

Papillary Carcinoma of Thyroid Gland in a Patient Treated with Recombinant Growth Hormone

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Abstract

The first successful treatment of growth hormone (GH) deficient children with GH extracted from human pituitary was introduced during late 1950's. The subsequent availability and use of recombinant GH (rhGH) for different clinical conditions raised the question of whether this new therapeutic modality increases the risk of certain conditions such as leukemia or malignancy. Herein, we report on a 22-year-old man who was diagnosed as a case of GH deficiency at the age of 11 years, was treated with rhGH for 6 years and who developed papillary carcinoma of the thyroid gland 6 years after cessation of the treatment.

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Keywords • Growth hormone • papillary carcinoma • thyroid gland • malignancy

Case Presentation

Our patient was the product of a full-term uncomplicated pregnancy and uneventful delivery in March 1975. At birth, he measured 48 cm in length, with a head circumference of 35 cm, and weight of 2570 gm.

At the age of five years, he presented with an apparent exophthalmus of the left eye which proved to be incidental with a positive history for two more cases in his family. Several studies including thyroid function tests, T₃ suppression test and thorough examination by an ophthalmologist using exophthalmometer were performed. Various radiological studies of the orbit revealed no abnormal finding. His parents had noted his poor linear growth for a few years and finally he was referred to our clinic when he was almost 10. At this time, his height was 124 cm and he weighed 22.5 kg. His bone age, as determined by x-ray of the left hand and wrist, was compatible with 8 years. L-dopa provocative test primed by propranolol showed a maximum rise of growth hormone (GH) to 5.4 ng/ml (normal >12 ng/ml). Serum TSH, T₄, T₃ and cortisol levels were all within normal limits. His growth rate was almost 3 cm/year measured over a period of more than 9 months. His physical examination was within normal limits except for a short stature and unilateral exophthalmus of the left eye. Family history was positive for two more cases of GH deficiency in his siblings. He was treated with recombinant human GH (rhGH) since the age of 11 years. The initial dose was 0.6 IU/kg/wk given subcutaneously in three divided doses administered at night for about one year. Concurrent with the foregoing treatment, the patient was also

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given 50 µg/kg/d of oxandrolone for six months. The rhGH was subsequently given in six divided doses. The patient did not have any apparent medical problems but some minor delay in the development of his secondary sex characteristics. His medication was discontinued at the chronological age of 16 years, when his final stature was 161 cm.

At the age of 22 years, he was referred to the surgical clinic because of cervical lymphadenopathy. Lymph node biopsy revealed metastatic carcinoma of the thyroid gland. Subsequent surgical procedures consisted of total thyroidectomy and neck dissection. Pathological examination of the tumor revealed a papillary carcinoma of the thyroid gland involving the left thyroid lobe with the right lobe of thyroid and isthmus being spared. Capsular and vascular invasion of the tumor were also present. Four of six lymph nodes removed at surgery were positive. Ablation therapy with ¹³¹I was done thereafter. Three times whole-body scanning over a 3-year period postoperatively revealed an athyroidic neck without any regional or distant metastasis. On his latest scanning, a small remnant of thyroid tissue was found. His most recent follow up (4 years after surgery) did not reveal any abnormal findings.

Discussion

The initial successful use of human GH for GH-deficient patients started in late 1950's by Raben.¹ After recombinant form of GH (rhGH) became available, GH hormone therapy has been widely used in various clinical conditions in children with genetically short statures, chronic renal failure, Turner syndrome, achondroplasia, β-thalassemia major and intrauterine growth retardation.⁴⁻⁸ Although the use of rhGH in most cases is still a matter of controversy, its only well-established indication is GH-deficiency.

Since the recognition of Creutzfeldt-Jakob disease,⁹ as a complication of administration of human pituitary extract to patients treated for GH-deficiency, attention is turned to the possibility of increasing risk of developing certain conditions through the use of rhGH. Some of the reported conditions include leukemias,^{7,10-12} transient lowering of T₄ level, slipped capital femoral epiphysis, worsening of scoliosis, gynecomastia, malignancies, pseudotumor cerebri, and rarely, diabetes mellitus. The incidence of complications is probably higher in patients who have a history of risk factors such as tumors, malignancies or irradiation.⁵ To the best of our knowledge, the association of GH therapy and papillary carcinoma of thyroid

gland has not been previously reported in the literature.

The most important consideration in the use of rhGH is an increasing risk of malignancies and leukemia. Though, no cause and effect relationship could be proven between rhGH therapy and development of most of the associated conditions, patients should be carefully selected for rhGH therapy.¹³

References

- 1 Raben MS: Treatment of a pituitary dwarf with human growth hormone. *J Clin Endocrinol metab* 1958;**18(8)**:901-3
- 2 Allen DB: Safety of human growth hormone therapy: current topics. *J Pediatr* 2001;**138**:448-9
- 3 Blethen SL: Complications of growth hormone therapy in children. *Curr Opin Pediatr* 1995;**7**:466-71
- 4 Van Vliet G, Styne DM, Kaplan SL, et al: Growth hormone treatment for short stature. *N Eng J Med* 1983; **309(17)**:1016-22.
- 5 Vimalachandra D, Craig JC, Cowell CT, Knight JF. Growth hormone treatment in children with chronic renal failure: A meta-analysis of randomized controlled trials. *J Pediatr* 2001;**139(4)**: 560-7
- 6 Yamate T, Kanzaki S, Tanka H, et al; Growth hormone treatment in Achrodroplasia. *J Pediatr Endocrinol* 1993;**6**: 45-52
- 7 Stanhope R: Growth hormone treatment of short stature due to intrauterine growth retardation. *Clin Endocrinol (Oxf)* 2000;**53**: 665-6
- 8 Cavallo L, Acquafredda A, Zecchino C, et al: Recombinant growth hormone treatment in short patients with thalassemia major: results after 24 and 36 months. *J Pediatr Endocrinol Metab* 2001;**14**: 1133-7
- 9 Buchanan CR, Preece MA, Milner RD: Mortality, neoplasia, and Creutzfeldt-Jakob disease in patients treated with human pituitary growth hormone in the United Kingdom. *BMJ* 1991;**302**:824-8
- 10 Ogawa M, Mori O, Kamijo T, et al: The occurrence of acute lymphoblastic leukemia shortly after the cessation of human growth hormone therapy. *Jpn J Clin Oncol* 1988; **18**:255-60
- 11 Shalet S.M: Leukemia in children treated with growth hormone. *J Pediatr Endocrinol* 1993;**6**:109-11
- 12 Fradkin JE, Mills JL, Schonberger LB, et al. Risk of leukemia after treatment with pituitary growth hormone. *JAMA* 1993;**270(23)**: 2829-32
- 13 Milner RD: Which children should have growth hormone therapy? *Lancet* 1986;**1**: 483-5.