

Pituitary Stalk Interruption Syndrome: Presentation of a Rare Case

Burcin Agrıdag Ucpınar¹ Ahmet Ucar² Evrim Ozmen³

¹Department of Radiology, Sisli Hamidiye Etfal Training and Research Hospital, Sisli, Istanbul, Turkey

²Division of Pediatric Endocrinology, Sisli Hamidiye Etfal Training and Research Hospital, Sisli, Istanbul, Turkey

³Division of Pediatric Radiology, Sisli Hamidiye Etfal Training and Research Hospital, Sisli, Istanbul, Turkey

Address for correspondence Burcin Agrıdag Ucpınar, MD, Department of Radiology, Sisli Hamidiye Etfal Training and Research Hospital, Sisli, Istanbul, Turkey (e-mail: drburcinagridag@gmail.com).

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Abstract

Pituitary stalk interruption syndrome is a congenital anomaly characterized by interrupted or thin pituitary stalk, hypoplastic or absent anterior pituitary, and an absent or ectopic posterior pituitary gland. The exact incidence rate of this syndrome is not known. However, the estimated incidence rate is 0.5/1,000,000 births. In this case report, we wanted to present a case of interrupted pituitary stalk syndrome, which presented with seizures and thyroid hormone deficiency. A 5-year-old female patient was admitted to our emergency department with vomiting, fever, and seizures with new onset. She had a twin who was ex-utero intrapartum in taken history. She was diagnosed with hypothyroidism and started on levothyroxine. Her height was in 25 to 50th percentile and her weight was in 10 to 25th percentile. She had mild mental retardation. On contrast-enhanced cranial magnetic resonance imaging scan, the pituitary stalk was absent, posterior pituitary was ectopic, and anterior pituitary was hypoplastic. The patient was diagnosed with interrupted pituitary stalk syndrome. After the symptoms were relieved, patient started on carbamazepine for epileptic seizures and hormone replacement therapy with levothyroxine and hydrocortisone. She was routinely followed up after the proper diagnosis. Leuprolide (gonadotropin-releasing hormone) and Norditropin (biosynthetic growth hormone) were added to medical therapy. Her height and weight were in 25th percentile after the long-term follow-up of approximately 10 years. On neurological examination, situation of mild mental retardation persisted. Pituitary stalk interruption syndrome is a very rare entity. However, radiologists should keep this syndrome in mind for patients who present with hypoglycemia, seizures, jaundice, cryptorchidism, and hypothyroidism in neonatal period and growth retardation with pituitary hormone deficiencies in childhood.

Keywords

- ▶ pituitary stalk transection syndrome
- ▶ pituitary stalk interruption syndrome
- ▶ growth retardation

Introduction

Pituitary stalk interruption syndrome (PSIS), also known as “Pituitary stalk transection syndrome,” is a congenital anomaly characterized by interrupted or thin pituitary stalk, hypoplastic or absent anterior pituitary, and an absent or

ectopic posterior pituitary gland.^{1,2} The exact incidence rate of this syndrome is not known. However, the estimated incidence rate is 0.5/1,000,000 births.^{3,4} This syndrome is characterized by pituitary hormone deficiencies and their symptoms and patients generally admit to clinics at the first

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decade of life with growth retardation. Patients usually present with isolated growth hormone (GH) deficiency; however, this deficiency may progress to multiple hormone deficiencies of pituitary gland.^{2,5} The mean age at the diagnosis varies and ranges between 4 and 5 in studies.^{6,7} Different hypotheses for the underlying mechanism of this syndrome have been discussed in the literature such as pituitary defects in antenatal period or ischemia resulting with defective reorganization of infundibular axons and ectopic localization of posterior pituitary.^{2,8,9} In this case presentation, we wanted to present a case of 5-year-old female with interrupted pituitary stalk syndrome, which presented with seizures, mental retardation, and thyroid hormone deficiency.

Case Presentation

A 5-year-old female patient was admitted to our emergency department with vomiting, fever, and seizures with new onset.

In history taking, she had a twin who died in utero at 3 months of gestational age. Her ex twin was in uterus during the gestation period. She was delivered at term via C-section. She had postnatal asphyxia due to hypoglycemia and experienced generalized tonic-clonic seizures and followed up in neonatal intensive care unit (NICU). She also had neonatal jaundice and treated in NICU. She was diagnosed with hypothyroidism and started on levothyroxine. She has been taking thyroid hormone supply since neonatal period. Unfortunately, there are no data about performed computed tomography (CT) and magnetic resonance imaging (MRI) in neonatal period. The patient was followed up in a tertiary hospital after the neonatal period without any definitive diagnosis.

On physical examination, she had coarse facial features at a first look. She was experiencing generalized tonic-clonic seizures, which were relieved after applying antiepileptic medication. She had a fever of 38°C. On neurological examination, she had bilateral grade 1 papilledema. In laboratory tests, she had hypoglycemia, low hemoglobin levels, and neutropenia. In hormone analysis, follicle-stimulating hormone level was below 0.1 mIU/mL, thyroid-stimulating hormone level was 0.005 mIU/L, adrenocorticotropic hormone level was 2.24 pg/mL, and somatomedin C level was 35.7, which were all below normal values. In performed GH stimulation test, GH peak was 3 ng/mL, which supported the deficiency of GH. Prolactin level was higher than normal, with a value of 42.04 ng/mL. Her height was in 25 to 50th percentile and her weight was in 10 to 25th percentile. Her head circumference was 49 cm, which was below the normal values as well. She had mild mental retardation. Noncontrast cranial CT scan in emergency settings revealed noncommunicating hydrocephalus with dilation of lateral and third ventricles. Patient was admitted to pediatric inpatient clinic for further follow-up. On contrast-enhanced cranial MRI scan, the pituitary stalk was absent, posterior pituitary was ectopic, and anterior pituitary was hypoplastic (►Figs. 1 and 2). The patient was diagnosed with interrupted pituitary stalk syndrome. After reliefment

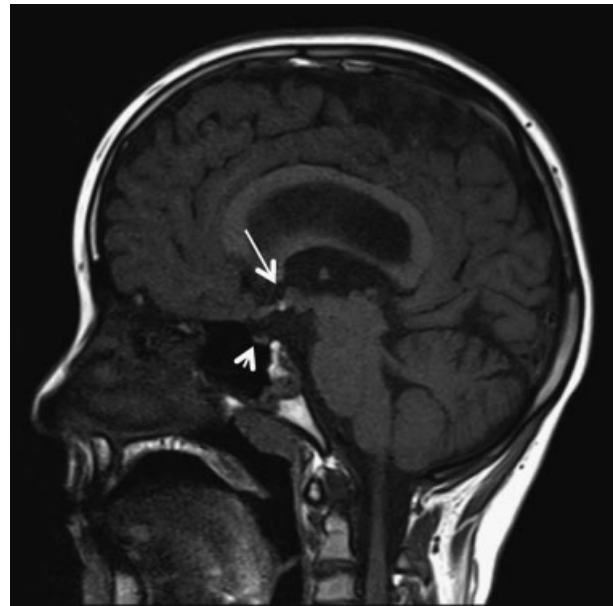


Fig. 1 T1-weighted sagittal magnetic resonance image of the patient showing ectopic neurohypophysis (long arrow) at the proximal part of the infundibular stalk and hypoplastic pituitary gland (short arrow).

of the symptoms, patient started on carbamazepine for epileptic seizures and hormone replacement therapy with levothyroxine and hydrocortisone. She was routinely followed up after the proper diagnosis. Leuprolide (gonadotropin-releasing hormone) and Norditropin (biosynthetic GH) were added to medical therapy. Her height and weight were in 25th percentile after the long-term follow-up of approximately 10 years period. On neurological examination, situation of the mild mental retardation persisted.

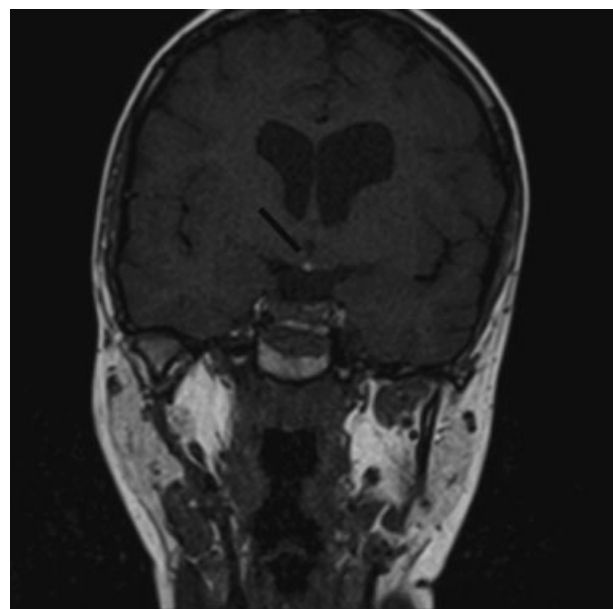


Fig. 2 T1-weighted coronal magnetic resonance image of the patient showing ectopic neurohypophysis (arrow). Pituitary stalk is absent.

Discussion

Pituitary stalk interruption syndrome is a very rare entity and it was first presented by Fujisawa et al¹⁰ in 1987. The incidence rate is 0.5/1,000,000 per birth. It has an X-linked inheritance.^{3,4} However, exact mechanism underlying this pathology is unclear. Birth-related complications like asphyxia, perinatal complications, and trauma during birth are thought to be possible underlying factors.^{2,8,9} In familial cases, some rare genetic mutations in the HESX1, LHX4, OTX2, SOX3, and PROKR2 genes can be seen.⁷ It is mainly characterized by primary hypopituitarism and tertiary hypothyroidism symptoms.

Our case presented with hypoglycemia, jaundice, and seizures during neonatal period. Exact diagnosis was delayed till our patient was at 5 years of age. Interrupted pituitary syndrome may present in a variety of ways. Earlier signs may include hypoglycemia, jaundice, cryptorchidism, and seizures; however, patients may also present with late term signs which can be listed as failure to thrive, short stature, and delayed puberty.⁵ All these symptoms tend to occur due to lack of pituitary hormones.

Diagnosis can be achieved after clinical suspicion of hypopituitarism and hypothyroidism symptoms; laboratory tests and exact diagnosis can be achieved via imaging methods. MRI, with detailed hormone analysis, is the main diagnostic method for the exact diagnosis.^{2,5} In our case, contrast-enhanced MRI revealed minimal dilation in ventricular system, hypoplastic anterior pituitary, thin pituitary stalk, and ectopic posterior pituitary which was located between pituitary stalk and hypothalamus. In some cases, pathologies can be limited to an interrupted pituitary stalk or an ectopic posterior pituitary gland. Most of the cases (98.3%) include hypoplasia of anterior pituitary gland and absent pituitary stalk. Another common feature is the presence of ectopic posterior pituitary, as cited above (91.4%). In differential diagnosis, suprasellar lipoma and ectopic posterior pituitary should be kept in mind. Suprasellar lipomas are benign lesions with equal subcutaneous fat intensity on MRI in suprasellar region, which may be misdiagnosed as an ectopic posterior pituitary. Even though they are usually asymptomatic, large lipomas may produce symptoms by compression of the adjacent structures. To distinguish suprasellar lipomas from PSIS, the presence of a normal-sized anterior pituitary and pituitary stalk with normal localization of posterior pituitary should be observed.

Ectopic posterior pituitary should also be kept in mind as differential diagnosis. Due to dysembryogenesis, the posterior pituitary locates characteristically at the median eminence on the floor of third ventricle, on noncontrast-enhanced T1-weighted images. Ectopic posterior pituitary may also cause hormone deficiencies with mostly GH deficiency. However, in some cases, panhypopituitarism may also be seen.

There are various reported cases in the literature. Gutch et al reported three cases of PSIS.³ Their first case was a 15-year-old boy who had a history of asphyxia at birth and was presented with delayed puberty. Their second case was a 11-

year-old boy with no remarkable previous history of any birth-related pathologies or any diseases, presented with short stature. Their third case was an 18-year-old boy who presented with short stature and delayed puberty and his previous history was unremarkable. Their exact diagnosis was achieved via MRI of the brain. Jang and Ko recently reported a case of PSIS.¹¹ Their case was a 24-year-old male patient who was evaluated for severe recurrent hyponatremia, due to chronic adrenal insufficiency with short stature, delayed puberty. These studies prove that PSIS can present with a variety of different symptoms and laboratory findings. There are also studies with large number of case series in literature.^{12,13} Guo et al represented clinical characteristics of 55 patients with PSIS.¹³ In our case, the patient had also a vanishing twin who was ex-utero intrapartum in the first trimester of the gestation. To our knowledge, there is no similar case in literature which states a patient with this syndrome and also having a twin with ex-utero intrapartum. Further cases are needed to reach a conclusion about the relationship of this syndrome with twin pregnancy.

Pituitary stalk interruption syndrome is a very rare entity. However, radiologists should keep this syndrome in mind for patients who present with hypoglycemia, seizures, jaundice, cryptorchidism, and hypothyroidism in neonatal period and growth retardation with pituitary hormone deficiencies in childhood period.

Learning Points

1. To keep the pituitary stalk interruption syndrome in mind, in the differential diagnosis of neonatal hypoglycemia, hypothyroidism, and convulsions.
2. To remind pituitary stalk interruption syndrome in cases of multiple pituitary hormone deficiencies in childhood.
3. To distinguish between imaging findings of pituitary stalk interruption syndrome, ectopic posterior pituitary gland, and pituitary lipomas.

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