Case Report

ISSN (Print): 2958-0307

Journal of Association of Clinical Endocrinologist and Diabetologist of Bangladesh

July 2022, Vol. 1, No. 2, pp. 69-71

Five cases of short stature and delayed puberty with primary empty sella syndrome

Rahman MA[1], *Morshed MS[2], Jahan S[3], Hasan M[4], Hasanat MA[5], Fariduddin M[6]

[1]Mohammad Atiqur-Rahman, Ex-resident, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [2]Md Shahed Morshed, Ex-resident, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [3]Sharmin Jahan, Associate Professor, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [4]Mashfiqul-Hasan, Ex-resident, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [5]Muhammad Abul Hasanat, Professor, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [6]Md Fariduddin, Professor, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

We reported five adolescent boys of proportionate short stature and delayed puberty. None of the patients had any risk factors or stigma of growth hormone and other pituitary hormone deficiency. But investigations revealed panhypopituitarism with empty sella detected by pituitary MRI in all cases. Children with primary empty sella syndrome require an active evaluation of hormonal status for long-term outcomes. *[J Assoc Clin Endocrinol Diabetol Bangladesh, July 2022; 1 (2): 69-71]*

Keywords: Empty sella syndrome, Panhypopituitarism, Short stature, Delayed puberty

***Correspondence:** Md Shahed Morshed, Emergency Medical Officer, Kurmitola General Hospital, Dhaka-1206, Bangladesh. Email: shahedk62@gmail.com, Cell: +88 01738-42019

Introduction

Empty sella syndrome (ESS) refers to a radiological or autopsy finding of sella turcica where the space is filled up by cerebrospinal fluid compressing the pituitary against the floor. A defect in the sellar diaphragm either congenital or compression by raised intracranial pressure/pituitary volume is known as primary ESS.[1] While ESS is a common finding in adults, it is usually rare in the pediatric population without endocrinopathies. However, several endocrinopathies especially multiple hormone deficiencies, isolated growth hormone deficiency, and gonadotropin abnormality are relatively common in children and adolescents with empty sella.[2,3] Hence, ESS with reduced sellar dimension in children is considered one of the mid-line defects in pituitary dwarfs.[4] Here we reported five cases of short stature who had also primary empty sella in pituitary MRI.

Case presentation

All five cases were admitted to the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU) for evaluation of short stature. Their age ranged from 12 to 17 years and all were male (Table-I). Their height and weight were far below the 3rd percentile for their age and sex, had proportional

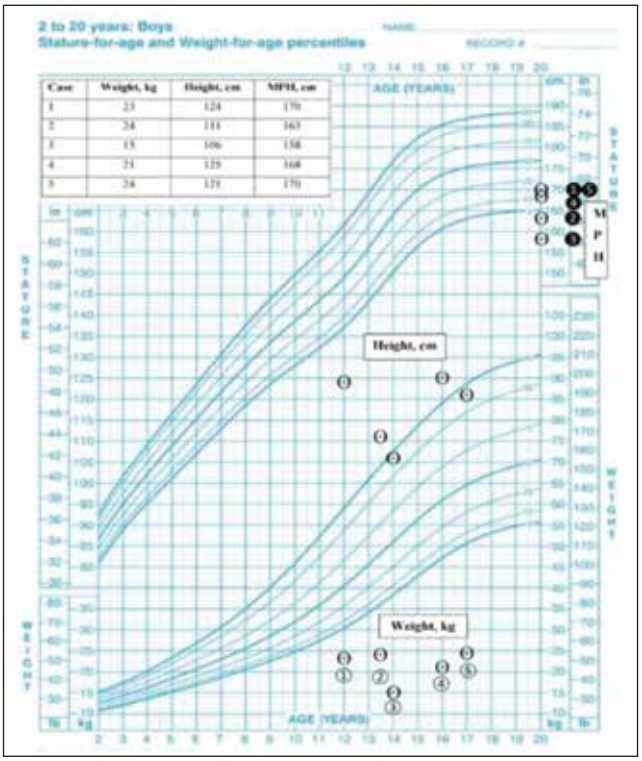

Figure-1: Height (cm), mid-parental height (MPH, cm), and weight (kg) of the study population in the growth chart

Table-I: Clinical and Laboratory findings of the patients

Investigations		Case- 1	Case- 2	Case- 3	Case- 4	Case- 5	Ref. values
Age, years		12	13½	14	16	17	
Sex				All boys			
Family history of short stature in 1st-degree relatives		Absent	Present	Absent	Absent	Absent	
Secondary sexual characteristics				Absent in all			
General investigations				Unremarkable in all			
Bone age, years							
Growth hormone, ng/ml							
	Post-levodopa	8-9	8-9	8-9	10-11	9-12	>10.0
	Post-exercise	0.07	0.09	0.13	0.10	0.39	
Thyroid axis	TSH, mIU/ml	0.12	0.06	0.14	0.19	0.31	0.47-3.41
	FT4, ng/dl	6.0	8.20	2.30	3.31	2.44	
Adrenal axis	Basal cortisol, nmol/L	0.65	0.74	1.0	1.20	0.82	0.80-1.80
	1h-stimulated cortisol, nmol/L	551	612	580	164	701	83-550
Gonadal axis	Luteinizing hormone, IU/ml	–	–	–	412	–	≥550
	Total testosterone, ng/dl	0.01	0.2	<0.01	0.13	0.25	0.02-0.30
Prolactin, ng/ml		12.10	9.20	16.40	15.90	17.80	31.0-733.0
Empty sella in pituitary MRI*		6.20	5.40	8.10	1.90	4.70	≤10.0
		Partial	Complete	Partial	Complete	Complete	

Cut-off for the category of empty sella with 50% of the space fulfillment by CSF.[1]

short stature (Figure-1). All of their antenatal and perinatal histories were uneventful with a normal milestone of development as well as a normal intelligent quotient. They had not yet developed any secondary sexual characteristics and had no features suggestive of chronic illness. Only one of them had a family history of short stature (Table-I). They had no history of headache, head injury, surgery, or irradiation to the head. None of them had any dysmorphic features including any mid-line defects. The general investigations were unremarkable, whereas the endocrine evaluation revealed features suggestive of panhypopituitarism in all cases (at least two axes affected). Growth and gonadal axes were affected in all cases. Hypothyroidism was present in two cases with low normal FT4 in one case. One patient had partial adrenal insufficiency. Bone age was delayed in all cases (Table-I). MRI of the pituitary revealed partial empty sella (<50% of sella) in two cases and complete empty sella in three cases (Figure-2). Levothyroxine and hydrocortisone were started in deficient patients. Unfortunately, growth hormones could not be initiated in any of them due to cost. Pubertal induction was done by intramuscular testosterone therapy.

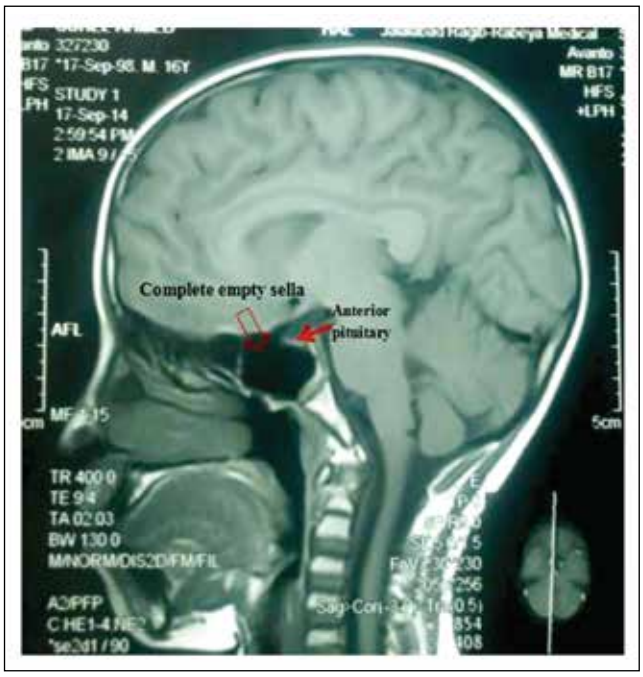

Figure-2: Complete empty sella in a 16-year boy with panhypopituitarism (case no- 4)

Discussion

ESS is a common finding in children with abnormal pituitary functions. However, hypoplastic anterior pituitary, ectopic posterior pituitary, and disrupted stalk rather than ESS are found to be associated with pituitary dwarfism.[5] Thus the association between ESS with pituitary dwarfism is questionable.[3,6] Despite that,

the association remained significant with multiple anterior pituitary hormone abnormalities.[3]

One in 35,000 children develops growth hormone deficiency (GHD) each year with a higher incidence in boys than girls.[7] Among 303 Danish children with childhood-onset GHD, only one had empty sella.[8] None of our patients had any risk factors or stigma of GHD. Despite having thyroid and adrenal axes involvement, their milestone of development and intelligence were normal. It is possible that multiple hormonal deficiencies evolved over time with ignorance of symptoms.[9] So, patients with GHD require lifelong monitoring for other anterior pituitary hormone deficiencies. Diabetes insipidus (DI) was also reported in ESS, however, none of our patients had features of DI.[3] Recombinant growth hormone therapy (GHT) is effective and safe in patients with GHD.[10] Unfortunately, none of our patients could afford the cost of GHT.

Conclusions

ESS is associated with multiple pituitary hormone deficiencies in children with short stature and hypogonadism. However, diagnosis of deficiencies may require active evaluation as clinical features may be absent.

Acknowledgement

We are grateful to the participant of the study for giving the consent to report the case.

Conflict of Interest

The authors have no conflicts of interest to disclose.

Financial Disclosure

The author(s) received no specific funding for this work.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Written informed assent was taken from the patients and their legal guardians.

How to cite this article: Rahman MA, Morshed MS, Jahan S, Mashfiqul-Hasan M, Hasanat MA, Fariduddin M. Five cases of short stature and delayed puberty with primary empty sella syndrome. J Assoc Clin Endocrinol Diabetol Bangladesh, 2022; 1 (2):69-71

Publication History

Received on: 12 February 2022

Accepted on: 24 April 2022

Published on: 1 July 2022

References

1. De Marinis L, Bonadonna S, Bianchi A, Maira G, Giustina A. Primary empty sella. J Clin Endocrinol Metab 2005;90(9):5471-7. doi: 10.1210/jc.2005-0288.
2. Lenz AM, Root AW. Empty sella syndrome. Pediatr Endocrinol Rev 2012;9(4):710-5.
3. Cacciari E, Zucchini S, Ambrosetto P, Tani G, Carlà G, Cicognani A, et al. Empty sella in children and adolescents with possible hypothalamic-pituitary disorders. J Clin Endocrinol Metab 1994;78(3):767-71. doi: 10.1210/jcem.78.3.8126155.
4. Zucchini S, Ambrosetto P, Carlà G, Tani G, Franzoni E, Cacciari E. Primary empty sella: differences and similarities between children and adults. Acta Paediatr 1995;84(12): 1382-5. doi: 10.1111/j.1651-2227.1995.tb13574.x.
5. Bozzola M, Adamsbaum C, Biscaldi I, Zecca M, Cisternino M, Genovese E, et al. Role of magnetic resonance imaging in the diagnosis and prognosis of growth hormone deficiency. Clin Endocrinol (Oxf) 1996;45(1):21-6.
6. di Natale B, Scotti G, Pellini C, Del Maschio A, Triulzi F, Petecca C, Uboldi F, Chiumello G. Empty sella in children with pituitary dwarfism: does it exist? Pediatrician 1987;14(4):246-52.
7. Lindsay R, Feldkamp M, Harris D, Robertson J, Rallison M. Utah Growth Study: growth standards and the prevalence of growth hormone deficiency. J Pediatr 1994;125(1):29-35. doi: 10.1016/s0022-3476(94)70117-2.
8. Stochholm K, Gravholt CH, Laursen T, Jørgensen JO, Laurberg P, Andersen M, et al. Incidence of GH deficiency - a nationwide study. Eur J Endocrinol 2006;155(1):61-71. doi: 10.1530/eje.1.02191.
9. Cerbone M, Dattani MT. Progression from isolated growth hormone deficiency to combined pituitary hormone deficiency. Growth Horm IGF Res 2017;37:19-25. doi: 10.1016/j.ghir.2017.10.005.
10. Hou L, Luo XP, Du ML, Ma HM, Gong CX, Li YC, et al. Efficacy and safety of recombinant human growth hormone solution in children with growth hormone deficiency in China: a multicenter trial. Zhonghua Er Ke Za Zhi 2009;47(1):48-52.