Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Pituitary stalk interruption syndrome: a case report and literature review

Abdullah Ali Alqarni[a,*], Khalid Mohamed Abdalla[d], Mohammed A. S. Alqarni[c], Jaber A. Alfaifi[b], Hisham G. A. Osman[d], Bandar S. Al Alhindi[a]

Background: Pituitary stalk interruption syndrome is a rare congenital anomaly of the pituitary gland characterized by growth hormones deficiency (with or without other pituitary hormone deficiencies) along with radiological features of a thin or interrupted pituitary stalk, an ectopic or absent posterior pituitary, or a hypoplastic or absent anterior pituitary.
Case presentation: A 10-year-old baby boy came with short stature. The laboratory investigations were done and showed low growth hormones and low thyroid-stimulating hormone. MRI showed an ectopic posterior pituitary, a small hypoplastic anterior pituitary, and an absent pituitary stalk.
Conclusion: Pituitary stalk interruption syndrome is a very rare entity. MRI is used to diagnose it. Early detection of this syndrome improve the patient symptoms especially before puberty.

Keywords: growth hormone, magnetic resonance imaging, pituitary stalk interruption syndrome

Introduction

Pituitary stalk interruption syndrome (PSIS) is a rare entity with an estimated incidence rate of 0.5/1 000 000 births and with male predominance[1,2]. The first-ever reported case was by Fujisawa *et al*.[3] in 1987 after surgical resection of the pituitary stalk in a patient with idiopathic pituitary dwarfism. While the etiology and pathophysiology of PSIS are not fully known, a strong relationship with birth trauma resulting in prenatal pituitary injury, including breech or footling presentation, dystocia, and cesarean delivery, has been observed[4,5]. PSIS is also thought to be caused by mutations in pituitary embryogenesis genes (PROP1, LHX3, HEXSX1, PROKR2, and GPR161)[6]. This syndrome is a congenital anomaly of the pituitary gland characterized by growth hormone (GH) deficiency (with or without other pituitary hormone deficiencies) along with radiological features of a thin or interrupted pituitary stalk, an ectopic or absent posterior pituitary, or a hypoplastic or absent anterior pituitary[3,7]. We report the example of a young boy who presented with short stature and was eventually diagnosed with PSIS. To the best of our knowledge, this is the first-ever reported case of PSIS from Saudi Arabia.

HIGHLIGHTS

- Pituitary stalk interruption syndrome is a very rare entity.
- Incidence rate of 0.5/1 000 000 births and with male predominance.
- MRI is used to diagnose it.
- Early detection of this syndrome improve the patient symptoms especially before puberty.

Case presentation

A 10-year-old boy was brought in general pediatric clinic due to concerns about his notably short stature compared to peers of his age. Upon conducting an initial assessment, a series of laboratory tests were performed to evaluate his hormonal levels, given the suspected endocrine nature of his growth delay.

Laboratory findings

The laboratory investigations revealed significantly reduced levels of GH and thyroid-stimulating hormone (TSH), which are critical for normal growth and metabolism. Specifically, the Somatomedin-C (IGF-1) level was markedly low at 8 ng/ml, with the reference range being 85–249 ng/ml. This finding is consistent with GH deficiency, which can contribute to the patient's short stature.

In addition to hormonal assays, MRI of the pituitary gland was conducted to explore the anatomical basis of the observed hormonal deficiencies. The MRI findings were notable for an ectopic posterior pituitary gland, a significantly underdeveloped anterior pituitary gland, and the complete absence of the pituitary stalk (Figs 1 and 2).

These radiological findings, in conjunction with the laboratory results, led to the diagnosis of PSIS.

The combination of the patient's clinical presentation, the hormonal assay results, and the MRI findings provided a clear picture, confirming the diagnosis of PSIS. This case highlights the importance of a thorough diagnostic workup, including both

[a]Department of Medicine, College of Medicine, University of Bisha, [b]Department of Child Health, College of Medicine, University of Bisha, [c]Hospital Director of Maternity and Children's Hospital and [d]King Abdullah Hospital, Bisha, Kingdom of Saudi Arabia

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: E-mail: abdullahasalmohsen@gmail.com (A.A. Alqarni).

Annals of Medicine & Surgery (2024) 86:5486–5488

Received 23 January 2024; Accepted 31 March 2024

Published online 17 April 2024

http://dx.doi.org/10.1097/MS9.0000000000002067

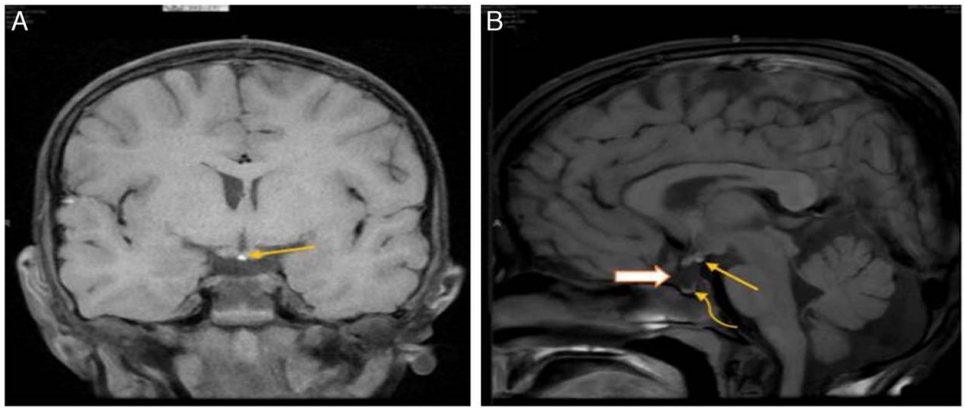

Figure 1. (A, B) Coronal and sagittal T1 precontrast shows ectopic posterior pituitary arrow, hypoplastic anterior pituitary curved orange arrow, and absent pituitary stalk open white arrow.

laboratory and imaging studies, in the evaluation of pediatric patients presenting with growth retardation.

Following the diagnosis, a multidisciplinary approach to management was initiated, involving pediatric endocrinology for hormonal replacement therapy and close monitoring of the patient's growth and development. This case underscores the critical role of early detection and intervention in managing rare endocrinological disorders such as PSIS, particularly in pediatric patients where growth and development are significantly impacted (Figs 1 and 2).

Discussion

Fujisawa *et al.*[3] first reported PSIS in 1987. PSIS has a male predominance, with a male-female sex ratio ranging from 2.3 to 6.9:1, indicating X-linked inheritance. The mean age of diagnosis is 9.4–11.6 years, with neonatal distress and breech delivery not affecting the presentation age[10]. The exact prevalence of this syndrome remains unknown. Less than 1000 cases were reported in the literature until 2010[11]. Its prevalence as a cause of GH deficiency is around 4%[4]. The age at diagnosis differs according to the severity of the hormone deficiency. When PSIS presents at birth, hypoglycemia, and failure to thrive are the most common symptoms. Growth retardation is usually the presenting complaint in childhood, whereas delayed puberty is usually the chief complaint when it manifests in adolescence and early adulthood[6,7]. Our case was a 10-year-old boy who presented to us with short stature and was eventually diagnosed with PSIS.

The pathogenesis is unknown, but perinatal anoxia and breech presentation at birth may cause pituitary stalk injury[9]. The relationship with undescended testes and micropenis and the occurrence of syndromal forms caused by genetic abnormalities in HESX1, LHX4, and SOX3 point to a prenatal origin[8,12]. El Chehadeh-Djebbar *et al.* reported the first case of PSIS in association with 17q21.31 microdeletion in 2011[1]. Approximately 20–50% of the patients have some associated congenital abnormality, mostly midline structural, for example, in the cleft lip and palate, an absent diaphragm, and axial skeletal anomalies, with the hypoplastic optic nerve being the most common, all of which suggest an association with improper embryonal migration of neural crest cells[13].

These patients have multiple hormonal deficiencies. Growth hormone deficiency is the most frequently existing deficiency and reaches 100% of all patients. Interestingly, considerable

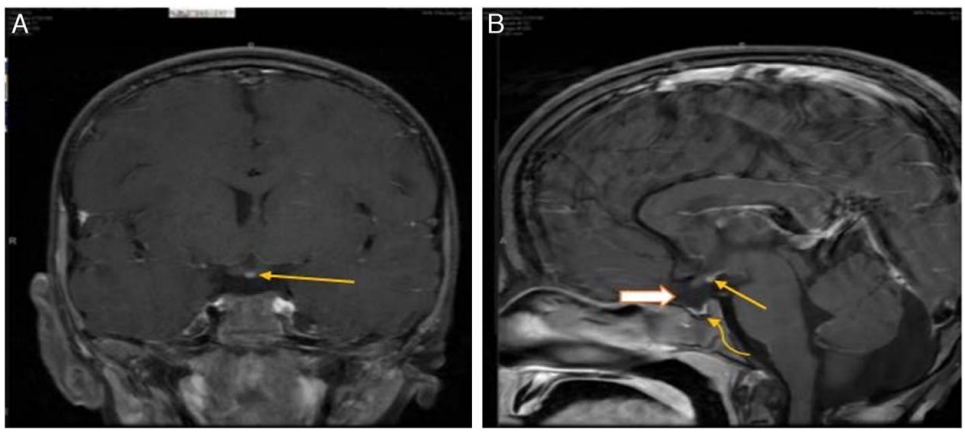

Figure 2. (A, B) Coronal and sagittal T1 postcontrast shows ectopic posterior pituitary arrow, hypoplastic anterior pituitary curved orange arrow, and absent pituitary stalk open white arrow.

heterogeneity in height has been reported. Few children maintain normal linear growth despite abnormal GH secretion[4]. Gonadotropin deficiency [luteinizing hormone (LH), follicle-stimulating hormone (FSH)] is frequently associated with other deficiencies. Adrenocorticotropic hormone (ACTH) deficiency can cause neonatal cholestasis and recurrent hyponatremia. Stimulation test for ACTH and cortisol measurement have shown their levels to be significantly lower in patients with PSIS[4]. Prolactin levels have shown a considerable degree of heterogeneity. It can be deficient, or hyperprolactinemia can be observed in 17% to one-third of patients. It varies depending on the severity of dopaminergic pathway disconnection[4]. Owing to different embryonic origins of the anterior and posterior pituitary, only a few patients have complained of central diabetes insipidus. In the neonatal period, features indicative of hypopituitarism, hypotonia, secondary adrenal deficiency with hypotension, prolonged cholestatic icterus, and repeated episodes of hypoglycemia are found in 33% of PSIS patients[4]. TSH deficiency may also be seen, but measurement may be within the normal limits in most patients with central hypothyroidism. Cases have been described with isolated sparing of TSH secretion with a deficiency of the remaining anterior pituitary hormones[4]. Our case had low GH and TSH levels.

PSIS MRI findings include hypoplasia or aplasia of the anterior pituitary, absence of the hyper-intense posterior lobe within the sella turcica and its presence as a hyper-intense nodule at the level of the median eminence or the pituitary stalk, and absence or thinned out pituitary stalk[8,10,14]. However, the presentation of this illness on MRI varies. The height of the anterior pituitary (from absence to normal), the appearance of the posterior pituitary lobe (ectopic at the base of the hypothalamus or along the pituitary stalk, absent, or normal), and the shape of the pituitary stalk (interrupted, thin, nonexistent, or normal) are all examples of these differences. An ectopic posterior pituitary can be the only abnormality[10]. Regarding our case, the MRI showed an ectopic posterior pituitary, a small hypoplastic anterior pituitary, and an absent pituitary stalk.

Conclusion

PSIS is a rare condition. However, radiologists should remember this syndrome for neonatal patients with hypoglycemia, seizures, jaundice, cryptorchidism, hypothyroidism, and children with growth retardation due to pituitary hormone deficits.

Ethical approval

Yes ethical approval was done at Research and Innovation Centre, King Abdullah Hospital, Bisha.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

None.

Author contribution

A.A.A. and K.M.A.I.: writing and diagnosis; M.A.S. and H.G.A.O.: diagnosis of the case; B.S.A.A. and J.A.A: writing the case.

Conflicts of interest disclosure

The authors declare no conflict of interest.

Research registration unique identifying number (UIN)

Name of the registry.

Guarantor

Abdullah AlQarni.

References

[1] El Chehadeh-Djebbar S, Callier P, Masurel-Paulet A, *et al*. 17q21. 31 microdeletion in a patient with pituitary stalk interruption syndrome. Eur J Med Genet 2011;54:369–73.
[2] Bar C, Zadro C, Diene G, *et al*. Pituitary stalk interruption syndrome from infancy to adulthood: clinical, hormonal, and radiological assessment according to the initial presentation. PLoS ONE 2015;10: e0142354.
[3] Fujisawa I, Kikuchi K, Nishimura K, *et al*. Transection of the pituitary stalk: development of an ectopic posterior lobe assessed with MR imaging. Radiology 1987;165:487–9.
[4] Vergier J, Castinetti F, Saveanu A, *et al*. Diagnosis of endocrine disease: pituitary stalk interruption syndrome: etiology and clinical manifestations. Eur J Endocrinol 2019;181:R199–209.
[5] Wang CZ, Guo LL, Han BY, *et al*. Growth hormone therapy benefits pituitary stalk interruption syndrome patients with short stature: a retrospective study of 75 Han Chinese. Int J Endocrinol 2016;2016: 1896285.
[6] Gosi SK, Kanduri S, Garla VV. Pituitary stalk interruption syndrome. BMJ Case Rep 2019;12:e230133.
[7] Reynaud R, Albarel F, Saveanu A, *et al*. Pituitary stalk interruption syndrome in 83 patients: novel HESX1 mutation and severe hormonal prognosis in malformative forms. Eur J Endocrinol 2011;164:457–65.
[8] Guo Q, Yang Y, Mu Y, *et al*. Pituitary stalk interruption syndrome in Chinese people: clinical characteristic analysis of 55 cases. PLoS ONE 2013;8:e53579.
[9] Arrigo T, Wasniewska M, De Luca F, *et al*. Congenital adenohypophysis aplasia: clinical features and analysis of the transcriptional factors for embryonic pituitary development. J Endocrinol Invest 2006;29:208–13.
[10] Pinto G, Netchine I, Sobrier ML, *et al*. Pituitary stalk interruption syndrome: a clinical-biological-genetic assessment of its pathogenesis. J Clin Endocrinol Metabol 1997;82:3450–4.
[11] "Pituitary stalk interruption syndrome," *Orphanet*. 2010. https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=12620&Disease_Disease_Search_diseaseGroup=Pituitary-stalk-interruption-syndrome-&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group%20of%20diseases=Pituitary-stalk-interruption
[12] Pham LL, Lemaire P, Harroche A, *et al*. Pituitary stalk interruption syndrome in 53 postpubertal patients: factors influencing the heterogeneity of its presentation. PLoS ONE 2013;8:e53189.
[13] Tauber M, Chevrel J, Diene G, *et al*. Long-term evolution of endocrine disorders and effect of GH therapy in 35 patients with pituitary stalk interruption syndrome. Horm Res Paediatr 2005;64:266–73.
[14] Van der Linden AS, van Es HW. Case 112: pituitary stalk transection syndrome with ectopic posterior pituitary gland. Radiology 2007;243: 594–7.