A Case of Craniopharyngioma Presenting as Precocious Puberty after a Period of Stunted Growth

Mauro Bozzola[1,*], Cristina Meazza[1], Sara Pagani[1] and Elena Bozzola[2]

[1]*Department of Internal Medicine and Therapeutics, Pediatric and Adolescent Unit, University of Pavia, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*

[2]*Department of Pediatrics, Pediatric and Infectious Diseases Unit, Bambino Gesù Children Hospital, IRCCS, Rome, Italy*

Abstract: A case of craniopharyngioma (CP) presenting as precocious puberty associated with growth acceleration after a period of stunted growth is reported in a 7.5-year-old girl.

The girl grew along the 25th percentile until the age of 4 years, when her height fell down to 3rd percentile until she was 7 years old. Then, a breast bud occurred, the growth rate increased and a diagnosis of precocious puberty was made.

Brain magnetic resonance imaging revealed an oval suprasellar mass pressing and flattening the hypophysis with ventral displacement of the optic chiasm suggesting a CP. No headache or other neurophthalmologic disturbances were documented. After resection of CP, the girl showed panhypopituitarism that was treated with hormonal substitutive therapy. A few months later, the major problem became the exponential increase of the weight due to the hyperphagia not responding to any diet regimen and leading the girl to develop a severe hypothalamic obesity. In fact, at the age of 8.3 years she showed an height of 118.8 cm (-1.53 SDS) and a weight of 37.5 Kg (BMI 2.14 SDS).

In conclusion, CP has a wide range of clinical manifestations, depending of the tumour size as well as the extent of endocrine deficiency and the age of the patient. In our patient the initial growth failure was, probably, due to the compressive action of CP. Then, the onset of precocious puberty was related to the stimulating effect of the neoplasia on gonadotropic pituitary cells.

Keywords: Craniopharyngioma, precocious puberty, growth.

INTRODUCTION

Cranioparyngioma (CP) is a non-glial intracranial tumour derived from a formation of embryonaltissue and is the most common tumours of the hypothalamic-pituitary region in childhood [1, 2]. Craniopharyngioma is usually manifested clinically by nonendocrine symptoms, such headache and visual disturbances; although up to 80% of patients have evidence of endocrine dysfunction at diagnosis [2]. The majority of patients presents with growth deceleration, while precocious puberty has very rarely been described in these patients [3, 4].

Here, we describe a girl in whom precocious puberty associated with growth acceleration after a period of stunted growth was a presenting sign of CP.

CASE REPORT

A 7.5-year-old girl was referred to our department for the evaluation of breast buds that had occurred 2 or 3 months before and that progressed rapidly over the next 3 months. She was born at term of an uneventful pregnancy with a weight of 2,840 g and a length of 49.0 cm. Paternal and maternal height were 173.5 cm and 149.3 cm, respectively. Both her parents were healthy and unrelated, and have had a normal puberty progression.

Physical examination revealed a height of 113.6 cm (-1.54 standard deviation score, SDS), a weight of 23.0 Kg (body mass index, BMI 1.12 SDS), a bone age of 8.5 years, and a growth velocity during the last year of 6 cm/year (0.42 SDS), no pubic nor axillary hair.

The history of the girl showed a regular growth along the 25th percentile until the age of 4 years, but a subsequent growth failure until she was 7 years old with no justification. No headache nor other neurophthalmologic disturbances were documented.

At the moment of the evaluation, i.e. 7.5 years, a pelvic scanner showed an uterus with length of 4.1 cm, ovaries of 2.0-2.5 ml with some fullicula of 0.7-0.9 cm, and endometrium of 0.2 cm. Basal and gonadotropin releasing hormone (GnRH)-stimulated levels of follicle-stimulating hormone (FSH) were 2.9 and 10.1 mIU/ml, respectively, and luteinizing hormone (LH) 0.5 and 9.1 mIU/ml, respectively. Moreover, 17β-estradiol values were 39.7 pg/ml (<10 pg/ml in prepubertal children), prolactin 4.9 ng/ml (range 1.9-25 ng/ml), free thyroxin

*Address correspondence to this author at the Internal Medicine and Therapeutics Department, Pediatric and Adolescent Unit, University of Pavia, Auxology Research Centre, Fondazione IRCCS Policlinico San Matteo, Piazzale Golgi, 2- 27100, Pavia, Italy; Tel: +39 0382 501270;
Fax: +39 0382 502876; E-mail: mauro.bozzola@unipv.it

(FT4) 9.8 pg/ml (normal range: 8-19 pg/ml), thyroid-stimulating hormone (TSH) 2.12 mIU/ml (normal range: 0.4-4 mIU/ml), 17-hydroxyprogesterone 0.4 ng/ml (normal range: 0.49-2.3 ng/ml). These clinical and laboratory data led to a diagnosis of precocious puberty and a treatment with GnRH analogue (triptorelin) was started.

Brain magnetic resonance imaging revealed an oval suprasellar mass pressing and flattening the hypophysis with ventral displacement of the optic chiasm suggesting a CP. Therefore, the girl underwent surgery for the resection of the CP and, after it, she showed panhypopituitarism treated with substitutive therapy including desmopressin 30 mg+30 mg+30 mg per day, hydrocortisone 5 mg +2.5 mg +2.5 mg per day and L-thyroxin 25 µg per day. Obviously, the treatment with GnRH analogue was discontinued.

After the surgery, the major problem was the exponential increase of the weight due to the hyperphagia not responding to any diet regimen and leading the girl to develop a hypothalamic obesity. In fact, at the age of 8.3 years she showed a height of 118.8 cm (-1.53 SDS), weight of 37.5 Kg (BMI 2.14 SDS) and growth velocity of 6.24 cm (1.22 SDS).

About six months after the surgery, growth hormone (GH) secretion was evaluated and GH response to arginine infusion revealed a peak less than 0.1 ng/ml suggesting a severe GH deficiency. After the evaluation of a normal tolerance to glucose, hrGH therapy was started at classical dose (0.020

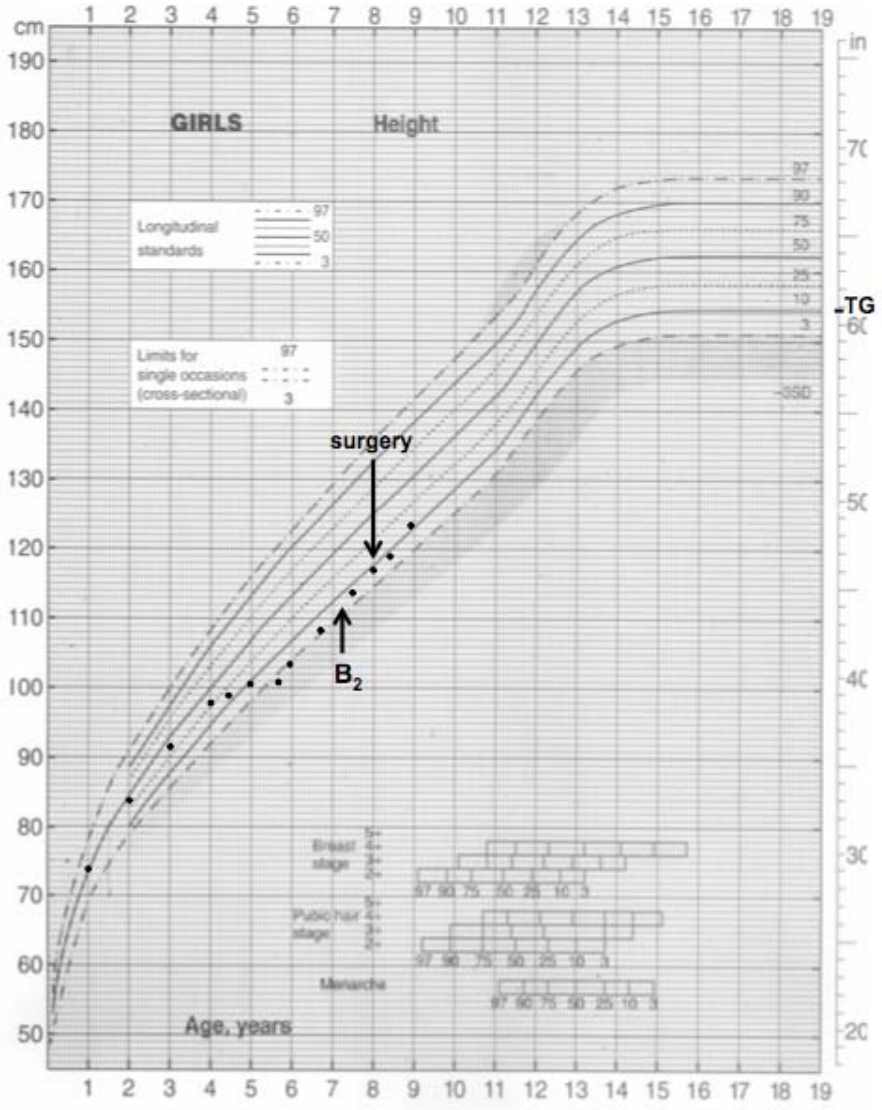

Figure 1: The subject's growth chart for height. The times of puberty start (B_2) and of tumour resection (surgery) are indicated by the corresponding arrows.
TH = Target Height.

mg/Kg/week subdivided in 5 daily subcutaneous injections). A significant increase in growth velocity was demonstrated in the first 6 months (from 1.22 to 2.81 SDS). Unfortunately, no effect on weight was observed because it increased from 37.5 to 45.0 Kg (BMI 2.37 SDS).

DISCUSSION

Craniopharyngioma in childhood often presents with non-specific manifestations of increased intracranial pressure, such as headache and nausea [5]. Other leading manifestations include endocrine deficits (52-87%) and involve the hypothalamic-pituitary axis, affecting the secretion of GH with subsequently pathological growth rate, gonadotropins, adrenocorticotropic hormone (ACTH) and TSH.

The patient had a normal growth velocity during the first years of life. Then, she firstly showed an arrest of growth, followed, one year later, by an increase of growth associated with the appearance of mammary gland. The suspicious of precocious puberty confirmed by the laboratory findings and pelvic scanner results, prompted us to perform brain imaging revealing the presence of CP. We may speculate that CP had a double effect, firstly inhibiting growth rate and then increasing it, due to the start of precocious puberty. Although precocious puberty is extremely rare as a presenting symptom of CP [4], in patients with other hypothalamic lesions it has been described that it early occurred in 19% of prepubertal ones, in particular in those with hamartoma and optic-pathway glioma [3]. Therefore, the decision to perform brain imaging in children with precocious puberty should be made on the basis of clinical and laboratory features.

It is well known that survivors of CP show a high incidence of obesity [6]. After tumour resection, also our patient experienced increased body weight, as already described in other studies [7]. In fact, it has been shown that about 50-60% of patients treated for CP during childhood were found overweight or obese after about 7 years form diagnosis [8]. It will be mandatory to continue a careful follow up until adulthood, since previous studies demonstrated that an early and rapid post-operative weight gain is a significant predictive factor for severe long-term obesity [9, 10].

In conclusion, CP has a wide range of clinical manifestations, depending of the tumour size as well as the extent of endocrine deficiency and the age of the patient. In our patient the initial growth failure was, probably, due to the compressive action of CP. Then, the onset of precocious puberty was related to the stimulating effect of the neoplasia on gonadotropic pituitary cells.

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