The Role of Growth Hormone Replacement in a Growth Hormone Deficient Patient With Underlying Cardiomyopathy and Severe Congestive Heart Failure

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It has been reported that growth hormone (GH) deficiency induced cardiomyopathy responds to growth hormone replacement therapy. We describe the case of a middle-aged male with cardiomyopathic heart failure and growth hormone deficiency of the adult secondary to surgical panhypopituitarism. We demonstrate clinical and hemodynamic improvement of cardiac function with growth hormone replacement therapy despite underlying structural heart disease. J Heart Lung Transplant 2005;24:110–14. Copyright © 2005 by the International Society for Heart and Lung Transplantation.

A 39-year-old male presented in 1998 to an emergency department with 12 hours of dyspnea, hypotension, and pulmonary edema. He required inotropic support to stabilize his clinical situation. He was transferred to the Queensland Heart and Lung Transplant unit for further management. Initial echocardiography demonstrated a heart that was globally dilated with evidence of severe biventricular dysfunction and severe mitral regurgitation due to annular dilatation. He was stabilized with medical therapy, which included diuretics and angiotensin converting enzyme (ACE) inhibitors. He remained in New York Heart Association (NYHA) class II–III congestive heart failure (CHF). He was listed for transplantation in April 1999. Carvedilol therapy was commenced and he reached target dose of carvedilol in August 1999. Due to clinical improvement, presumably secondary to carvedilol, he was removed from the transplantation list in October 1999.

His past medical history included a Ewing's sarcoma of the lower tibia diagnosed at age 12. He was treated with an above the knee amputation and 2 years of chemotherapy which included monthly courses of adriamycin (total dose 480 mg/m^2), vincristine, cyclophosphamide (total dose 600 mg/m^2), and dacarbazine. There was no known family history of cardiomyopathy.

His history was also significant for a non-secretory pituitary adenoma diagnosed in 1996. He underwent a craniotomy and pituitary clearance, which resulted in panhypopituitarism. He received pituitary hormone replacement therapy with prednisone (10 mg daily), thyroxine (150 μcg daily), testosterone enanthate (250 mg IM biweekly), and desmopressin acetate (10 μcg nasal spray twice daily). He tolerated replacement therapy without clinical features of iatrogenic Cushing's syndrome and had clinical and biochemical features of adequate thyroid and androgen replacement.

The patient did well for 1.5 years on his heart failure therapy, which included target dose β-blockers (carvedilol 25 mg bid). He presented again in July 2001 with decompensated heart failure and hypotension requiring inotropic support for 10 days. He had his ACE inhibitor reduced to small doses and his carvedilol dose reduced by one-half. He remained in NYHA class III–IV CHF. A right heart catheterization (Table 1) revealed elevated pulmonary pressures and a transpulmonary gradient elevated above the values acceptable for cardiac transplantation.

After consultation with the endocrinology service, he was commenced on growth hormone (GH) replacement to improve hemodynamics and potentially to improve the pulmonary pressures as a "bridge" to cardiac transplantation. A diagnosis of GH deficiency was considered likely given his panhypopituitarism and low serum insulin-like growth factor-I (IGF-I; see Table 2) that could not be explained on the basis of other known pathologies. Insulin hypoglycemia testing, the gold standard for the diagnosing GH deficiency, was considered an unacceptable risk given his cardiac status.

After ethics approval was granted, and baseline echo-

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Table 1. Hemodynamic Data: Growth Hormone Protocol

RHC (in mmHg)	Baseline	Week 15
RA	4	3
PA	51/27 36	21/11 19
PCWP	20	15
SVR	1310	1383
PVR	272	67
CO	4.3	4.8
CI	2.0	2.1
TPG	16	4

RHC, right heart catheterization.

cardiographic measurements, hemodynamic parameters, and biochemical measures were performed the patient was commenced on recombinant human growth hormone (r-hGH) subcutaneously at 1 U/day (Humatrope; Eli Lilly & Company, West Ryde, Australia). Serial biochemical assays revealed a prompt rise in IGF-1 level (age corrected 95% confidence intervals for normal values: 7–36 nmol/l; Bioclone acid-ethanol extracted RIA) that prompted reduction of the daily dose of GH dose to .75IU during week 2 of replacement therapy (Table 2).

Serial echocardiographic data (Table 3) demonstrated that there was a progressive improvement in right ventricular size and function over the first 4 weeks of replacement therapy with normal values then maintained for the duration of the study. There was also an improvement in the qualitative grades of mitral and tricuspid regurgitation during the study period, and a trend to improved ejection fraction in the absence of wall thickness changes.

Hemodynamic data (Table 1) was obtained at baseline and at week 15 of replacement therapy, which

Table 2. Biochemical Data: Growth Hormone Protocol

Growth hormone dose	Baseline (Height 181 cms; Weight 94 kgs)	Week 1 (1 IU daily)	Week 2 (22.10 ↓ .75 IU)	Week 4	Week 6	Week 8	Week 12	Week 15	Week 21	Week 28	Week 33
Date	19–20.09.01	08.10.01	15.10.01	29.10.01	12.11.01	26.11.01	20.12.01	14.01.02	25.02.02	18.4.02	22.05.02
Na mmol/liter	134			137		136	135			138	139
K mmol/liter	4.1			4.2		4.3	4.5			3.8	4.2
Cl mmol/liter	98			100		102	99			105	105
HCO_3 mmol/liter	27			28		25	26			24	26
Urea mmol/liter	9.5			6.6		5.5	5.6			4.7	5.7
Creat umol/liter	.12			.11		.11	.11			.10	.11
Glucose mmol/liter	4.4	5.1	4.8	5.4	4.8	5.7	5.6		5.1	4.6	5.0
T.Bill mmol/liter	8			9		8	8			13	14
T.Prot g/liter	74			78		70	73			68	74
Albumin g/liter	40			39		35	38			39	42
AST IU/liter	10			19		13	14			30	16
AP IU/liter	63			77		60	60			56	66
GGT IU/liter	21			20		20	16			15	19
Growth hormone mU/L (<6.0)	<0.5					29				1.3	
HbA1C % (<6.0)	5.2									6.0	5.6
IGF-1 nmol/L (10–40)	6	39		43	36	36	29		24	21	
Insulin level mU/L (<20)	6	21		22	9	22	11		15	4	
WCC 10^9/liter	10.1			7.1			6.7			5.0	
RCC 10^{12}/liter	4.49			4.2			4.0			4.3	
Hb mmol/liter	131			128			123			130	
MCV fl	87			89			92			88	
Plt 10^9/liter	271			282			289			253	
HCT%	.39			.36			.37			.38	
Diff: N 10^9/liter	5.1			5.07			5.07			1.8	
L 10^9/liter	4.0			1.19			1.19			2.4	
M 10^9/liter	.71			.53			.28			.52	
TSH mU/liter	<0.05			<0.05		<0.05	<0.05		<0.05	<0.05	<0.05
Free T4 nmol/liter	21			22		21	23		17	13	16
Cholesterol mmol/liter	6.2						5.7		5.5	5.8	
Triglycerides mmol/liter	1.1						1.0		1.2	1.2	
Weight (kgs)	94					102		102.5			