Letter to the Editor

Pituitary Stalk Interruption Syndrome (PSIS)

Sir,

A 3-yr and six-mth old boy was referred for evaluation of recurrent hypoglycemic seizures from the early neonatal period. A product of non-consanguineous marriage, he had an uneventful antenatal period and normal birth with no history of prolonged physiological jaundice. There was no history of polyuria or polydipsia. On general assessment he was an active child with average intelligence. He had short stature with height less than 3rd centile and weight at 50th centile. Physical examination was normal with no evidence of micropenis or midline craniofacial defects. His bone age was around 1 yr (assessed by Greulich and Pyle chart). Investigations done in the recent past including liver and renal functions, serum electrolytes, hemogram, serum aminoacid, urine for aminoacids and organic acid and CT scan brain were all normal. During the peak of a hypoglycemic episode (Random plasma glucose 25 mg/dl) which occurred spontaneously during the hospital stay hormonal evaluation was done which revealed inappropriately low levels of growth hormone (0.84 ng/ml) and cortisol (15.8 mcg/dl) and a normally suppressed insulin (3.95 mIU/ml). Baseline thyroid profile showed low free T_4 (0.80 ng/dl) and inappropriately low TSH (1.61 mIU/ml) and normal prolactin (18.1 ng/ml). MRI brain with gadolinium contrast revealed empty sella with normal anterior and posterior clinoid processes. A small focus, hyperintense signal in T1 weighted images (posterior pituitary) was visualized in the hypothalamic region and the pituitary stalk was not visualized even after gadolinium enhacement. Thus the overall clinico-radiological and biochemical profile confirmed the diagnosis of congenital panhypopituitarism secondary to anterior pituitary hypoplasia with ectopic posterior pituitary (Pituitary Stalk Interruption Syndrome) and he was started on appropriate hormonal replacement therapy.

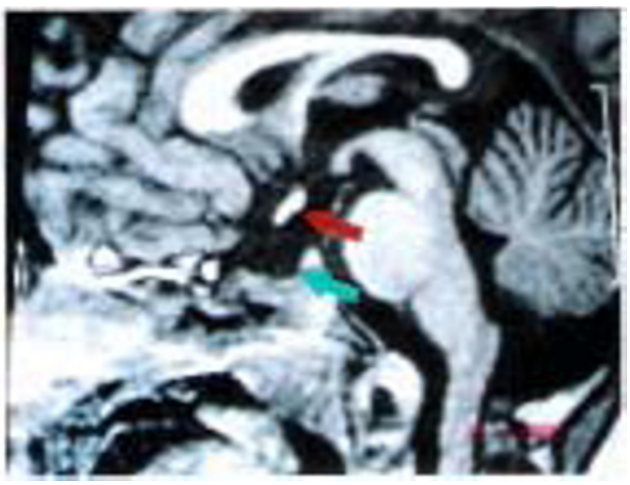

Fig. 1. MRI brain with contrast reveals empty sella, anterior pituitary hypoplasia, ectopic posterior pituitary bright spot and non-visualization of stalk.

DISCUSSION

Idiopathic Growth Hormone Deficiency (GHD) occurs in 1/4000 to 1/10000 live births.[1] Previous studies have shown that an anatomical abnormality of the hypothalamo- pituitary region by magnetic resonance imaging (MRI) is a marker of severe and often permanent GHD.[1,2,3,4,5,6] The complete form of this abnormality is the Pituitary Stalk Interruption Syndrome (PSIS) the hallmark of which is Ectopic Posterior Pituitary (EPP). It is also characterized by absence or faint visualization of pituitary stalk and absent or hypoplastic anterior lobe (adenohypophysis). Clinically, the syndrome is associated with either isolated GH deficiency (GHD) or multiple anterior pituitary hormone deficiency (MPHD) (i.e.) growth hormone deficiency associated with abnormality of atleast one of the other anterior pituitary hormones, but normal posterior pituitary function as observed in our case.[1,2] Depending on the age at diagnosis, the common modes of presentation include neonatal hypoglycemia, prolonged neonatal (physiological) jaundice, micropenis, cryptorchidism and short stature.[1,2] Infrequently, the radiological entity of PSIS may be associated with other midline craniofacial anomalies like Chiari malformation, septo-optic dysplasia, single central incisor or absent left internal carotid.[1,2,5] Studies have correlated adenohypophyseal function to the absence of pituitary stalk and it has been observed that MPHD is usually associated with absence of pituitary stalk.[2,7] This may progress from isolated GHD to MPHD even during second or third decade of life.[8]

The pathogenesis of PSIS is unclear. Pituitary gland development is a complex multi-step process involving the fusion of adenohypophysis (Rathke's pouch, ectodermal) with the neurohypophysis (posterior pituitary, neurectodermal origin). The whole sequence of events during early embryogenesis is well orchestrated and controlled by transcription factors including Pit-1, PROP -1, HESX1 and LHX. One of the explanations for PSIS is a traumatic hypothesis involving transection of the stalk during breech delivery followed by hypertrophy of the proximal axons with subsequent reorganization leading to EPP. However, a significant percentage of patients with this abnormality were delivered normally and no clear cause and effect role could be established in

a large series of congenital growth hormone deficiency.[6] Hence a defective induction of mediobasal structure of the brain during early embryogenesis was entertained which could also explain the associated midline brain abnormalities.[6] Our patient neither had a history of breech delivery nor any other midline structural defects. Studies which looked at genetic abnormalities in PSIS have not demonstrated any abnormalities in the transcription factors.[1,9]

Thus, non-visualization of pituitary stalk even after gadolinium enhancement in magnetic resonance imaging (MRI) may thus indicate profound adenohypophyseal dysfunction. Hence management not only includes appropriate hormonal replacement but also close follow up for monitoring of other hormonal deficiencies especially if initially presenting with isolated GHD.

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REFERENCES

1. Pinto G, Netchine I, Sobrier L, Brunelle F, Souberbielli E, Brauner R. Pituitary Stalk Interruption Syndrome: A clinical – Biological – Genetic Assessment of its pathogenesis. *J Clin Endocrinol Metab* 1997; 82 : 3450-3454.
2. Chen S, Leger J, Garel C, Hassan M, Czernichow P. Growth Hormone Deficiency with Ectopic Neurohypophysis: Anatomical variations and relationship between the visibility of the pituitary stalk asserted by Magnetic Resonance Imaging and anterior pituitary function. *J Clin Endocrinol Metab* 1999; 84 : 2408-2413.
3. Maghnie M, Salati B, Silvia B, Rallo M, Tinelli C, Autelli M, et al. Relationship between the morphological evaluation of the pituitary and the growth hormone (GH) response to GH – Releasing Hormone plus Arginine in Children and adults with congenital hypopituitarism. *J Clin Endocrinol Metab* 2001; 86: 1574-1579.
4. Hamilton J, Blaser S, Daneman D. MR Imaging in Idiopathic Growth Hormone deficiency. *Am J Neuroradiol* 1998; 19: 1609-1615.
5. Patkar D, Patankar T, Krishnan A, Prasad S, Shah H, Limdi J. MR Imaging in children with ectopic pituitary gland and anterior hypopituitarism. *J Postgad Med* 1999; 45 : 81-83.
6. Triulzi F, Scotti G, Di Natale B, Pellini C, Lukezic M, Scognamiglio M, Chiumello G. Evidence of a congenital midbrain anomaly in pituitary dwarfs: a magnetic resonance imaging study in 101 patients. *Pediatrics* 1994; 93 : 409-415.
7. Ultmann MC, Siegel SF, Hirsch WL, Finegold DN, Foley TP Jr. Pituitary stalk and ectopic hyperintense T1 signal on magnetic resonance imaging. Implications for anterior pituitary dysfunction. *Am J Dis Child* 1993; 147 : 647-652.
8. Crowne EC, Shalet SM. Adult panhypopituitarism presenting as idiopathic growth hormone deficiency in childhood. *Acta Paediatr Scand* 1991; 80 : 255-258.
9. Arrigo T, Wasniewska M, De Luca F, Valenzise M, Lombardo F, Vivenza D. Congenital adenohypophysis aplasia: Clinical features and analysis of transcriptional factors embryonic pituitary development. *J Endocrinol Invest* 2006; 29(3) : 208-213.