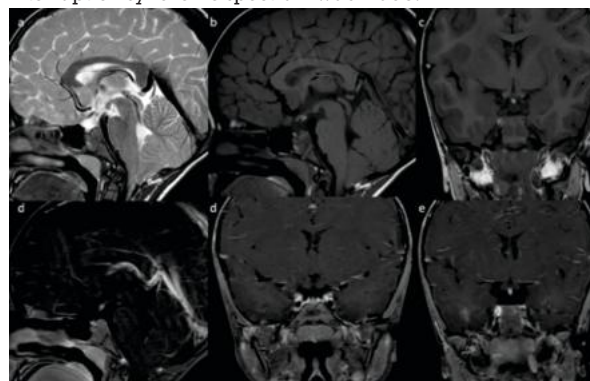


Figure 1:

Sagittal T2(a), T1(b) and coronal T1(c) non contrast images depicting small sized sella tursica, small anterior pituitary gland, thin pituitary stalk with T1W hyperintensity seen at the proximal part of the infundibular stalk s/o an ectopic pituitary. Post contrast sagittal (d), coronal (e and f) images show homogeneous enhancement of the pituitary gland (within the sella and ectopic tissue) as well as the infundibulum.

Case 2

A 15 year old male child presented with complains of short stature, dysmorphic facies and intellectual disability. Antenatal and perinatal history was unremarkable. There was no history of premature delivery, low birth weight, delayed cry or history of intensive care unit (ICU) admission following birth. The family history was unremarkable. No other comorbidity or surgical history was present. The parents gave a history of delayed motor and language milestones. On examination, the child had a height of 135 centimeters and weight of 45 kg. Upper body to lower body ratio was normal. The child was conscious and oriented with a normal systemic examination. Biochemical evaluation revealed deficiency of vitamin D (16.8 ng/ml), with growth hormone, parathyroid hormone, cortisol, thyroid profile and IGF 1 to be within normal limits. X ray of wrist revealed bone age between 12 to 18 years. The child subsequently underwent a contrast enhanced dynamic MRI scan on a 3 Tesla MRI machine (Siemens Magnetom Skyra) to assess for any pituitary cause of short stature. Written informed consent was obtained from the parents prior to investigation. Intravenous gadolinium at a dose of 0.2 mmol/kg was administered via a pressure injector

at the rate of 3 mL/s and thin section images of the sella (Table 1). MRI revealed a small sized native pituitary gland measuring 3x6x8 mm in size. The native pituitary gland had intermediate signal intensity on sagittal T1WI (appearing isointense to grey matter) with homogenous post contrast enhancement. A round, ectopic soft tissue measuring 4x4 mm, appearing hyperintense on T1WI (relative to the native sellar tissue) with homogeneous post contrast enhancement was seen in adjacent to the proximal part of the pituitary stalk. The pituitary stalk was thin and deviated to the left and measured 0.7 mm in calibre. (Figure 2) Based on the clinical, biochemical and radiological findings, a diagnosis of pituitary stalk interruption syndrome was made.

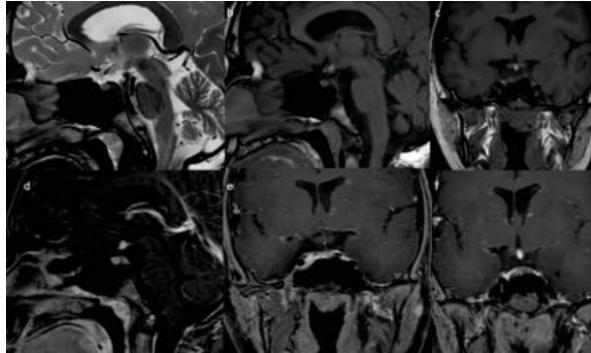


Figure 2

Sagittal T2(a), T1(b) and coronal T1(c) non contrast images depicting a small anterior pituitary gland, thin pituitary stalk with T1W hyperintensity seen at the proximal part of the infundibular stalk s/o an ectopic pituitary. Post contrast sagittal (d), coronal (e and f) images show homogeneous enhancement of the pituitary gland (within the sella and ectopic tissue) as well as the infundibulum.

DISCUSSION

Pituitary stalk interruption is a rare entity characterized by a triad of anterior pituitary hypoplasia (or aplasia), ectopic posterior pituitary and an absent or thinned pituitary stalk.^[1] Although the exact prevalence of PCIS is unknown, few studies describe an incidence of about 0.5 cases per 1,000,000 births.^[1,2,3] It is a rare cause of hormonal dwarfism, with about 7% cases of non acquired growth hormone (GH) thought to be due to PCIS.^[1] Average age of presentation is also variable, ranging from 4.8 to 19.7 years, with a male preponderance.^[1,2] In our case, both patients were male with both pre-pubertal and pubertal age of presentation (one patient was 6 years old and the other patient was 15 years old).

PSIS occurs secondary to failure of axonal extension of neurons from the hypothalamus to the posterior sella.^[4] Genetic mutation is considered to be the most common etiology.^[2] Another theory attributes PCIS developing secondary to adverse perinatal events, such as complicated deliveries, breech delivery or traumatic birth (with PCIS resulting from stretching of the pituitary stalk, causing mechanical rupture of the stalk).^[1] Association with congenital midline developmental anomalies has also been described.^[1]

Clinical presentation is variable and non-specific, relating to either an isolated growth hormone deficiency or a combination of anterior pituitary hormone deficiencies.^[1,2] PCIS should be a differential diagnosis in children presenting with growth retardation and delayed puberty.^[1] In cases of PCIS presenting at birth, failure to thrive and hypoglycemia are the most common symptoms.^[3] In older patients and early adulthood, symptoms include growth retardation and delayed secondary sexual characteristics.^[1,3] However, cases of PCIS without growth retardation have also been reported.^[1] PCIS may be associated with extra-pituitary manifestations in upto 30-50% of cases.^[5] Associated anomalies of midline structures include cleft lip, septo-optic dysplasia, optic nerve

hypoplasia, corpus callosum aplasia and holoprosencephaly.^[5,6] In our case, both patients had short stature and delayed bony growth with normal secondary sexual characters. One patient had dysmorphic facies. No evidence of cerebral midline anomalies was seen in our case.

Hormonal profile is heterogeneous, with deficiencies of anterior pituitary hormones (most commonly growth hormone (GH), adrenocorticotrophic hormone (ACTH) or thyroid stimulating hormone (TSH)).^[3,4,7] Prolactin levels may be increased or decreased.^[3,4,5] In our case, both patients had a deficiency of GH and 1 patient had PTH deficiency.

Diagnosis is often delayed, hinging on a combination of clinical history, biochemistry and MRI findings.^[1] Contrast enhanced MRI is the cornerstone for the diagnosis, with the typical triad of anterior pituitary hypoplasia (or aplasia), ectopic posterior pituitary and an absent or thinned pituitary stalk.^[1,3] Often, the only visible abnormality on MRI is an ectopic posterior pituitary.^[1] A pituitary gland height of less than 3.5 mm and volume less than 150 mm³ may be considered abnormal.^[6] Cut-off for defining pituitary stalk hypoplasia are variable, with Fatima et al and Hussain et al defining a cut-off of 1 mm and Agha et al defining a cut-off of less than 2.5 mm at the level of optic chiasm.^[3,6] The ectopic pituitary tissue is most commonly seen in the infundibular recess (60.4%) or hypothalamus (18.9%). This variation in location is an important prognostic factor, as posterior pituitary located in the median eminence or hypothalamus is associated with a greater number of anterior pituitary hormone deficiencies.^[2]

Early diagnosis is important to prevent the significant morbidity and mortality associated with PCIS, as well as to allow patient to reach a normal height before puberty.^[2,4] Management of PSIS is conservative with lifelong hormone replacement and follow-up.^[1,3]

CONCLUSION

Pituitary stalk interruption is a rare entity characterized by of hypoplastic or aplastic anterior pituitary, ectopic posterior pituitary and absent or thinned pituitary stalk. Clinical symptoms and imaging findings are heterogeneous. Dynamic contrast enhanced MRI is the cornerstone of diagnosis. Management is conservative with lifelong follow-up and hormone replacement treatment.

Table 1: MRI Protocol for Imaging of PCIS

Sequence	Area of interest	Plane	Slice Thickness	Field of View	Matrix
Non contrast T1WI	Sella	Coronal	2 mm	155 mm	256
Non contrast T1WI	Sella	Sagittal	2 mm	160 mm	256
Non contrast T2WI	Sella	Coronal	2 mm	140 mm	320
Non contrast T2WI	Sella	Sagittal	2 mm	150 mm	320
Dynamic post contrast imaging	Sella	Coronal	2 mm	180 mm	192
T2WI	Brain	Axial	4 mm	240 mm	512
T2WI	Brain	Sagittal	4 mm	220 mm	512

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