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Short Communication

Primary empty sella and associated pituitary hormonal abnormalities in children: An observational study

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Abstract

Objective: To find out the spectrum of pituitary hormonal abnormalities in children with primary empty sella syndrome. **Materials and Methods:** This retrospective observational hospital-based study was carried out in a tertiary care teaching hospital. Children referred to the pediatric endocrinology clinic with clinical features of pituitary hormonal abnormalities were evaluated. Children who were found to have empty sella were included in the study and hormonal profile of these children were studied. **Results:** There were 14 patients in the study group. Isolated growth hormone deficiency was the most common associated abnormality (64%) followed by multiple pituitary hormone deficiencies in 5 (35%) children. Hypothyroidism was observed in 4 patients (28%) and hypocortisolism in 2 cases (14%). Hypogonadism was observed in one girl on follow-up (7.1%). **Conclusions:** Significant numbers of children with pituitary hormone abnormalities have primary empty sella as a cause. Therefore, these children need to be evaluated for all pituitary hormones and should be regularly followed up for evolving hormonal deficiencies.

Key words: *Empty sella, Growth hormone deficiency, Multiple pituitary hormone deficiencies*

Empty sella is a radiological diagnosis of a sella turcica that is partially or completely filled with cerebrospinal fluid (CSF). The empty sella turcica is defined as an intrasellar herniation of the suprasellar subarachnoid space with compression of the pituitary gland [1], which in many cases is thinned out against the sellar floor. The empty sella may be classified as primary or secondary.

The primary empty sella is an idiopathic form of empty sella which occurs in persons without any known pituitary insult. Here, deficiency of the diaphragm sella is the primary defect. This allows suprasellar cisterns to herniate into sella exposing the pituitary to the CSF pulsations with compression of the gland [2]. Sella may be of normal size or enlarged. On the contrary, secondary empty sella develops after pituitary surgery, irradiation, hemorrhage, infarct, infection, or other insult to the pituitary gland.

Endocrine abnormalities in the empty sella syndrome have been studied by different groups; though, the data is limited in children [3]. Isolated growth hormone (GH) deficiency is the most common abnormality noted. Multiple pituitary hormone deficiencies, precocious puberty, delayed puberty, hyperprolactinemia etc., have also been described. There is a great paucity of literature on pituitary hormonal abnormalities in children with primary empty sella syndrome. Therefore, this study was undertaken to find out the spectrum of pituitary hormonal abnormalities in children with primary empty sella syndrome.

MATERIALS AND METHODS

This retrospective hospital-based case study was conducted at a tertiary care center in North Kerala, over a period of 6-year from January 2009 to January 2015. Ethical clearance was obtained from the Institutional Ethics Committee for reviewing the case records. All children referred to the pediatric endocrinology clinic with clinical features of pituitary hormonal abnormalities were evaluated initially for hormonal deficiencies by clinical examination and laboratory investigations.

Those children who were found to have at least one of the hormonal deficiencies were further evaluated by 1.5 tesla magnetic resonance imaging scan to delineate the pituitary anatomy. A retrospective analysis of the case records was done and those children who were found to have empty sella were included in the study. Those children who had any of the predisposing factors for a secondary empty sella were excluded. Following laboratory investigations were done in all the recruited patients. All tests were done by automated chemiluminescence immunoassay method.

- Routine general laboratory tests, which included complete blood picture, renal and liver function tests, calcium

profile, and X-ray for bone age assessment (Greulich pyle method)
- Thyroid profile (FT3, FT4), thyroid stimulating hormone (TSH) levels
- GH secretion was tested after stimulating with clonidine at a dose of 0.15 mg/m^2 orally. Blood samples were drawn at 0, 30, 60, 90, 120 min thereafter. A peak level of GH <5 ng/ml was taken as evidence of complete GH deficiency and 5-10 ng/ml as partial GH deficiency. Patients in pubertal age (bone age >10 years) were primed with sex hormones prior to GH testing
- Insulin-like growth factor-1 (IGF-1) and IGF binding protein-3 were determined at diagnosis, and age-specific cutoffs were taken
- Basal cortisol testing was done at 8 am. Value more than 5 mcg/dl was taken as sufficient. For those who had lower values, adrenocorticotrophic hormone (ACTH) was also estimated
- Luteinizing hormone (LH) and follicle-stimulating hormone levels were estimated after the age of 13 years in girls and 14 years in boys. Leuprolide acetate was given subcutaneously at a dose of 1000 mcg and LH was estimated at 0 min, 1 h, and 2 h. A stimulated value >5 IU/L was taken as normal.

RESULTS

There were 14 patients in the study group. All of them except one presented with short stature. One child presented with features of adrenal insufficiency following an episode of fever. Clinical presentation and associated hormonal defects are shown in Table 1. Out of the total of 14 patients, 6 were females (42.8%) and 8 were males (57.1%). Mean age at diagnosis was 9.3±5 years. The youngest patient was 4 years, and the oldest one was 15 years old. All, except one, had GH deficiency (92%). Isolated GH deficiency was noted in 9 children (64.2%). Five children had multiple pituitary hormone deficiencies (35%). Hypothyroidism was observed in 4 patients (28%), out of which 1 was a case of primary hypothyroidism (antibody negative). Hypogonadism was observed in one girl on follow-up (7.1%) and hypocortisolism in 2 cases (14%). None of the children had features of diabetes insipidus, and none of the children was obese.

Table 1: Clinical presentation and hormonal deficiencies of children with empty sella

Age in years	Sex	Clinical features	Hormones deficient
6.5	F	Short stature	GH
15	M	Seizures, shock, dullness	ACTH, cortisol, primary hypothyroidism
13	M	Short stature	GH
9	M	Short stature	GH
12	F	Short stature	GH, hypothyroidism, cortisol
11	F	Short stature, delayed puberty	GH, hypogonadism
8	M	Short stature	Partial GH deficiency
4	M	Short stature	GH
5	M	Short stature	GH
7	F	Short stature	GH
12	F	Short stature	GH, hypothyroidism
8	F	Short stature	GH
8.5	M	Short stature, constipation	GH, hypothyroidism
9.5	M	Short stature	GH

GH: Growth hormone

DISCUSSION

Empty sella is an infrequent finding in children. In adults, it is more commonly found in older, obese, and multiparous women and may be asymptomatic. However, in children, empty sella is more likely to be associated with clinical symptoms and endocrinopathies. The incidence of empty sella is 1.2% in the general population to 68% in children with known endocrinopathies [4]. There is a definite female preponderance in the case of adult empty sella as reported by several researchers but the sex distribution in children has not been reported [5]. In this study group, there is a slight male preponderance (57%).

Children with growth retardation and abnormal hypothalamic-pituitary functions have a high incidence of empty sella. However, empty sella is detected in considerable number (10%) of children with normal hypothalamic-pituitary function [6]. GH deficiency is the single most common hormonal dysfunction described in children with primary empty sella [7]. In the present study also, the most common abnormality noted was GH deficiency. Short stature was the most common presenting feature. 64% of the children had isolated GH deficiency, and the rest had associated other hormonal abnormalities.

One child presented with isolated ACTH deficiency, and he had associated primary hypothyroidism. He presented with seizure, hypoglycemia, and shock following an episode of fever. Further investigations showed low cortisol and low ACTH, the other pituitary hormones being normal; he had low T3, T4, and high TSH and was negative for anti-thyroglobulin and anti-thyroperoxidase antibody. Gulcan et al. have reported a similar case [8]. Obesity has been reported as a common finding associated with empty sella in adults [3], but none of the patients in this study were found to be obese.

Hypogonadotropic hypogonadism was noted in one child on follow-up. The exact prevalence cannot be determined because some of the study subjects were young and hypogonadotropic

hypogonadism can be detected only after the bone age of 13 years. None of the children had diabetes insipidus or precocious puberty. Two children had hypocortisolism. Cacciari et al. [9] have described hypogonadism associated with empty sella.

Our study has a limitation as this is a cross-sectional study. Since pituitary hormonal abnormalities can evolve over time, these children need to be followed up over longer periods of time to know the actual occurrence of hormonal deficiencies.

CONCLUSION

This study shows that primary empty sella is not a rare finding in children with pituitary hormonal deficiencies. Children with empty sella need to be evaluated for all pituitary hormones and should be regularly followed up for evolving hormonal deficiencies.

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