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Pituitary stalk interruption syndrome (PSIS): do not miss this diagnosis

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Abstract

Background: Pituitary stalk interruption syndrome (PSIS) is one of the rare endocrinological aetiologies of the abnormal short stature. This is a syndrome characterized by a specific triad, an absent or hypoplastic anterior pituitary gland, thin or absent infundibulum, and ectopic posterior pituitary location. This type of pituitary dwarfism is usually presented in the first decade of life and may be first isolated with normal other pituitary hormones.

Results: Only 3 out of 117 dwarf patients (2.5%) were found to have pituitary stalk interruption syndrome.

Conclusion: Although of rare incidence, pituitary stalk interruption syndrome (PSIS) is an entity which leads to pituitary dwarfism and should be kept in mind while investigating a child with pituitary dwarfism and radiologists should be aware of its rarely encountered diagnostic MRI findings for early diagnosis and treatment.

Background

Child short stature is defined as a height that is 2 or more standard deviations below the mean for age and gender. Many pathogeneses of short stature were well known, including skeletal dysplasia and hormonal disorders. Such endocrinological pathogenesis due to pituitary growth hormone deficiency may also be familial, syndromic or isolated idiopathic as a result of developmental anomaly, malnutrition and chronic debilitating disease. The pituitary gland (hypophysis) is the magistrative endocrine gland, as it is the source of the organizing hormones of the whole endocrine glands in the body. Normally, the gland is located at the sella turcica, below the hypothalamus, which is the overseer of the pituitary gland [1, 2].

The pituitary gland is composed of 2 lobes: the anterior lobe (the adenohypophysis) and the posterior lobe (the neurohypophysis). The adenohypophysis has hypothalamic regulation through a portal system (circulatory), while the neurohypophysis activity has direct neural

hypothalamic control. Each lobe has a specific group of different hormones, so pituitary gland deficiency can lead to a wide range of clinical conditions, e.g. hypothyroidism, central diabetes insipidus, or growth retardation. Proportional growth retardation usually has a hormonal cause, such as growth hormone deficiency, called pituitary dwarfism. Unlike skeletal dysplasia which is a disproportionate dwarfism, the hormonal dwarfism may be associated with some mental disability [3, 4].

One of the rare aetiologies of the hormonal dwarfism is the pituitary stalk interruption syndrome (PSIS), which is also known as pituitary stalk transection syndrome. This is a syndrome characterized by a specific triad, an absent or hypoplastic anterior pituitary gland, thin or absent infundibulum, and ectopic posterior pituitary location. This type of pituitary dwarfism is usually presented in the first decade of life and may be first isolated with normal other pituitary hormones. However, deficiencies of other hormones present afterwards, with end stage anterior pan-hypopituitarism, with preservation of posterior pituitary function, regardless it is usually ectopic in location [5, 6].

The aim of this study was to detect the incidence of pituitary stalk interruption syndrome in cases of pituitary

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dwarfism in our institute and to highlight the magnetic resonance imaging (MRI) findings in such syndrome.

Methods

Approval of this retrospective study was obtained from the research ethics committee in our institute. All the study procedures were performed in agreement with the Declaration of Helsinki regarding research involving human participants. An informed consent was obtained from the parents of every patient.

The study population

This study included 117 patients, whom referred to do pituitary MRI, investigating their hormonal dwarfism, who were treated at our hospital from November 2019 to March 2022. It was a retrospective study, through revision of the patients records. The clinical data including height and weight of the children and their growth charts were reviewed as well as the laboratory data including growth hormone and other pituitary hormones levels. PACS MRI pituitary images were then reviewed. Inclusion criteria included all short stature children, below 15 years, with height that is 2 or more standard

deviations below the mean for age and gender with laboratory evidence of growth hormone deficiency. Exclusion criteria included all patients with other proven metabolic causes or dysplasias as an aetiology for dwarfism.

MRI protocol

All MRI examinations were performed through Intera 1.5 T, Closed Magnet MRI, Philips Medical Systems, 5656 AE Eindhoven, Netherlands. The examinations were done with a dedicated head coil. Thin slices (three millimetre thickness) for the sella turica were taken including T1 weighted (T1W) and T2 weighted images (T2W) images in the coronal and sagittal planes. T1W sequences were repeated after administration of intravenous gadolinium with a dose of 0.1 mmol/kg. General anaesthesia were used in children younger than seven years old.

Imaging evaluation

Two experienced pediatric neuroradiologists (10&8 years experience), reviewed the images in the same session and agreed together on the findings followed by writing a detailed report. Images were carefully revised for evaluation the size and the components of the pituitary gland.

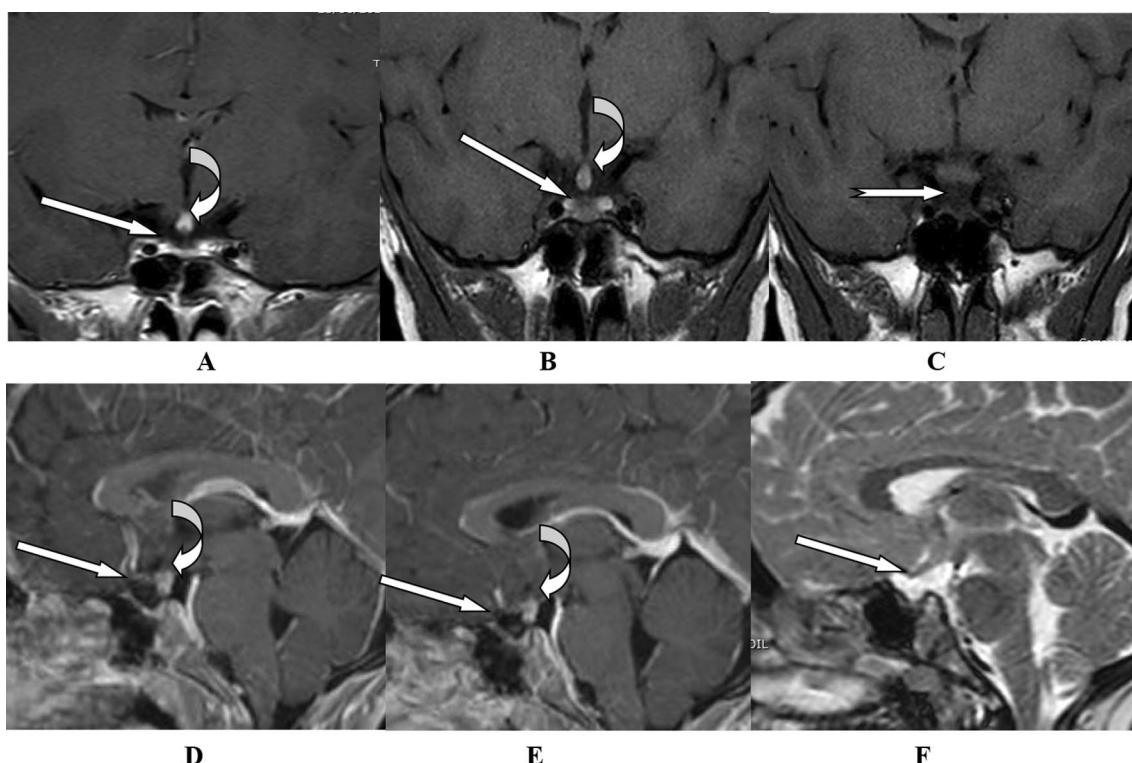


Fig. 1 A 7-year-old girl with signs of pituitary dwarfism. MRI of the sella was performed. Coronal non contrast (**A**) & coronal post contrast T1w (**B**, **C**), Sagittal T1 contrast (**D**, **E**) and Sagittal T2w images (**F**) showing: hypoplastic anterior pituitary gland (Arrows), hypothalamic ectopic posterior pituitary (Curved Arrows) and absent stalk (Notched arrow)

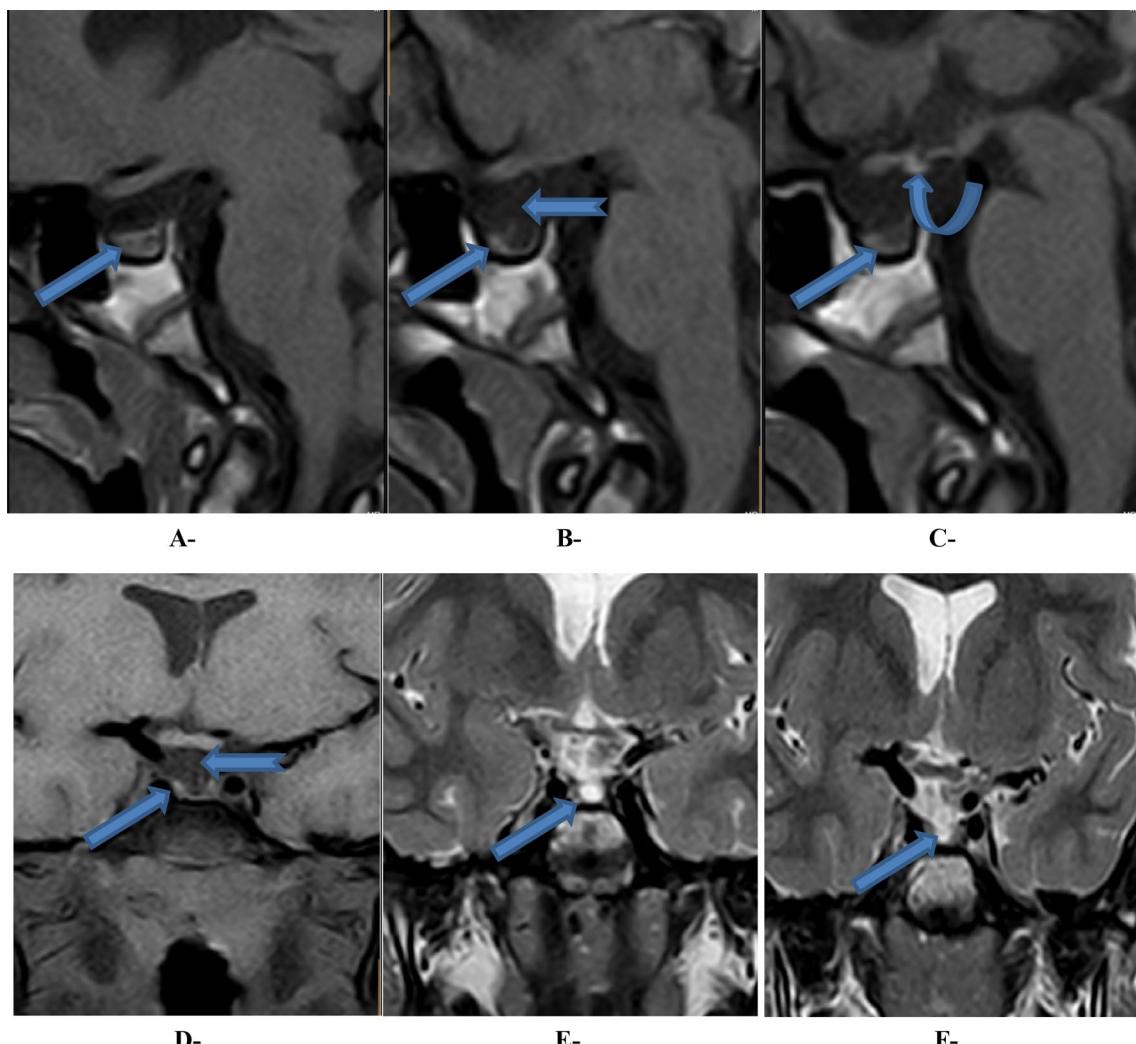


Fig. 2 An 8-year-old boy with signs of pituitary dwarfism. Sagittal T1w non contrast (A–C), Sagittal T2w (D), Coronal T1w (D) and Coronal T2w (E, F) showing: hypoplastic anterior pituitary gland (Arrows), hypothalamic ectopic posterior pituitary (Curved Arrows) and absent stalk (Notched arrow)

The size was considered abnormal, if the height is less than 3.5 mm, and the volume is less than 150 mm^3 . The pituitary stalk was considered hypoplastic, if its AP diameter at optic chiasm level is less than 2.5 mm [7, 8]. The site and signal of the posterior pituitary lobe was assessed as well as the hypothalamus.

Statistical analysis of the data

Data were then fed to the computer and analysed using IBM SPSS software package version 20.

Results

The study included 117 patients all of which presenting with height that is 2 or more standard deviations below the mean for age and gender and with laboratory evidence

of growth hormone deficiency. Their ages ranged between 4 and 14 years and included 55 males (47%) and 62 females (53%). After review of the images, three patients (2.5%) were found to have PSIS, all sharing the same features including hypoplastic anterior pituitary, defective or absent stalk and hypothalamic ectopic site of the posterior pituitary lobe. The three patients included a 7-year-old girl, and two boys aging 8 and 10 years, respectively.

The heights of the gland were 1, 1.2 and 1.5 mm in heights, respectively, and the pituitary stalk was absent in the three patients. The site of the ectopic posterior pituitary marked by the T1W hyperintense bright spot was in the region of the tuber cinereum in the three patients. Figures 1, 2, 3 are showing the different MRI findings encountered in the three patients.

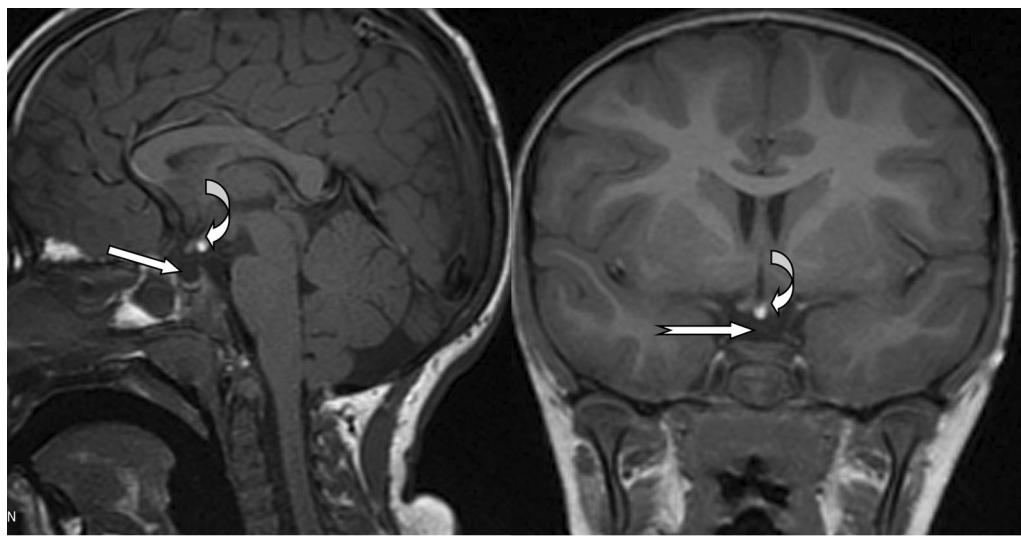


Fig. 3 A 10-year-old boy with signs of pituitary dwarfism. T1w non contrast sagittal (**A**) and coronal (**B**) MRI sequences showing hypoplastic anterior pituitary gland, hypothalamic ectopic posterior pituitary and absent stalk

Discussion

PSIS is an uncommon congenital cause of with its reported incidence is around 0.5 per one million births [9, 10]. In this study, three patients out of 117 patients presenting with pituitary dwarfism were diagnosed with this syndrome with percent around 2.5% confirming rarity of this syndrome.

Various hypotheses have been proposed to this syndrome such as defective migration of the pituitary gland during intrauterine life or ischemia with subsequent reorganization of the infundibular axons and development of ectopic posterior pituitary [11, 12].

The key imaging diagnostic findings of this syndrome are the absence of the pituitary stalk combined with ectopic site of the bright T1W posterior pituitary in the infundibular recess of the hypothalamus together with hypoplasia of the pituitary gland [10]. This was encountered in the three patients with confirmed diagnosis in this study.

Reported associated anomalies were noted to involve the midline structures (e.g. cleft lip, optic nerves hypoplasia and cerebral midline congenital anomaly). This may suggest that the gene responsible for these midline defects is the same responsible for PSIS. However, owing to the limited number of the diagnosed cases of PSIS, there is still no complete standard edited sources for the full clinical presentation of this disease, which is usually complex and diverse. Some shared signs were reported, as neonatal hyperbilirubinemia, hypoglycemia and small external genitalia, however the dwarfism and growth is

the most common presentation adolescent presentation [13]. In this study, signs of dwarfism were noted in the three diagnosed patients without other definite associated anomalies.

Conclusion

Although of rare incidence, pituitary stalk interruption syndrome (PSIS) is an entity which leads to pituitary dwarfism and should be kept in mind while investigating a child with pituitary dwarfism and radiologists should be aware of its rarely encountered diagnostic MRI findings for early diagnosis and treatment.

Abbreviations

MRI: Magnetic resonant imaging.; PSIS: Pituitary stalk interruption syndrome.

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None.

Author contributions

MA: Corresponding author, collected data and the major editor. MS: Clinical pathology consultant, who helped in growth hormone level tests. AA: Shared in writing of the research and interpretation and gathering of the clinical and radiological data. MSA: Major sharer in data collection and analysis. All authors read and approved the final manuscript.

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Availability of data and materials

Available on request with the corresponding author. The authors declare that they had full access to all data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Declarations

Ethics approval and consent to participate

Written consents were assigned by the head of the family of the included patients, and the study was approved by the ethics committee of our institute (Almana General Hospital- KSA-Eastern Province).

Consent for publication

All researchers are accepting to publish this original article. This study is not previously published.

Competing interests

The authors declare that they have no competing interests.

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