

Primary Empty Sella Syndrome and Central Precocious Puberty in a Boy with Recurrent Headache. A Case Report

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Abstract

Central precocious puberty (CPP) is commoner in girls in comparison to boys. Its Causes are idiopathic in over 80% girls while being secondary to central nervous system pathologies in 80% boys. CPP in association with empty sella syndrome, a condition often linked with idiopathic intracranial hypertension, is rare. We report a case of a boy with CPP and recurrent headaches in whom empty sella was diagnosed. Management consisted of GnRH analog therapy. Follow-up (clinical, ophthalmologic, and repeat MRI) remained uneventful. ES as cause of CPP must be known and close surveillance considered as secondary complications may occur.

Keywords: *Primary Empty Sella; Central Precocious Puberty; Headaches; Etiology*

Abbreviations

ES: Empty Sella; CPP: Central Precocious Puberty; IIH: Idiopathic Intracranial Hypertension; CSF: Cerebrospinal Fluid; MRI: Magnetic Resonance Imaging; BMI: Body Mass Index; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; S-DHEA: Dehydroepiandrosterone Sulfate; 17(OH)P: 17 Hydroxyprogesterone; TSH: Thyroid Stimulating Hormone; ACTH: Adreno Corticotropin Hormone

Introduction

Precocious puberty is defined by the early occurrence of secondary sexual characteristics in children (< 8 years in girls, and < 9 years in boys). It is relatively common, with a reported incidence that is between 1/5'000 to 1/10'000 [1]. Central precocious puberty (CPP) is commoner in girls with etiology that is often idiopathic (over 80% cases), in comparison to boys in whom it is secondary to a lesion in 80 to 95% cases, so that central nervous system tumours and/or lesions are feared in this population group.

Primary empty sella (ES), also known as arachnoidocele, is an anatomical condition characterized by a sella turcica that is partially, less than 50% filled with cerebrospinal fluid (CSF) and pituitary thickness > 3 mm or completely, more than 50% filled with CSF and pituitary thickness < 2 mm.

ES is consequent to herniation of the subarachnoid space into the sella [2]. Primary ES as cause of CPP is rather rare, with only few cases reported in the literature [3-5], it has, however, been reported in several children as well as adult patients with idiopathic intracranial hypertension [5].

The association of primary ES with CPP and headaches in the same patient is, to our knowledge, very rare.

In spite the precise causality relationship between primary ES and CPP remaining a matter of debate, this entity needs to be known and considered in children with CPP.

We report a case of a boy who presented with clinical signs of precocious puberty and recurrent headaches, in whom primary ES was diagnosed on radiological investigation.

Case Report

A 10.4-year-old boy was referred to our clinic for signs of precocious puberty evolving since a year and half. He was a product of normal term pregnancy, with birth weight of 3080g, birth length of 46,5 cm and head circumference of 34 cm. He often complained of headache that had not been investigated, but he had, however, received antibiotic treatment for sinusitis. The boy's mother suffered from migraine, had her menarche at the age of 13.6 years, the father was healthy. One of the boy's 3 sisters had past history of CPP diagnosed at the age of 6.0 years, for which GnRH analog therapy was administered. The younger brother aged 5 years was healthy.

Upon clinical examination, height was 143.5 cm (+ 1.09 SDS, Sempé French growth curves) [6], weight 37 Kg, BMI 18 kg/m², blood pressure was 100/70 mm Hg, pubertal stage A1P3G3 (Tanner's staging), with testicular length of 3.7 x 2.5 cm, in favour of enhanced precocious puberty. He was investigated, and his results showed, on endocrine work-up, basal FSH 8 UI/l, peak 14.7 UI/L, basal LH level of 3.4 UI/L peaking at 37.7 UI/L on the LHRH test. LH/FSH ratio was 2,5, plasma testosterone 15.8 nmol/L, delta-4 androstenedione 3.1 nmol/L (N 1.5 - 17), S-DHEA 1104 nmol/L (N 2600 - 4000), 17(OH)P normal, morning cortisol 301 nmol/L, TSH 1.92 mUI/L, FT4 13.9 pmol/L, Prolactine 4.7 ng/ml (N 2.2 - 8.6), normal plasma electrolytes, and normal GH secretion (Ornithine test). Bone age assessed by Greulich and Pyle method [7] was 12 years.

The head MRI revealed the presence of an important arachnoidocele that compressed anterior pituitary lobe against the floor of pituitary sella, with pituitary gland height measured at 2.3 mm (Figure 1). There were no signs in favour of raised intracranial pressure. Ophthalmologic tests (visual acuity, visual field, fundus examination, etc.) were unremarkable.

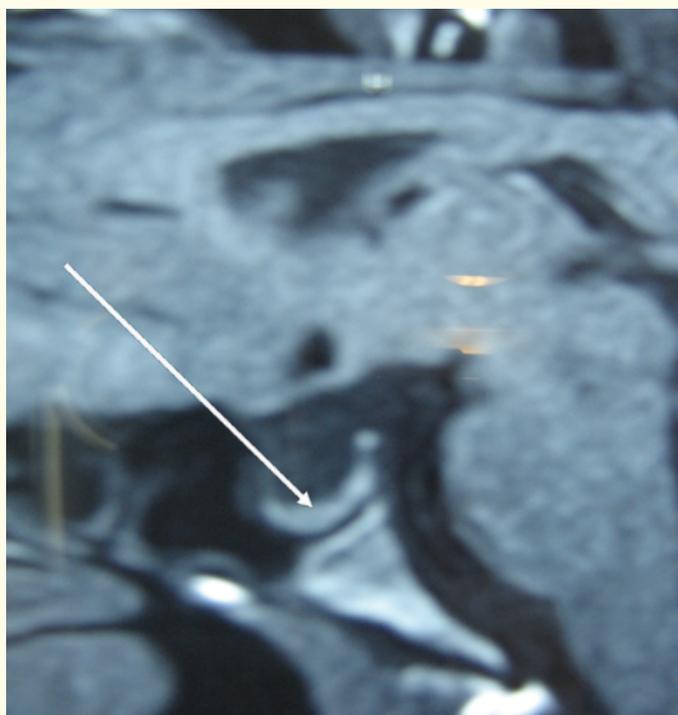


Figure 1: Arachnoidocele (arrow), with flattened anterior pituitary lobe.

The boy was managed with GnRH agonist therapy for two years, was reviewed clinically twice a year and had control MRI two years after the first, with results that were identical to the previous. He grew up and attained his predicted final height [173 cm (-0.08 SDS) at age 17 years], and complained less often of headaches.

Comments

Primary ES has been linked with various hypothalamic-pituitary dysfunctions in children, with an estimated frequency of 10.9% among patients with hypothalamic-pituitary endocrinopathies [8].

Its precise prevalence in general pediatric population remains, however, difficult to ascertain. In a study by Takanashi, *et al.* the frequency of ES in children without any pathology was estimated at 1.2% [9]. In this same study, primary ES was present in all patients with idiopathic intracranial hypertension (IIH), a known cause of headaches, and a symptom that our patient complained of, despite the absence of ophthalmologic and cranial MRI signs. Although the later may be absent in about 19% children with IIH, our patient did not meet the set criteria to be considered as suffering from this disorder due to lack of some additional symptoms (nausea, vomiting, transient visual obscurations, tinnitus, etc.) and CSF study required for the diagnosis [10]. In spite of cases of CPP secondary to primary ES having been reported, this pathological association remains rare [3-5].

Establishing a pathophysiological link between primary ES with CPP, and even with other reported endocrinopathies (growth hormone deficiency, gonadotropin deficiency, ACTH and TSH deficiencies, and diabetes insipidus) is a difficult task for several reasons:

- In a post-mortem histologic study of an adult male patient with ES and flattened thin rim of adenohypophyseal tissue discovered incidentally, Bergeron, *et al.* found, that all five anterior pituitary cell types were identifiable by immunohistochemistry in adequate number and with normal intracellular granules [11]. This inferring that ES did not affect anterior pituitary functions.
- The fact that pituitary height is not correlated with associated endocrinopathies adds to the complexity of physiopathological mechanisms that would explain the relationship between ES and reported endocrine disturbances [12]. On the other hand, however, cases of resolution and/or pituitary hormones remittance after reduction of intracranial pressure either by lumbar puncture or medical treatment with acetazolamide have been also reported [13,14].

This, therefore, support there could be causality relationship between primary ES and anterior pituitary hormone disturbances. Lack of correlation between the extent of pressure exerted on the pituitary gland by the arachnoidocele (as translated by the pituitary height), 2.3 mm in our patient, prompts us to question as to whether this malformation leads to suppression of inhibitory inputs to GnRH neurons, as consequence of which CPP occurs.

Management of children with CPP secondary to primary ES is classical, with GnRH analogs. We added symptomatic treatment for headaches and this was sufficient. Follow-up consisted of bi-annual clinical examinations, regular ophthalmologic surveillance with control MRI two years after diagnosis all of which were unremarkable.

Conclusion

Primary ES is a possible cause CPP in children, additional investigations in children with this disorder must include screening for all pituitary function, along with ophthalmologic assessment especially in those children with symptoms suggestive of IIH. CPP management in this case is similar to that of classical precocious puberty, the overall prognosis is good. We suggest bi-annual follow-up during treatment and empirically 3 to 4 years after treatment to make sure no other endocrinopathies occur.

Conflict of Interest

No conflict of interest to declare.

Bibliography

1. Partch CJ and Sippell WG. "Pathogenesis and epidemiology of precocious puberty. Effects of exogenous oestrogens". *Acta Pathologica, Microbiologica, et Immunologica Scandinavica* 109.S103 (2001): S144-S155.
2. Shulman DI, et al. "Hypothalamic-pituitary dysfunction in primary empty sella syndrome in childhood". *Journal of Pediatrics* 108.4 (1986): 540-544.
3. Scire G, et al. "Primary empty sella and endocrinopathies in childhood: high prevalence among children with precocious puberty". *European Journal of Pediatrics* 147.6 (1988): 665-666.
4. Rapaport R and Lograno R. "Primary empty sella syndrome in childhood: association with precocious puberty". *Clinical Pediatrics (Phila)* 30.8 (1991): 466-471.
5. Zucchini S, et al. "Primary empty sella: differences and similarities between children and adults". *Acta Paediatrica* 84.12 (1995): 1382-1385.
6. Sempé M, et al. "Auxologie method et sequences". Théraplix. Paris (1979).
7. Greulich WW and Pyle SI. "Radiographic Atlas of Skeletal Development of the Hand and Wrist". (2nd edition) California: Stanford University Press (1959).
8. Cacciari E, et al. "Empty sella in children and adolescents with possible hypothalamic-pituitary disorders". *Journal of Clinical Endocrinology and Metabolism* 78.3 (1994): 767-771.
9. Takanishi J, et al. "Empty sella in children as a key for diagnosis". *Brain and Development* 23.6 (2001): 422-423.
10. Aylward SC. "Pediatric idiopathic intracranial hypertension: a need for clarification". *Pediatric Neurology* 49.5 (2013): 303-304.
11. Bergeron C, et al. "Primary empty sella a histologic and immunocytologic study". *Archives of Internal Medicine* 139.2 (1979): 248-249.
12. De Marinis L, et al. "Primary Empty Sella". *Journal of Clinical Endocrinology and Metabolism* 90.9 (2005): 5471-5477.
13. Quintos JB, et al. "Transient pituitary dysfunction, empty sella, pseudotumor cerebri in a morbidly obese adolescent". *Pediatric Endocrinology Reviews* 3.4 (2006): 576-578.
14. Zagardo MT, et al. "Reversible empty sella in idiopathic intracranial hypertension: an indicator of successful therapy?" *American Journal of Neuroradiology* 17.10 (1996): 1953-1956.

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