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Case Report

Pituitary Stalk Duplication: A Radiological Surprise in a Child With Short Stature

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ABSTRACT

Objective: Pituitary stalk abnormalities are one of the causes of hypopituitarism. Isolated pituitary stalk duplication with a single pituitary gland is extremely rare with only a few cases reported to date. The present case has a different clinical picture as compared to the cases that were previously reported in the literature.

Case Report: A 2 years 6-month-old male child, a product of nonconsanguineous marriage, presented with short stature, micropenis with unilateral undescended testis, and delayed motor milestones. His bone age was delayed by 6 months. On further evaluation, he was found to be euthyroid, with stimulated growth hormone (GH) and stimulated gonadotropin levels were suboptimal, whereas the cortisol and the prolactin were normal. Magnetic resonance imaging of the pituitary revealed pituitary stalk duplication with a single pituitary gland of normal dimensions and fused tuber cinereum and mammillary body.

Discussion: To our knowledge, only 7 cases with isolated pituitary stalk duplication were reported. The presenting complaint could be primarily of hypopituitarism like short stature or a neurologic complaint or ocular abnormality. The pituitary hormone deficiencies are variable with GH deficiency being the most common as seen in our case. Other associated features could be the morning glory disc anomaly, moyamoya disease, pituitary adenoma or hypoplasia, split hypothalamus, and sellar dermoid.

Conclusion: Pituitary stalk duplication is a developmental disorder that is diagnosed only by imaging. Patients should be evaluated for hypopituitarism, particularly the GH and gonadotrophins deficiency, and also screened for associated neurologic and ocular abnormalities.

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Introduction

Pituitary gland, the master endocrine gland, is regulated by the hypothalamus and is composed of the anterior lobe, posterior lobe, and stalk that connects the pituitary to the hypothalamus.[1] Of the multiple etiologies of hypopituitarism, pituitary stalk disorders are very rare. Pituitary stalk duplication (PSD) is usually associated with pituitary gland duplication and midline defects. However, isolated PSD with normal pituitary gland is extremely rare with only a few cases reported to date.[2] The manifestations range from isolated growth hormone deficiency (GHD) to panhypopituitarism. PSD as reported previously is commonly associated with multiple other neurologic or ocular abnormalities.[3,4] The diagnosis is by magnetic resonance imaging (MRI). Here we present an interesting case of short stature with micropenis and motor milestone delay showing PSD on imaging.

Case Report

A 2 years 6-month-old male child born of a nonconsanguineous marriage presented with poor height gain and motor developmental delay. He was unable to walk without support currently. However, his intellectual development was as per age. His appetite and food intake were normal. There were no

Abbreviations: GH, Growth hormone; MRI, Magnetic resonance imaging; PSD, Pituitary stalk duplication; PSIS, Pituitary stalk interruption syndrome.

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Table 1
Biochemical Investigations

Biochemical Parameter	Value	Normal Values
Stimulated GH (ng/mL)	4.3	>10
LH (mIU/mL)		
Baseline	<0.1	
Stimulated peak	3.2	>8
FSH (mIU/mL)		
Baseline	1	
Stimulated peak	4.5	>8
Serum cortisol (mcg/dL)	11.1	6-18
Serum testosterone (ng/dL)	2.5	<20
FT3 (pg/mL)	2.93	2.02-4.4
FT4 (ng/dL)	1.13	0.9-1.7
TSH (μIU/mL)	1.49	0.7-4.2
Prolactin (ng/mL)	10	4-15

Abbreviations: FSH = follicular stimulating hormone; FT3 = free T3; FT4 = free T4; GH = growth hormone; LH = luteinizing hormone; TSH = thyroid stimulating hormone.

symptoms of polyuria, polydipsia, bony pain, lethargy, poor feeding, or failure to thrive. There is no family history of short stature, delayed puberty, or pituitary tumors. On examination, his height was 84 cm (<third centile, 2.13 standard deviations below the mean for age and sex) and his weight was 12 kg (between 10 and 25th centile for age and sex). The mid-parental height was 168 cm, and upper segment to lower segment ratio was 1.3 (proportionate short stature). Genital examination revealed micropenis with a stretched penile length of 2 cm (normal 4-5 cm), testicular volume of 1 cc on the right side with left undescended testis, and a well-formed scrotum, no ambiguity was noted. There were no midline defects like cleft lip, cleft palate, hypertelorism, mid-facial hypoplasia, or other malformations. Radiograph of the left hand with wrist showed a bone age of 2 years. Audiometry and ocular examination were normal. Biochemical investigations are listed in Table 1. MRI of the brain and pituitary was done that revealed duplication of the pituitary stalk with single pituitary gland of normal size (4.2 × 6.1 × 8.5 mm), fusion of tuber cinereum, and mammillary bodies (Fig. 1 and 2). Biochemically GHD was confirmed, and the patient was started on growth hormone replacement therapy with a dose of 30 μg/kg of body weight per day. The patient was followed up at 1 and 3 months and had no any adverse effects. He was advised for regular follow-up to assess for the further adverse effects and development of other pituitary hormone deficiency.

Highlights

- Case of isolated pituitary stalk duplication that is very rare
- Varied hormone deficiency at presentation
- Review of case reports of pituitary stalk duplication

Clinical Relevance

We describe a unique case of isolated pituitary stalk duplication with a normal pituitary gland. Here we summarize the unique presentation giving an idea of when to suspect, how to diagnose, and follow-up. Since the pituitary stalk defects are congenital, timely follow-up for the development of hormone deficiencies and appropriate management is indicated. Here we also summarized various case reports of pituitary stalk duplication and their associated anomalies indicating that when a stalk duplication is diagnosed, the patient has to undergo comprehensive screening for these anomalies and be treated accordingly. This case report provides very good clinical insights into pituitary stalk duplication.

Discussion

This patient who presented mainly with short stature, micropenis, and delayed motor milestones had GHD and hypogonadotropic hypogonadism. On MRI pituitary, he was found to have PSD and single normal sized pituitary gland.

Pituitary duplication is a rare finding with only around 40 cases described in the literature. On the other hand, isolated stalk duplication with normal pituitary is very rare with only a few cases reported to date. The etiopathogenesis is not well

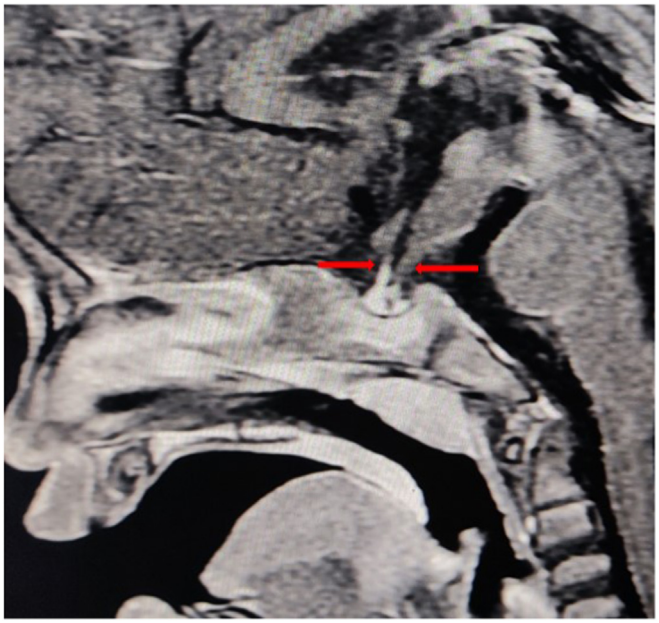

Fig. 1. Sagittal section of the pituitary showing the duplicated stalk (red arrows).

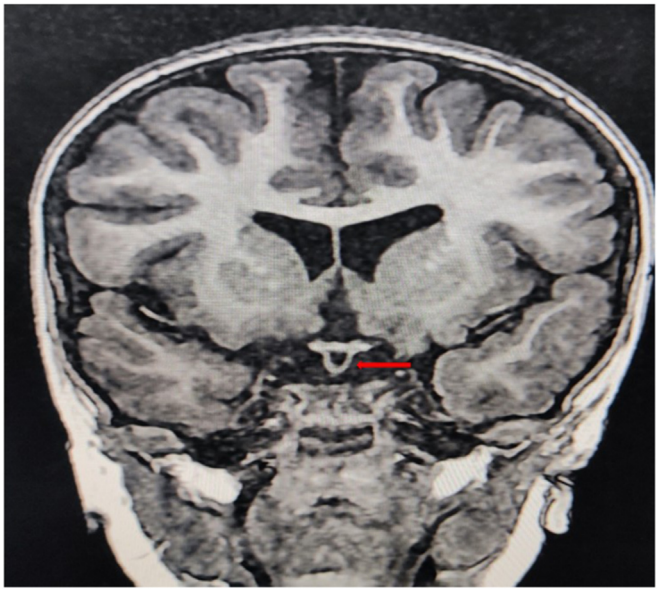

Fig. 2. Coronal section showing the duplicated pituitary stalk (red arrow).

Table 2
Review of Case Reports on Pituitary Stalk Interruption Syndrome

Author	Presenting Features	Associated Abnormalities	Pituitary Hormone Deficiencies	Genetic Testing
Özdemir et al[2]	12-year-old boy, short stature	Marked anterior pituitary hypoplasia, split hypothalamus, and downward extension of third ventricle	GHD	-
Loddenkemper et al[3]	2-year-old girl, ocular abnormality	Bilateral morning glory disc anomaly, Moyamoya disease	Hyperprolactinemia	PAX6 gene negative
Scala et al[4]	4.5-year-old girl, growth failure	Hypoplasia of the anterior pituitary, duplication of the pituitary stalk, atrial septal defect	GHD	Deletion of ROBO1 gene
Madhusudhan and Kandpal[6]	11-year-old boy, short stature	Sellar dermoid and herniation of the third ventricle	All anterior pituitary hormones	-
Petridis and Barth[7]	53-year-old male, headache	Anterior pituitary adenoma and hydrocephalus due to aqueductal stenosis	Hyperprolactinemia, GHD	-
Khodeiry et al[8]	Decreased vision	Morning glory disc anomaly and Moyamoya disease	GHD	-
Accornero et al[9]	18-year-old girl, chorea	No	Subclinical hypothyroidism	TTF-1

Abbreviation: GHD = growth hormone deficiency.

established but is attributed to alteration of genes involved in the development of the pituitary like RPX/ HESX-1, PAX-6, SIX-1,3, Isl-1, PITX1 and 2, PROP-1, and many others.[5] Of these, ROBO 1, PAX 6, and TTF-1 were studied among the PSD cases.[3,4,9] However, the pathologic role of these genes in the causation of PSD is not well established. The duplication can develop at various stages of pituitary development, based on which the presentation varies, in the form of either both the gland and stalk or only one of them being duplicated.[3] Other acquired factors implicated in the causation of PSD are pituitary adenoma and sellar dermoid which have been reported.[6,7] However, it is not clear whether the sellar tumors are the cause or just an association with PSD.

Structurally the pituitary gland can be normal as in our case or hypoplastic as reported by 2 others.[2,4] Of all the cases reported, GHD is the most common pituitary hormone abnormality as seen in our case. Hyperprolactinemia has also been reported,[3,6] which could be primarily due to a stalk defect or the associated pituitary tumor, which is not seen in our case. Our case also had hypogonadotropic hypogonadism, whereas one case was reported to have anterior panhypopituitarism.[5] The posterior pituitary hormone deficiency has not been reported in PSD cases. Although the gland is normal in size, our case had hormonal deficiencies. This could be explained by the fact that the functioning of the pituitary is dependent on the trophic hormones from the hypothalamus that are carried through the stalk which is defective. These patients can develop hormone deficiencies at varied points of time and so are to be regularly followed up for deficiencies in a later time especially gonadotrophins, thyrotrophin, and corticotrophin.

Most of the reported cases of PSD were associated with varied other anomalies like duplication of the hypothalamus,[2] morning glory disc anomaly of the eye, and moyamoya disease.[3,8] Table 2 summarizes the case reports of isolated PSD. Our case had an associated anomaly of fused tuber cinereum and mammillary body which was not reported in the previous cases.

Scala et al[4] reported a 4.5-year-old girl and her father, both harboring the genetic mutation of ROBO1 gene. The girl had ventral-dorsal duplication of the pituitary stalk and hypoplasia of the anterior pituitary with isolated GHD. On the other hand, her father had normal pituitary hormone levels but the MRI revealed pituitary stalk interruption syndrome (PSIS). This case report shows that PSD could be a spectrum of PSIS, particularly in the mutation of the ROBO1 gene.[4]

The management of patients with PSD varies according to the age of presentation, hormone deficiencies, and the presence of other associated pathologies. Appropriate hormone replacement therapy and follow-up for other hormone deficiencies are crucial. A detailed ophthalmologic, neurologic, and neuroradiologic evaluation and follow-up are necessary to avoid missing a concomitant pathology in these patients.

The genetic study that gives a further idea about the cause could not be performed in this case, which is a limitation of our report.

Conclusion

PSD is a rare disorder and MRI has an invaluable role in diagnosis. PSD may develop multiple pituitary hormone deficiencies over a period of time of which GHD is the most common. So, a diagnosis of PSD should prompt regular follow-up for timely diagnosis and treatment of hormone deficiencies. A comprehensive screening for other developmental anomalies like midline defects, ocular anomalies, and neurologic abnormalities with appropriate action is advised.

Disclosure

The authors have no multiplicity of interest to disclose.

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We acknowledge that consent has been obtained from the parents of the child.

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