International Journal of Scientific Reports
Kumble A et al. Int J Sci Rep. 2021 Jun;7(6):312-315
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164

DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20211953

Case Report

A case of pituitary stalk interruption syndrome diagnosed in a 2-year-old child masquerading as syndrome of inappropriate antidiuretic hormone secretion

Ali Kumble, Abhishek K. Phadke*, Sapheliya Nazar

Department of Paediatrics, Indiana Hospital and Heart institute, Mangalore, Karnataka, India

Received: 06 April 2021
Accepted: 10 May 2021

***Correspondence:**
Dr. Abhishek K. Phadke,
E-mail: phadke18@gmail.com

ABSTRACT

Pituitary stalk interruption syndrome (PSIS) is included under the spectrum of midline abnormalities and is considered as a part of the holoprosencephaly (HPE) wide spectrum. Genetic basis has been identified in few familial cases. PSIS have anterior pituitary hormone deficiencies and a wide spectrum of clinical presentation. The typical clinical manifestations of PSIS are growth retardation, hypoglycemia and delayed puberty. We report a case of PSIS with hyponatremic seizures as initial presentation. Two-year-old girl with growth and development appropriate for age, presented with acute respiratory infection and generalized tonic clonic seizures. There was history of similar illness two weeks prior and was treated for hyponatremia. Child had euvolemic hyponatremia and symptomatic hypoglycemia. Serum cortisol level was observed to be low and thyroid function test was abnormal. MRI brain showed hypoplastic anterior pituitary and ectopic posterior pituitary (hallmark of PSIS) and absent septum pellucidum. Child was treated with hormone replacement therapy with hydrocortisone and thyroxine. Child improved and is on follow up. Clinical suspicion, early diagnosis and treatment prevent worsening of endocrine impairment, permanent short stature and associated morbidities with PSIS.

Keywords: Pituitary stalk interruption syndrome, Anterior pituitary hormone deficiencies, Euvolemic hyponatremia, Hormone replacement therapy

INTRODUCTION

Pituitary stalk interruption syndrome (PSIS) belongs to the spectrum of midline abnormalities and is usually associated with other midline extra pituitary malformations like septo-optic dysplasia and absent septum pellucidum. PSIS is considered as a part of the holoprosencephaly (HPE) wide spectrum.[1] The estimated incidence rate of PSIS is 0.5/1,00, 000 births with male predominance.[2] PSIS is characterized by triad of ectopic posterior pituitary, thin or absent pituitary stalk and anterior pituitary hypoplasia with variable degree of anterior pituitary hormone insufficiency. The timing of onset is variable from newborn to pre-pubertal period but most commonly in the pre-pubertal period with growth failure. PSIS is characterized by a wide spectrum of clinical manifestations. The cause of PSIS is still unknown and many theories are proposed like perinatal injuries, defective organogenesis due to genetic or environmental factors during pregnancy. Rare mutations of PROP1, HESX1, LH4, OTX3 and SOX3 can be the cause of PSIS in familial cases. According to recent studies, mode of delivery and/or neonatal hypoxemia are not the cause of PSIS, but are direct or indirect consequence of the hypothalamic-pituitary lesion.[2,3]

The clinical features of PSIS in the early neonatal period include cryptorchidism, micropenis, hypoglycaemia and jaundice. The most common presenting clinical feature of PSIS in childhood is short stature. Although this is a rare

disorder, a clinician and radiologist should always think of pituitary stalk interruption syndrome in case of short stature with growth hormone deficiency alone or multiple hormone deficiencies, because PSIS patients have an excellent prognosis to achieve normal height according to their age if they are diagnosed before the fusion of epiphyses. PSIS is characterized by the following triad: thin (<1 mm) or interrupted pituitary stalk connecting the hypothalamus to the pituitary gland, ectopic posterior lobe and hypoplasia or aplasia of the anterior lobe.[4]

PSIS clinical manifestations includes permanent anterior pituitary hormone deficiencies at birth with a severe hormonal phenotype including hypoglycemia and jaundice and ACTH deficiency causing neonatal cholestasis. Other manifestations during childhood appears gradually and generally progresses into pan hypopituitarism. ACTH deficiency causes recurrent hyponatremia. ACTH measurement and cortisol level after stimulation test are significantly lower. Serum TSH level measurement may be within the normal limits in most patients with central hypothyroidism.[4]

MRI is the key to diagnosis which reveals numerous anatomical variations in case of PSIS concerning the anterior lobe (absence, hypoplasia, normal), the posterior pituitary lobe (absence, ectopic along the stalk, ectopic at the hypothalamus base, normal in the sella turcica) and/or the stalk. Midline defects involving the central nervous system, mainly brain and eyes like Arnold-Chiari malformations, septal agenesis, aqueductal stenosis, optic nerve hypoplasia, coloboma of the retina, craniopharyngeal canal and central respiratory failure are observed. Craniofacial structures may also be altered with cleft lip or palate and dental anomalies such as single central incisor. Distinct but inconstant facial features were reported, such as sparse fine hair, broad forehead with frontal bossing, hypotelorism, anteverted helix, high nasal bridge, bulbous nasal tip, deep philtrum with a thin upper lip, short chin.[4,5]

The heterogeneity of PSIS presentation warrants the need to establish clinical, MRI and endocrine phenotype of the case. During the literature review, we found that there are very few reported cases of severe hyponatremia associated with PSIS and hypopituitarism. We report a patient with PSIS, who presented with severe hyponatremia and hyponatremic seizures as the initial presentation.

CASE REPORT

Two-year-old girl presented to the emergency department with complaints of fever, cough and one episode of generalized clonic tonic seizures, lasting for 10 minutes. She was developmentally normal with growth appropriate for age.

Child was born to a 24 -year-old primigravida mother out of non-consanguineous wedlock. She was a booked antenatal case with regular visits with her obstetrician. Antenatal ultrasound scan done in each trimester was told to them to be normal. Child was born late preterm at 36 weeks of gestation by normal vaginal delivery at an outside hospital. Baby cried soon after birth with a birth weight of 2600 g and length 48 cm. In view of borderline blood sugars on day 1 of life, baby was referred to our hospital for further management. At admission on day 2 of life, baby was active, sucking well, vitals stable, no facial dysmorphism and no obvious congenital anomalies. Baby's GRBS was 38 mg/dl. Baby was treated with maintenance dextrose containing IV fluids for 48 hours along with oral feeds, following which blood sugars normalized. Baby also had physiological neonatal hyperbilirubinemia requiring treatment with phototherapy for 24 hours. Blood culture and septic markers were negative. By day 5 of life, baby was on full feeds orally, euglycaemic and hence discharged. Subsequently, child was on regular monthly follow up with paediatrician and the child's growth and development was noted to be normal. Routine immunizations were given as per the schedule.

At 2 years of age, child had an episode fever followed by 1 episode of generalized tonic clonic seizures, for which she was admitted and evaluated at our hospital. At admission: child was drowsy, airway patent, hemodynamically stable. Laboratory investigations revealed severe hyponatremia with serum sodium of 116 mmol/l, normal serum potassium (4.72 mmol/l) with normal blood sugars (GRBS- 75 mg/dl) and blood gas analysis. Child was treated with IV antibiotics, IV acyclovir, IV antiepileptic and IV fluids. CSF analysis was normal. Child was euvolumic with decreased serum osmolality (253 mosm/kg), raised urine osmolality (477 mosm/l) and raised urinary sodium (31 mEq/l). Serum cortisol (63 mcg/dl), 17-OH progesterone (3.28 ng/ml) and TSH levels (4.43) were normal. Provisional diagnosis of SIADH was done based upon decreased serum osmolality, raised urine osmolality and urinary sodium. Child responded to sodium correction, fluid restriction and oral salt supplementation and was discharged on oral antiepileptic.

Child was brought back after 2 weeks with generalized clonic tonic seizures, Serum sodium was noted to be 118 mmol/L and GRBS-52 mg/dl. Child was managed with IV fluid- NS and dextrose for hyponatremia and hypoglycemia. In view of recurrent severe hyponatremia and hypoglycemia, serum cortisol level (8 am) was repeated, which was 7 mcg/dl (reference level 10-20 mcg/dl (8 am). Possibility of anterior pituitary abnormality was considered. MRI of brain with contrast revealed ectopic posterior pituitary bright spot and anterior pituitary hypoplasia and non-visualization of stalk with absent septum pellucidum (Figure 1), which clinched the diagnosis. Thyroid function tests showed normal TSH level of 3 mU/l (reference range- 0.4 to 5 mU/l) and low FT4 levels of 0.61 ng/dl (reference 0.7 to 1.9 ng/dl). The cause of severe hyponatremia was diagnosed to be due to hypopituitarism. Child was started on oral hydrocortisone

at 10 mg/m^2/day and thyroxine 50 mcg/day. Child symptomatically improved by day 4 of admission with normal serum sodium and blood sugar levels and was discharged. On regular follow up, child's serum sodium and thyroid function tests were noted to be normal on regular medications. Presently child is on thyroxine and hydrocortisone with normal dietary sodium. Parents were counseled regarding the need for stress dose of steroids during period of illnesses. Child is on follow up and at 4 years and 6 months, child's weight is at 50th centile and height at 25th centile as per WHO and IAP combined growth chart (Figure 2). Bone age assessed by radius ulna staging tanner white III (RUS TW III) was 3 years and 6 months at chronological age of 4 years and 6 months (Figure 3) Delay in bone age by one year is noted. Child is growing well, IGF-1 level is within normal limits (measured- 45 ng/ml, reference range-15 ng/ml to 216 ng/ml at 4 years of age). The need for growth hormone studies and growth hormone administration on follow up is discussed with parents.

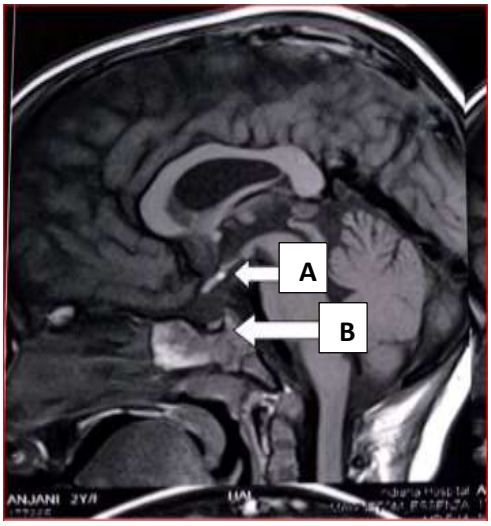

Figure 1: MRI brain with contrast (A) ectopic posterior pituitary bright spot; (B) anterior pituitary hypoplasia and non-visualization of stalk.

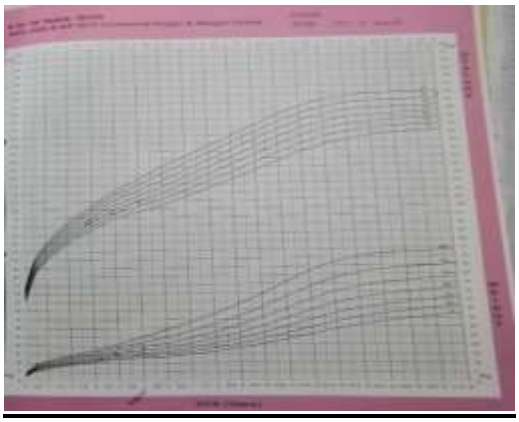

Figure 2: Growth chart.

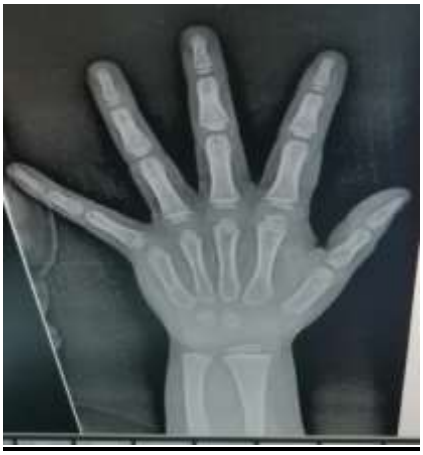

Figure 3: Left hand and wrist X-ray showing bone age. Chronological age=4 years and 6 months and bone age= 3 years 6 months.

DISCUSSION

The typical clinical manifestations of PSIS are growth retardation, hypoglycemia and delayed puberty. However, few cases are reported with seizures accompanied by hyponatremia. In case report by Juan Li et al[6], hyponatremic seizures were observed along with short stature and hormone replacement therapy helped to raise the sodium concentration to a normal level and in termination of seizures. Seizures as first presentation in PSIS has been observed.[6,7] It was observed in our case as well that on starting hormone replacement therapy, hyponatremia was resolved.

During stress such as respiratory illness in our case, patients with hypopituitarism become symptomatic due to hypocortisolism. It was observed in study by Diederich et al that in hypopituitarism, plasma ADH rises due to failure of endogenous cortisol to suppress vasopressin secretion from posterior pituitary leading to "SIADH- like syndrome". Even though clinical course is similar to SIADH, with decreased serum osmolality and raised urine osmolality and response to fluid management is poor and hyponatremia is rapidly corrected by steroids. Similar course of events were observed in our study.[8]

We had planned to do a targeted genetic sequencing in this case later on. Genetic defects were identified in less than 5% of cases, consisting of mutations, deletions, sequence variations, chromosomal defects such as 18p deletion, X chromosome translocations affecting SOX3 and 17q21.31 microdeletion.[9,10]

CONCLUSION

An early diagnosis and treatment of PSIS can prevent the patient from developing a permanent short stature. MRI is a gold standard in the diagnosis of PSIS and the ectopic posterior pituitary is the hallmark of the disease. Progressive worsening of the endocrine impairment is

observed and therefore, regular assessment of pituitary function with long-term follow-up for PSIS is essential. The signs and symptoms of PSIS during the neonatal period and infancy are often overlooked and therefore diagnosis is delayed. Early diagnosis and treatment of this rare disease can prevent permanent short stature and thus provide an excellent opportunity to reach their target height with GH therapy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Gutch M, Kumar S, Razi SM, Saran S, Gupta KK. Pituitary stalk interruption syndrome: Case report of three cases with review of literature. J Pediatr Neurosci. 2014;9(2):188-91.
2. Arrigo T, Wasniewska M, Luca F, Valenzise M, Lombardo F, Vivenza D, et al. Congenital adenohypophysis aplasia: clinical features and analysis of the transcriptional factors for embryonic pituitary development. J Endocrinol Invest. 2006;29(3):208-13.
3. Pinto G, Netchine I, Sobrier ML, Brunelle F, Souberbielle JC, Brauner R. Pituitary stalk interruption syndrome: a clinical-biological-genetic assessment of its pathogenesis. J Clin Endocrinol Metab. 1997;82(10):3450-4.
4. Bar C, Zadro C, Diene G, Oliver I, Pienkowski C, Jouret B, et al. Pituitary Stalk Interruption Syndrome from Infancy to Adulthood: Clinical, Hormonal, and Radiological Assessment According to the Initial Presentation. PLoS One. 2015;10(11):142354.
5. Bansal N, Patel P, Panasara P, Khandelwal S, Patel D, Mrugesh. Atypical cause of short stature with growth hormone deficiency: Pituitary stalk interruption Syndrome. Eurodad. 2018.
6. Li J, Jia H, Chakraborty A, Gao Z. A case of pituitary stalk interruption syndrome with intermittent seizures as the first presentation. Neuro Endocrinol Lett. 2016;37(7):469-72.
7. Vergier J, Castinetti F, Saveanu A, Girard N, Brue T, Reynaud R. Diagnosis of endocrine disease: Pituitary stalk interruption syndrome: etiology and clinical manifestations. Eur J Endocrinol. 2019;181(5):199-209.
8. Diederich S, Franzen NF, Bahr V, Oelkers W. Severe hyponatremia due to hypopituitarism with adrenal insufficiency: report on 28 cases. Eur J Endocrinol. 2003;148(6):609-17.
9. Voutetakis A, Sertedaki A, Dacou VC. Pituitary stalk interruption syndrome: cause, clinical manifestations, diagnosis, and management. Curr Opin Pediatr. 2016;28(4):545-50.
10. Chehadeh DS, Callier P, Masurel PA, Bensignor C, Mejean N, Payet M, Ragon C, et al. 17q21.31 microdeletion in a patient with pituitary stalk interruption syndrome. Eur J Med Genet. 2011;54(3):369-73.

Cite this article as: Kumble A, Phadke AK, Nazar S. A case of pituitary stalk interruption syndrome diagnosed in a 2-year-old child masquerading as syndrome of inappropriate antidiuretic hormone secretion. Int J Sci Rep 2021;7(6):312-5.