CASE REPORT

Osamu Motoyama · Akira Hasegawa · Takeshi Kawamura · Atushi Aikawa · Kikuo Iitaka

Adult height of three renal transplant patients after growth hormone therapy

Received: May 29, 2007 / Accepted: July 12, 2007

Abstract
Three girls with normal growth hormone secretion had received renal transplantation when aged 2 to 6 years. They had had severely retarded growth (SD for height score was –7.4 to –3.7) at the time of transplantation. After renal transplantation, steroid was withdrawn and they were treated with recombinant human growth hormone; they subsequently reached adult heights of 145 to 156 cm. The SD for adult height score was –2.6 to –0.3. The adult height in two patients was over their target height, calculated using the mean of the parents’ height. This report shows the efficacy of steroid withdrawal and recombinant human growth hormone therapy in achieving adult height in these three girls after renal transplantation.

Key words Growth · Adult height · Growth hormone · Renal transplantation · Steroid withdrawal

Introduction
In children after renal transplantation retarded growth remains a significant problem. Graft dysfunction and corticosteroids (steroids) used for immunosuppressive therapy are thought to be the main factors causing this problem. The SD score (SDS) for height has been improved in children with well-functioning grafts who received steroid reduction using a calcineurin inhibitor. But the adult height of most child renal transplantation patients is short, mainly because of their severely retarded growth by the time of transplant. Our experience of the short-term effects of recombinant human growth hormone (rhGH) therapy after renal transplantation was previously reported. We report here three girls with normal growth hormone secretion who had severely retarded growth at the time of transplantation, in whom steroid was withdrawn and rhGH treatment was given after renal transplantation and who reached adult height. To our knowledge, adult height after rhGH therapy and steroid withdrawal in renal transplant patients has not been reported.

Case reports
The three girls described here were of normal weight and length at birth. After undergoing peritoneal dialysis since infancy (patients 1 and 2), and from 2 years of age (patient 3), they each received renal transplantation from one of their parents. They received an immunosuppressive regimen with methylprednisolone (MPL), cyclosporine (CyA), and mizoribine. Azathioprine was added for patient 2. None of the three had any rejection episodes clinically during the course. The results of provocation tests for GH secretion, done before the start of rhGH therapy, were normal. Thyroid function was normal. The rhGH (somatropin) was given at a dose of 1.0 IU/kg (0.33 mg/kg) per week in patients 1 and 2 and at a dose of 0.5 IU/kg (0.17 mg/kg) per week in patient 3, given as a subcutaneous injection, divided into six evening doses. Clinical trial of rhGH therapy for 1 year was planned. Height SDS and target height were calculated as:

\[
\text{Height SDS} = \frac{\text{height of the patient} - \text{mean height for girls of the same age}}{\text{height SD for girls of the same age}}.
\]

Target height = mean of parents’ height – 6.5 cm.

Adult height was defined as having been achieved in all three patients, because their heights had not increased for more than 3 years at the last observation. Details of their growth are shown in Table 1 and Fig. 1. Target height was 158.5 cm in patient 1, 148.5 cm in patient 2, and 154.0 cm in
Bone age was evaluated using the Japanese version of the Tanner-Whitehouse 2 (TW-2) method [radius-ulna-short bone (RUS) score]. At the start of rhGH therapy, breast development (Tanner’s stage 2) was noted in patients 1 and 2. The peak level of luteinizing hormone after luteinizing hormone-releasing hormone administration was 7.7 mIU/ml in patient 1 and 20.6 mIU/ml in patient 2. In patient 3 during rhGH therapy, Tanner’s stage was 1.

As for graft function during the course, serum creatinine level and creatinine clearance, calculated by the method of Schwartz et al., are shown in Table 1. Serum creatinine level at the last follow-up was 1.3 mg/dl in patients 1 and 2, and 0.6 mg/dl in patient 3. There was no avascular necrosis, slipped capital femoral epiphysis, or malignancy.

### Patient 1

A 21-year-old woman with a hypoplastic kidney had received renal transplantation at the age of 2 years. Two years after transplantation, MPL was discontinued. At 3, 7, and 9 years after transplantation, histopathologic findings of routine serial graft biopsies revealed signs of acute rejection, but clinically the patient showed no symptoms of rejection, and laboratory tests showed no abnormal changes. Each time, she received high-dose MPL by bolus injection for 3 consecutive days to prevent rejection, but oral MPL therapy was not started. She was started on rhGH at 9 years of age (bone age, 10 years) and rhGH was continued for 1.4 years. She started menstruating at 11 years of age and reached adult height at 15 years of age.

### Patient 2

A 22-year-old woman with congenital nephrotic syndrome had received renal transplantation when she was 5 years old. Therapy with rhGH had started when she was 10 years old (bone age, 10 years) and was continued for 7 years. Because of the patient’s and her parent’s desire, long-term rhGH therapy was not started. She was started on rhGH at 9 years of age (bone age, 10 years) and rhGH was continued for 1.4 years. She started menstruating at 11 years of age and reached adult height at 15 years of age.