Follow-up of Two Cases of Medulloblastoma with/without Growth Hormone Therapy

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Introduction

Central nervous system (CNS) tumors are the most common solid malignancies in childhood with an incidence of 7 in one million children (1). One of the most frequent malignant CNS tumors in childhood is medulloblastoma. Although higher survival rates (60%) have been achieved with craniospinal radiotherapy and chemotherapy in medulloblastoma, the side effects on the growing young child are a major problem (2,3). Medulloblastoma survivors without growth hormone (GH) therapy attain an adult height between -2.9 and -5.0 standard deviation score (SDS), but with GH, the reported final height SDS was -1.9 (4).

Databases revealed a recurrence rate of 5% for medulloblastoma patients on GH treatment and similar for untreated ones (5). Here, we present two cases to emphasize the importance of GH therapy in medulloblastoma.

Case Reports

Case 1

A seven-year-old boy was referred to our clinic by an oncologist for assessment of primary hypothyroidism. He had a medulloblastoma operation 1.5 years ago. The radiotherapy and chemotherapy were completed 1 year and 2 months ago, respectively. On presentation to our clinic, his height was 118.7 cm (-0.73 SD) and weight was

Table 1. Demographic and basal hormonal evaluation with stimulation tests in the patients

	Case 1	Case 2
Age of diagnosis of medulloblastoma	5.6 y	7.6 y
Age at medulloblastoma therapy completed	7 y	8.7 y
Radiotherapy doses cGy (total and spinal)	5400 and 3600	5500 and 3740
Age at first endocrinology visit	7.2	12.2
Bone age	6.5	12
Height SDS	-0.73	-0.92
MPH SD	-0.45	-0.78
Free T4 (ng/dL)	0.5 (1.0-1.8)	0.99 (0.79-1.44)
TSH (mIU/mL)	99 (0.27-4.2)	11 (0.36-5.8)
L-T4 replacement	+	+
Peak cortisol (µg/dL) (low-dose ACTH test)	30.0	19.6
Prolactin (ng/mL) (N: 4.6-21.4)	16	8.1
Growth velocity (first year)	2.3 cm/year	2.9 cm/year
IGF-1 (ng/mL)	34 (66-436)	128 (322-776)
IGFBP-3 (µg/mL)	1.97 (2.6-6.2)	3.9 (4.6-7.3)
GH stimulation test		
Clonidin peak GH (ng/mL)	8.3	1.9
L-dopa peak GH (ng/mL)	6.8	3.9
GH therapy	-	+
Last visit		
Age	16.5	15.6
Bone age	16	13.5
Height (SDS)	138.5 (-5.69)	162.7 (-1.41)

SDS: standard deviation score, T4: thyroxine, TSH: thyroid stimulating hormone, ACTH: adrenocorticotropic hormone, IGF-1: insulin-like growth factor-1, IGFBP-3: IGF binding protein, GH: growth hormone

18.8 kg (-1.69 SD). Midparental height SDS was -0.45. He had no palpable thyroid gland on physical examination and heterogeneous thyroid tissue on ultrasound. He had primary hypothyroidism (thyroid stimulating hormone: 99 mIU/mL, N: 0.27-4.2; free thyroxine: 0.5 ng/dL, N: 1.0-1.8). L-thyroxine replacement was initiated and euthyroid state was achieved within a month. At follow-up visit, growth velocity was 1.8 cm/6 months despite euthyroidism. Hormonal evaluation and stimulation tests of the patient are given in the Table 1. The height SDS has continued to decrease during the follow-up and GH treatment was offered when height dropped below 2 SDS after 3 years of medulloblastoma-free period. However, his parents rejected the GH treatment due to fear of recurrence. His growth rate was around 2.3-2.7 cm/year during the follow-up. He also developed hypergonadotropic hypogonadism after the age of 10 years (follicle stimulating hormone: 46 mIU/mL, luteinizing hormone: 7.2 mIU/mL, T: 1.5 ng/mL at the age of $12^{9/12}$ yrs), however, needed replacement after the age of 16. His final height was 138.5 cm (-5.69 SD) at 16.5 years old. He is still on L-thyroxine and testosterone replacement therapy.

Case 2

A $12^{3/12}$-year-old boy was referred to our clinic for routine endocrinology follow-up. He was operated for medulloblastoma 4.5 years ago and was treated with radiotherapy (total 9140 cGy, spinal 3740 cGy) and chemotherapy. On presentation to our clinic, his height was 145.5 cm (-0.92 SD) and weight was 55 kg (0.86 SD). MPH was 171.4 cm (-0.78 SD). He was prepubertal on physical examination. His initial laboratory tests and stimulation tests are given in the Table 1. Since he had GH deficiency with low growth velocity (2.9 cm/year during puberty), GH treatment was started after 5 years of medulloblastoma-free period at the age of $13^{3/12}$ yrs. The height velocity was 7.9 cm/year in the first year of treatment and 5.6 cm/year in the second year. His current height is 162.7 cm (-1.41 SD) at the age of $15^{7/12}$ yrs, while bone age is 13.5. The patient is still on GH and L-T4 replacement therapy without any side effect or relapse of medulloblastoma.

Conclusion

GH deficiency, hypothyroidism and hypogonadism in patients having medulloblastoma and radiotherapy are common, however, the effect of GH treatment is variable and carries concerns regarding disproportionate growth related to spinal radiotherapy and recurrence risk. In our two cases, we showed that in spite of partial GH deficiency, height was much more severely affected in Case 1 due to development of the disease at a younger age and refusal of GH treatment.

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