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Case Report

Short Stature Without Neurological Manifestations in a Child with a Suprasellar Tumor

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Abstract

Addressing the problem of short stature in pediatrics is challenging because normal somatic growth depends on a complex interaction between genetic, nutritional, and hormonal factors. We report a 14-year-old girl with deceleration of growth velocity and delayed puberty but no other discernible neurologic or ophthalmologic symptoms or signs. Clonidine and insulin tolerance tests confirmed growth hormone deficiency, and magnetic resonance imaging disclosed a suprasellar mass. This case demonstrates that growth failure may be the only early sign of suprasellar tumor. Rigorous pursuit of the cause of a growth disorder should thus be considered, as it may disclose a potentially serious but treatable condition. (*Tzu Chi Med J* 2009;21(2):161–164)

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1. Introduction

In the pediatric population, short stature has an incidence of 3 in 100 (1). The causes of growth disorder are diverse, as normal somatic growth depends on the complex interaction between genetic, nutritional, and hormonal factors (2). The range of clinical conditions associated with short stature is vast, making the task of identifying a specific diagnosis daunting. However, certain causes, such as brain tumor, may cause irreversible damage or death if diagnosed too late (3). It is therefore absolutely necessary to examine the patient thoroughly and systematically think through an appropriate differential diagnosis. We report our experience with a child whose only manifestation of an intracranial lesion was short stature with decelerated growth.

2. Case report

A 14-year-old girl was seen in our pediatric endocrine clinic with the chief complaint of short stature that had been noted in elementary school. Her height was 132 cm (>3 standard deviations below the mean) and weight was 34 kg (2 standard deviations below the mean) (Fig. 1) (4). Her target height was 159 cm (5). Her 16-year-old sister was 154 cm tall and her 12-year-old sister was 152 cm tall. The patient had been born at term by a normal spontaneous vaginal

delivery without perinatal insult. According to her teacher and family, she had no eating problems or emotional disturbance. She had a grade B average in school. She denied nausea, headache, visual disturbance, polyuria, or polydipsia. Her growth velocity was slow at less than 3 cm/year. Her breast and pubic hair were Tanner stage 1. A pediatric neurologist found no neurologic abnormalities.

Her thyroid stimulating hormone (TSH) level was 1.42 μIU/mL, free thyroxine was 1.06 ng/dL, α-fetoprotein was < 2.76 ng/mL, human chorionic gonadotropin was 0.39 ng/mL, prolactin was 9.59 ng/mL, estradiol was < 10 pg/mL, luteinizing hormone was < 3 mIU/mL, follicle-stimulating hormone was < 2 mIU/mL, cortisol was 23.41 μg/dL, sodium was 144 mmol/L, potassium was 3.9 mmol/L, and her karyotype was 46,XX. Her bone age was 8.5 years. Visual fields by Goldmann perimetry were within normal limits. Clonidine and insulin tolerance tests showed growth hormone deficiency with a peak growth hormone level of 0.46 ng/mL (Table 1).

Magnetic resonance imaging (MRI) revealed a space-occupying, predominantly cystic, suprasellar lesion with peripheral wall enhancement (Fig. 2). A craniopharyngioma or pilocystic astrocytoma was suspected. The patient and her family refused craniotomy, so gamma knife surgery was performed. Therefore, no tissue was available for pathology examination. The patient was regularly followed, and MRI after treatment showed partial tumor regression.

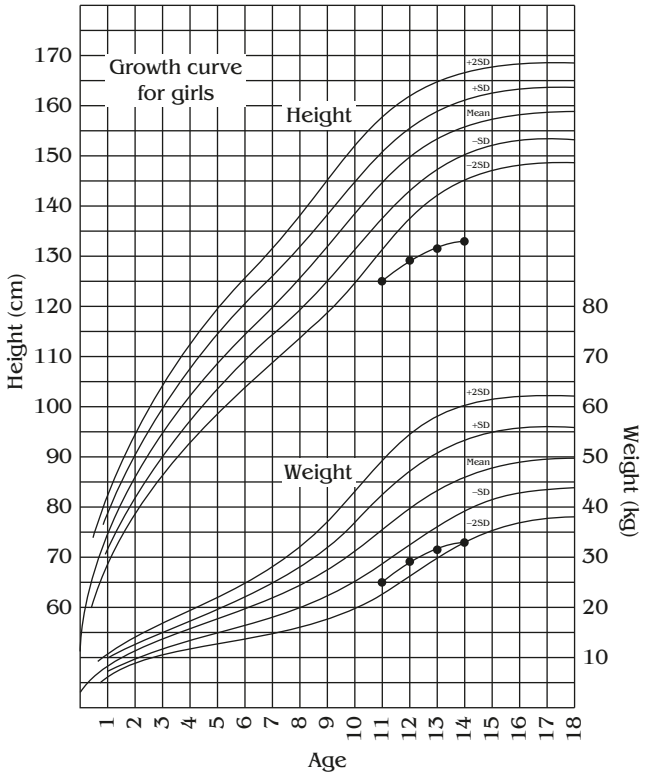

Fig. 1 — Patient's growth record showing progressive deceleration of growth compared with the norm [4]. (The patient's height and weight prior to age 11 were not available.)

3. Discussion

This case demonstrates that a sellar or suprasellar tumor might initially present with growth failure alone, without discernible neurologic and ophthalmologic manifestations. Intracranial tumors must be included in the differential diagnosis of growth disorders, even if the latter is the only presenting symptom.

Growth abnormality accounts for 27.6% of all diagnoses in a pediatric endocrine clinic, where it is the most common presenting complaint [6]. Constitutional growth delay, growth hormone deficiency, systemic disease, dysmorphic syndromes, and poor nutrition are the commonest causes. Patients with heights more than three standard deviations below the mean are likely to have organic etiologies [7,8]. However, the possible causes are so diverse that accurate diagnosis is challenging, especially when patients are less severely affected. This is particularly true for growth hormone deficiency, for which there is no diagnostic gold standard. Stimulation tests used to assess growth hormone levels include insulin-induced hypoglycemia, arginine, levodopa, clonidine, glucagon, and exercise tests [9]. Some experts use a combination of two or three of these tests to reduce the chance of false positives. Our patient had very low peak levels of growth hormone on both insulin-induced hypoglycemia and

Table 1 — Clonidine and insulin tolerance test (ITT) results

Time (min)	Growth hormone level (ng/mL)		Cortisol level (μg/dL)	Glucose level (mg/dL)
	Clonidine test	ITT	ITT	ITT
0	0.26	0.09		83
15		0.1		48
30	0.14	0.18		36
45		0.19	21.56	58
60	0.13	0.32	24.38	53
90	0.2	0.46	23.41	76
120	0.18	0.18		85

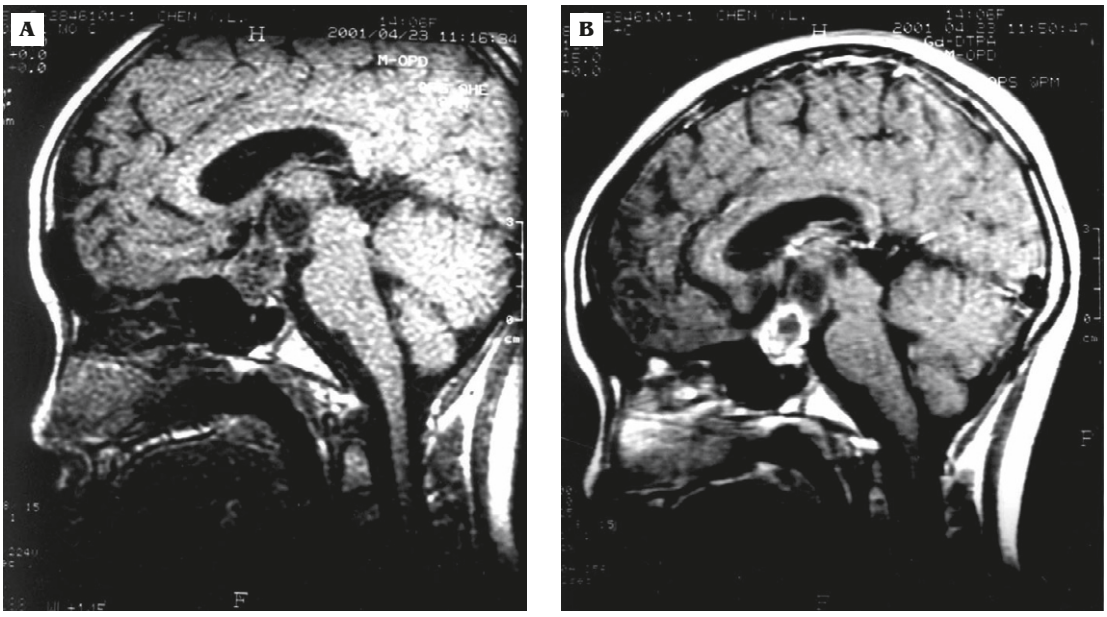

Fig. 2 — (A) T1-weighted sagittal image (TR 400/TE 25) without gadolinium shows a space-occupying suprasellar lesion with mixed solid and cystic components. The cystic portion has low signal intensity. (B) T1-weighted sagittal image with gadolinium reveals enhancement of the solid component of the tumor.

clonidine tests. In addition, she had very short stature and significant delays of bone age and puberty in spite of normal thyroid tests. Taken together, these features were most compatible with chronic growth hormone deficiency [10].

Having demonstrated growth hormone deficiency, however, we must still seek a reason for the deficiency. Tumors in the sella or above as well as other anomalies of the central nervous system account for only about 9% of patients with growth hormone deficiency [11]. Conversely, half of children with suprasellar or sellar neoplasms have growth hormone deficiency with or without the deficiency of other pituitary hormones [12]. As well as endocrine deficiencies, these tumors commonly present with neurologic deficits and visual defects [13], which is why our patient's presentation is unusual. It was the growth hormone deficiency that directed attention to the central nervous system, resulting in discovery of a suprasellar mass.

The differential diagnosis of such masses is broad, including such disorders as craniopharyngioma, pituitary adenoma, germ cell tumor, glioma, meningioma, vascular lesions, and inflammatory processes [14]. Craniopharyngiomas account for 80–90% of neoplasms arising in the pituitary region [15]. On MRI, their appearance depends on the proportion of the solid and cystic components, the contents of the cyst, and the amount of calcification [16]. Although large amounts of calcification may appear as areas of low signal in T1-weighted and T2-weighted images, calcification is better observed by computed tomography. Our patient's MRI showed a cystic suprasellar lesion mixed with solid components. She did not undergo computed tomography, so that we could not be certain that the tumor was a craniopharyngioma, although it was likely.

Surgical resection is the treatment of choice for craniopharyngiomas, with radiation used adjuvantly if complete resection is not accomplished. Stereotactic radiosurgery achieves tumor control in a substantial number of patients who have small volume lesions. It may be particularly useful for well-defined residual tissue after surgery or for the treatment of small solid recurrent tumors, especially after failure of conventional radiotherapy [17–19].

When a sellar or suprasellar tumor is diagnosed in a patient such as ours, the possibility of hormone deficiencies in addition to that of growth hormone should be considered, including TSH, thyroxine, adrenocorticotropic hormone, cortisol, gonadotropins, and gonadal steroids. Signs of diabetes insipidus should be searched for. The defect can be localized to the hypothalamus if there is a normal response to the administration of hypothalamic-releasing hormones for TSH, adrenocorticotropic hormone, or gonadotropins. Pituitary function can be assessed using an insulin stress test in conjunction with thyrotropin and gonadotropin releasing hormone tests [20].

While tumors in the suprasellar region are usually benign, either infiltration or a mass effect may be lethal. Therefore, early diagnosis is essential to avoid serious morbidity and mortality. Failure to consider the possibility of such a tumor is more likely when the presentation is atypical, as it was in our patient.

The key is recognizing the likelihood of an underlying organic cause in patients with severe growth failure and then conducting a thorough search for that underlying cause.

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References

1. Rappold GA, Fukami M, Niesler B, et al. Deletions of the homeobox gene SHOX (short stature homeobox) are an important cause of growth failure in children with short stature. *J Clin Endocrinol Metab* 2002;87:1402–6.
2. Vogiatzi MG, Copeland KC. The short child. *Pediatr Rev* 1998;19:92–9.
3. Lee JS, Tsai WY, Liu HM, Lin MY, Tu YK. Growth retardation as the initial manifestation of intracranial tumors: report of two cases. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi* 1994;35:157–62.
4. Hsiao RL, Miau TS, Lu CC, et al. A survey on weight and height of children (1 month–7 years) and plotting of growth curves (1 month–18 years) in Taiwan, 1987–1988. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi* 1990;31: 166–75.
5. Luo ZC, Albertsson-Wikland K, Karlberg J. Target height as predicted by parental heights in a population-based study. *Pediatr Res* 1998;44:563–71.
6. New MI, Obeid J, Wilson RC, et al. Profile of the pediatric endocrine clinic at New York-Presbyterian Hospital, New York Weill Cornell Center. *J Clin Endocrinol Metab* 1999;84: 4444–9.
7. Voss LD, Mulligan J, Betts PR, Wilkin TJ. Poor growth in school entrants as an index of organic disease: the Wessex growth study. *BMJ* 1992;305:1400–2.
8. Newman CB, Levine LS, New MI. Endocrine function in children with intrasellar and suprasellar neoplasms: before and after therapy. *Am J Dis Child* 1981;135:259–66.
9. Aimaretti G, Baffoni C, DiVito L, et al. Comparisons among old and new provocative tests of GH secretion in 178 normal adults. *Eur J Endocrinol* 2000;142:347–52.
10. Parks JS, Felner EI. Hypopituitarism. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. *Nelson Textbook of Pediatrics*, 18th edition. Philadelphia: Elsevier Saunders, 2007:2293–9.
11. Mahoney CP. Evaluating the child with short stature. *Pediatr Clin North Am* 1987;34:825–49.
12. Zargar AH, Laway BA, Masoodi SR, Wani AI, Salahuddin M. An aetiological profile of short stature in the Indian subcontinent. *J Paediatr Child Health* 1998;34:571–6.
13. Shin JL, Asa SL, Woodhouse LJ, Smyth HS, Ezzat S. Cystic lesions of the pituitary: clinicopathological features distinguishing craniopharyngioma, Rathke's cleft cyst, and arachnoid cyst. *J Clin Endocrinol Metab* 1999;84:3972–82.
14. Freda PU, Post KD. Differential diagnosis of sellar masses. *Endocrinol Metab Clin North Am* 1999;28:81–117.
15. Lafferty AR, Chrousos GP. Pituitary tumors in children and adolescents. *J Clin Endocrinol Metab* 1999;84:4317–23.
16. Karavitaki N, Wass JA. Craniopharyngiomas. *Endocrinol Metab Clin North Am* 2008;37:173–93.
17. Weil MD. Stereotactic radiosurgery for brain tumors. *Hematol Oncol Clin North Am* 2001;15:1017–26.
18. Kobayashi T, Kida Y, Mori Y, Hasegawa T. Long-term results of gamma knife surgery for the treatment of craniopharyngioma in 98 consecutive cases. *J Neurosurg* 2005;103:482–8.
19. Hayward R. The present and future management of childhood craniopharyngioma. *Childs Nerv Syst* 1999;15:764–9.
20. Harsoulis P, Marshall JC, Kuku SF, Burke CW, London DR, Fraser TR. Combined test for assessment of anterior pituitary function. *BMJ* 1973;4:326–9.