

Arachnoid Cyst with GnRH-dependent Sexual Precocity and Growth Hormone Deficiency

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The coexistence of gonadotropin-releasing hormone (GnRH)-dependent sexual precocity and growth hormone deficiency in patients with arachnoid cysts is rarely reported, and its pathogenesis is not well recognized. This report describes an 11-year-old female who had a huge intracranial arachnoid cyst with initial symptoms and signs of sexual precocity. Her brain magnetic resonance imaging revealed distorted hypothalamus with a thin and stretched pituitary stalk. After treatment with cysto-peritoneal shunting and gonadotropin-releasing hormone analogue, her puberty was arrested and subnormal growth rate was observed. Catch-up growth was detected after growth hormone therapy. Hence, coexistence of gonadotropin-releasing hormone-dependent sexual precocity and growth hormone deficiency in this patient was confirmed. © 2004 by Elsevier Inc. All rights reserved.

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Introduction

Intracranial arachnoid cysts, which comprise 1% of intracranial mass lesions [1], are developmental anomalies

of the arachnoid membrane [2]. Many arachnoid cysts are clinically silent and are identified only incidentally [3]. Nevertheless, suprasellar arachnoid cysts, which constitute 9% of all arachnoid cysts [4], are frequently symptomatic [4,5] and related to gonadotropin-releasing hormone (GnRH)-dependent sexual precocity [6,7]. Not until recently has it been clarified that suprasellar arachnoid cysts may actually affect many aspects of the hypothalamic-pituitary function [8-11]. However, so far only few studies have reported combined sexual precocity and growth hormone deficiency associated with arachnoid cysts [9-11]. Thus we report here an 11-year-old Taiwanese female with combined GnRH-dependent sexual precocity and growth hormone deficiency associated with an extensive intracranial arachnoid cyst. She was relieved from the progression of sexual precocity and achieved a normal growth rate after treatment with both gonadotropin-releasing hormone analogue and recombinant human growth hormone.

Case Report

This 11-year-old female's medical history is not noteworthy except that she suffered from a scalp laceration and a fracture of the right parietal bone after a traffic accident when she was 3 years of age. Early breast development was first observed by parents when she was 6 years 8 months old, and it became more prominent in the next year. She suffered another traffic accident when she was 7 years and 7 months old. She suffered from head injury, with an egg-sized hematoma on her left forehead. A head computed tomographic scan was performed at a community hospital owing to headache and vomiting. No intracranial hemorrhage was evident, but a huge arachnoid cyst occupying mainly the left temporal area was detected unexpectedly. One month after the event (7 years and 8 months old), she was found to have menarche, and two more menses were observed in the following 2 months. She was then brought to our hospital for further evaluation.

Brain magnetic resonance imaging revealed a huge arachnoid cyst occupying the left anterior and middle cranial fossae, the suprasellar, retrosellar, and prepontine areas, and also the left ambient cistern area (Fig 1). Also, the left hypothalamus was distorted and the pituitary stalk was stretched; however, the pituitary gland was normal in size (Figs 1 and 2). At that time, her height was 131.6 cm (+1.04 S.D.); her weight was 32.6 kg (+1.82 S.D.). Breast was at Tanner stage III, and pubic hair was at Tanner stage I. The neurologic examination was normal. She had no mental or emotional problems, and her appetite, sleep, and learning were all normal. Her bone age was read between 12 and 13 years at the chronological age of 7 years and 11 months. Her thyroid function test indicated serum T4 9.1 $\mu\text{g/dL}$ and thyroid stimulating hormone 1.6 $\mu\text{IU/mL}$. After intravenous administration of insulin, her serum growth hormone and cortisol levels rose to a peak of 2.9 ng/mL and 25.5 $\mu\text{g/dL}$ at 30 minutes, respectively. Her serum growth hormone level only reached a peak of 2.3 ng/mL after clonidine stimulation. Her baseline

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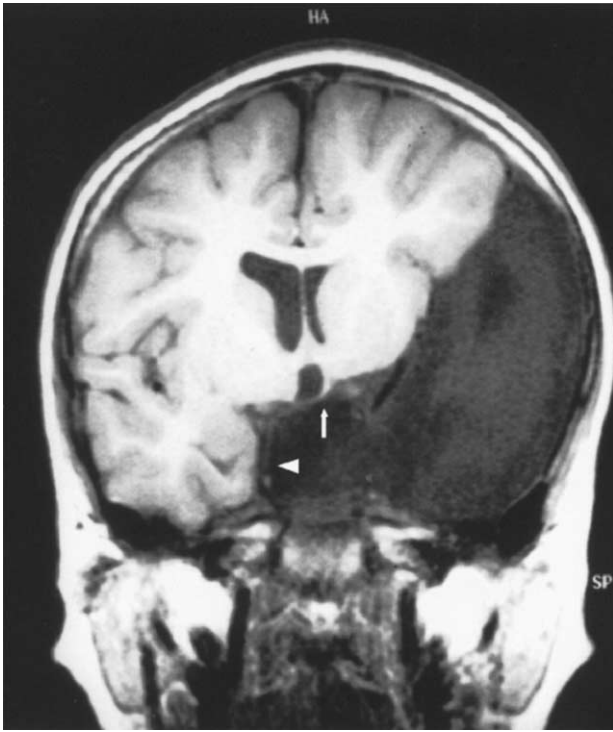


Figure 1. Coronal T_1 -weighted magnetic resonance image without contrast medium (TR = 650 ms, TE = 14 ms) revealed a large arachnoid cyst, which extended to the suprasellar region with distorted left hypothalamus (arrow) and pituitary stalk (arrowhead).

serum estradiol was 44 pg/mL. After intravenous administration of GnRH, her serum follicle-stimulating hormone level rose from 5.6 IU/L to 27.6 IU/L at 90 minutes and serum luteinizing hormone level rose from 5.8 IU/L to 49.0 IU/L at 30 minutes, which was a pubertal response. Therefore arachnoid cyst-associated GnRH-dependent sexual precocity and growth hormone deficiency was diagnosed. She then underwent a cysto-peritoneal shunt at 8 years of age. The postoperative course was smooth. She was discharged and monitored at our pediatric endocrine clinic.

In the subsequent 6 months, her breast size increased and she had another four episodes of menstruation with a duration of 1 day only. She

grew 2.8 cm during this period (growth rate: 5.6 cm/year). A follow-up head magnetic resonance imaging 6 months after the operation revealed only slight reduction of the size of the arachnoid cyst. Hence, she began to receive gonadotropin-releasing hormone analogue (Leuplin-depot) therapy.

The follow-up GnRH stimulation test indicated that her hypothalamic-pituitary-gonad axis was well suppressed by gonadotropin-releasing hormone analogue therapy in the following 1 year. However, she grew only 3.7 cm during this period. Hence, the recombinant human growth hormone (Genotropin) at the dose of 0.21 mg/kg/week has been administered subcutaneously. She then grew 8.8 cm during the first year of growth hormone therapy. Therefore growth hormone deficiency in this case was confirmed by her response to growth hormone therapy. In addition, dysfunction of the previous cysto-peritoneal shunt was suspected and a revision surgery of the shunt was performed 18 months after the previous operation. The follow-up head magnetic resonance imaging performed 19 months after the revision operation demonstrated marked reduction of the size of the arachnoid cyst. She is still receiving gonadotropin-releasing hormone analogue and growth hormone therapy. She is 151.2 cm tall, and her head circumference is 57 cm. Her bone age is 13 year 6 months at a chronological age of 10 years 11 months.

Discussion

Arachnoid cysts are benign congenital anomalies caused by accumulation of cerebrospinal fluid in cystic structures formed within two layers of arachnoid membranes [2,3]. Although the largest part of the cyst in our patient is located in the left temporal area, it actually involved multiple cisterns. The involvement of the suprasellar cistern by arachnoid cysts, as observed in our case, tends to cause endocrine dysfunction [9]. Expansion of arachnoid cysts is thought to be one of the major causes for the progression of clinical symptoms and signs [12]. Several hypotheses have been offered to explain the mechanism of cyst expansion, but controversy still exists [13,14].

Among the endocrine disorders associated with suprasellar arachnoid cysts, sexual precocity is the most common one [6,7]. There are also few cases of growth

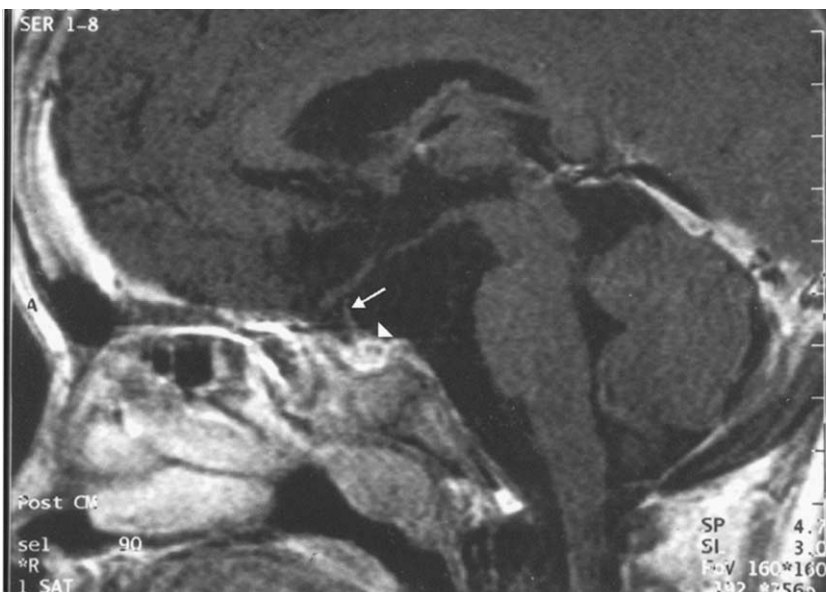


Figure 2. Sagittal T_1 -weighted magnetic resonance image with gadolinium enhancement (TR = 500 ms, TE = 14 ms) demonstrated poorly enhanced hypothalamus, displaced and distorted pituitary stalk (arrow), and normal-sized pituitary gland (arrowhead).

hormone deficiency reported in this situation [5,9], but the combination of sexual precocity and growth hormone deficiency in the same patient is extremely rare [9-11].

GnRH-dependent sexual precocity is caused by premature activation of the hypothalamic-pituitary-gonad axis, which is possibly related to the disruption of the neural pathway that normally inhibits the GnRH pulse generator. Because the hypothalamus is sensitive to pressure [15], GnRH-dependent sexual precocity was present in certain patients with hydrocephalus and was thought to be caused by the damage to the hypothalamus as a result of increased intracranial pressure or increased mass of cerebrospinal fluid [15]. Although arachnoid cysts, when compressing the aqueduct, may cause obstructive hydrocephalus [4], hydrocephalus was not obvious in our patient. On the other hand, because the compression and distortion of the left hypothalamus region was well documented in the brain magnetic resonance imaging of our patient, it is likely that the arachnoid cyst may cause the development of GnRH-dependent sexual precocity through such a pressure effect.

The pathogenesis of growth hormone deficiency is intriguing in our patient. Isolated growth hormone deficiency was also observed in some patients with chronic hydrocephalus, and the compression of the hypothalamus or pituitary by increased pressure was thought to be responsible for it [15]. Because in our patient the pituitary gland in magnetic resonance imaging was normal and only the secretion of growth hormone was subnormal, it is more likely that growth hormone deficiency in our patient was also caused by the pressure effect of the expanding arachnoid cyst on the hypothalamus.

We selected cysto-peritoneal shunting as the initial therapy for our patient, as Harsh et al. suggested [12]. We monitored her head magnetic resonance imaging several times after the operation, and marked reduction of the size of the arachnoid cyst was observed after the second operation. However, abnormal progression of puberty was still observed after the first operation. This phenomenon is not uncommon. Indeed, Pierre-Kahn et al. [5] have documented that some endocrine disorders persisted after treatment despite the satisfactory decrease in the volume of cysts, possibly because the permanent tissue damage occurred before the decompression surgery. The growth rate of our patient decelerated (3.7 cm/year) after the treatment with gonadotropin-releasing hormone analogue for 1 year. Such a phenomenon confirmed the coexistence of growth hormone deficiency, which was no longer masked by the growth-enhancing effect of estrogen. Recombinant human growth hormone therapy was commenced, and she had catch-up growth after the addition of growth hormone. Because our patient has a satisfactory response to therapy, we are optimistic about her final height.

Coexistence of GnRH-dependent sexual precocity and growth hormone deficiency in a patient with a large arachnoid cyst extending to involve the suprasellar region may be explained by the pressure-related compression on the adjacent hypothalamic region. More importantly, our observation underscores the possibility that the frequency of growth hormone deficiency in patients with GnRH-dependent sexual precocity as a result of arachnoid cysts might be underestimated because of the masking effect of sex hormones on the growth of such patients. Hence, evaluation of growth and sexual development in patients with arachnoid cysts during follow-up visits is recommended. Bone age study and GnRH test are indicated when abnormal progression of puberty is suspected. On the other hand, it is equally important to examine the growth hormone status in these patients despite normal growth so that they can receive appropriate therapy as soon as possible to prevent compromise of their final height.

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