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Cardiovascular Imaging In-a-Month

●Slowly Developing Heart Failure Associated With Hormonal Disorder

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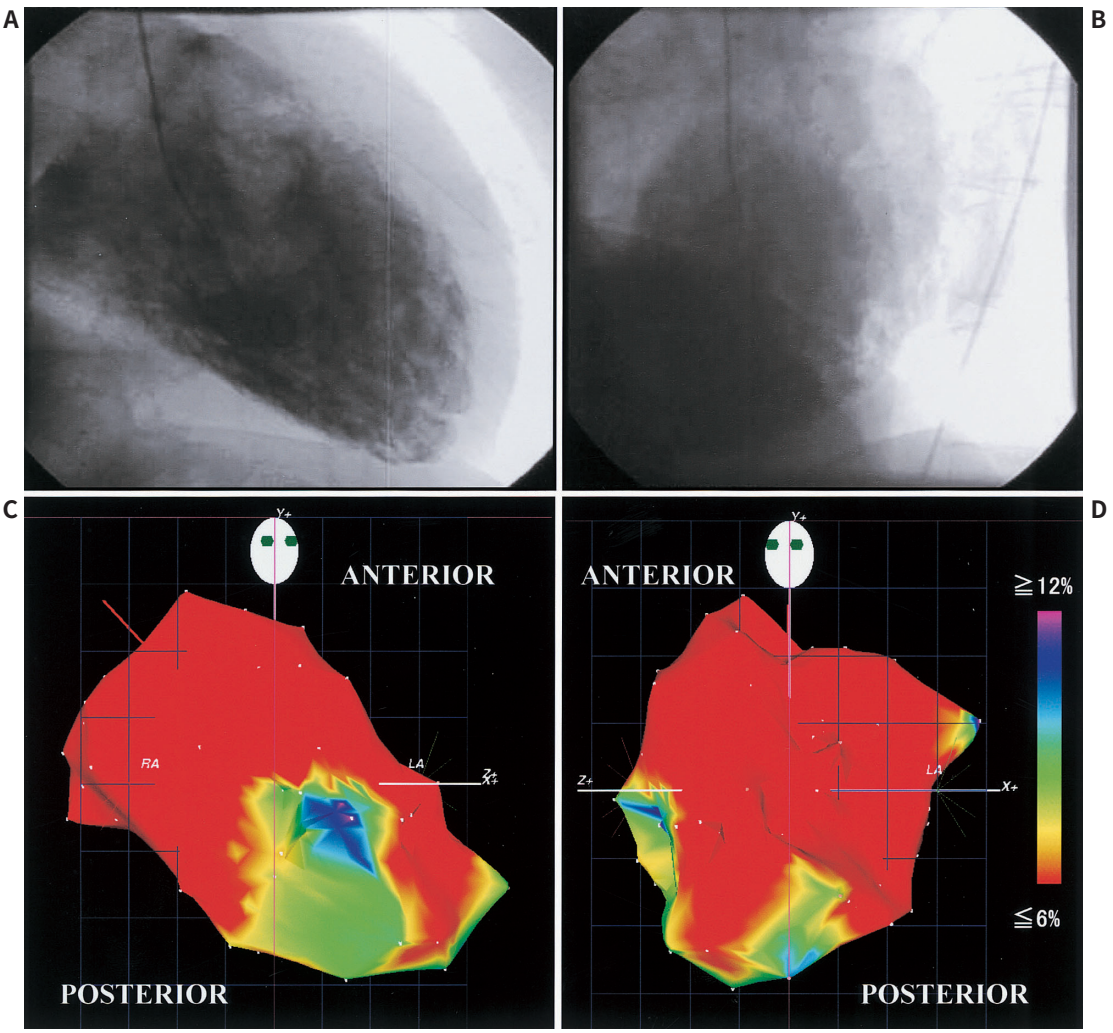

Fig. 1

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CASE

A 47-year-old man (height 176 cm, weight 78 kg) was admitted complaining of breathing difficulties and breath seizure during sleep in June 2000. The diagnosis was repetitive paroxysmal nocturnal dyspnea. His blood pressure was 106/80 mmHg and pulse rate was 100 beats/min. Cardiac catheterization showed the coronary arteries appeared intact and the left ventricle was enlarged (**Figs. 1−A**, **B**). Biopsy examination showed interstitial fibrosis and myocyte/myofibrillar hypertrophic changes, without disarray, in the left ventricle. Cardiac stasis was confirmed by the Biosense-Webster NOGA system (Johnson & Johnson), which revealed severely depressed contractility on local shortening mapping (**Figs. 1−C**, **D**). B-type natriuretic peptide (BNP) level was 620 pg/m*l*.

Points for Diagnosis

Serial chest radiography obtained during the last 9 years showed enlargement of the cardiothoracic ratio (**Figs. 2−A, B, C**). Echocardiography had revealed diastolic dimension (Dd) of 48 mm, fractional shortening (FS) of 40%, and interventricular septal thickness (IVST) of 12 mm in 1991. At that time the diagnosis was mild cardiomegaly. Echocardiography showed Dd of 76 mm and FS of 20%, and IVST of 10 mm in 1994, and Dd of 88 mm, FS of 10%, and IVST of 7 mm in 2000.

The patient was suspected of having growth hormonal disorder because of characteristic facial features such as enlargement of the nose and the lips. His blood growth hormone (GH) level was

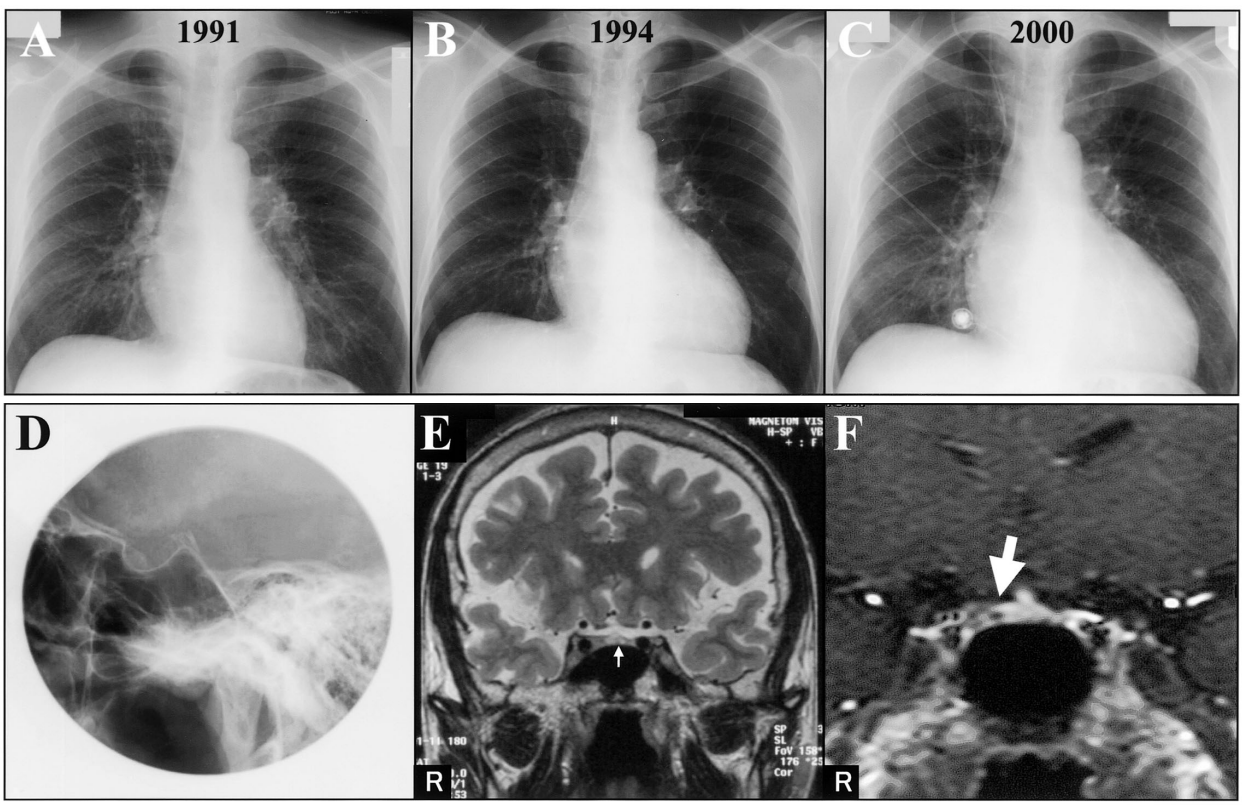

Fig. 2

Table 1 Diagnostic stress tests

	Cut-off	Before	30 min	60 min	90 min	120 min
75 g OGT test						
Glucose (mg/dl)		147	337	245	203	184
Growth hormone (ng/ml)	<0.42	5.84	5.45	7.46	7.96	5.70
TRH stress test						
Prolactin (ng/ml)	<30.0	16.0	21.0	17.0		18.0
Growth hormone (ng/ml)	<0.42	4.49	16.1	7.62		5.26
Somatostatin stress test						
Growth hormone (ng/ml)	<0.42	4.94	1.41	0.85		1.61

OGT=oral glucose tolerance; TRH=thyrotropin-releasing hormone.

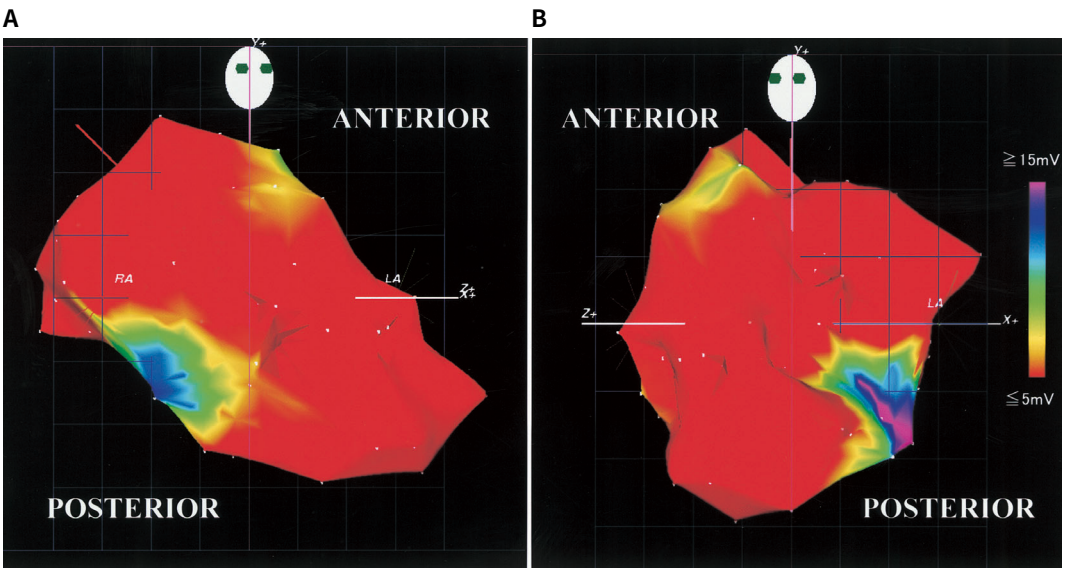

Fig. 3

9.43 ng/ml (normal < 0.42 ng/ml) and insulin-like growth factor (IGF)-I (somatomedin C) level was 936 ng/ml (normal < 270 ng/ml). These parameters were not suppressed by either oral glucose or thyrotropin-releasing hormone stress, although somatostatin stress did result in suppression (**Table 1**). Brain magnetic resonance imaging revealed a lesion in the right side of the pituitary gland, suggestive of microadenoma (**Figs. 2-E, F**). These results established the diagnosis of late-stage cardiomyopathy associated with acromegaly.

The patient was treated with renivase, spironolactone, furosemide, warfarin and carvedilol during 2 months admission. The patient was treated with intermittent subcutaneous infusions of slow-release form of octreotide (somatostatin analogue Sandostatin, 100 μg daily) in September 2000, in addition to medication for heart failure. GH and IGF-I levels were reduced to 2.45 and 370 ng/ml, respectively, accompanied by partial normalization of cardiac function (Dd: 77 mm; FS: 12%; BNP: 250 pg/ml), but the patient suddenly died in June 2001. The cause of death was not clear, but fatal arrhythmias were possibly involved.

The interaction between GH and IGF-I is involved in the intricate steps of cardiac development and excessive levels of these hormones can alter cardiac structure and function. Recent experimental data from animal models suggest that an increased level of IGF-I may be a possible causative factor for the development of ventricular hypertrophy[1]. Cardiac or hepatic IGF-I stimulates IGF receptors in the myocardium, which in turn induce muscle specific proto-oncogene expression,

and increase the size of cardiomyocytes. In clinical studies, concentric left ventricular hypertrophy has been frequently recognized, although in the absence of wall stress, a condition that is accompanied by impaired ventricular diastolic performance[2,3]. If the disease is not treated or treated unsuccessfully, cardiac contractility slowly deteriorates. Long-term exposure to an elevated IGF-I level promotes cardiac collagen accumulation, leading to cardiac remodeling due to extensive interstitial fibrosis in which the impairment of systolic dysfunction is a recognized consequence[1,2]. Hormonal disorders can be overlooked until finally documented in the terminal stage of cardiomyopathy.

The NOGA system is a catheter-based diagnostic tool used for the investigation of local myocardial contractility and viability[4]. The system records 50−100 endocardial electrograms derived from a sensor-tipped catheter electrode, and reconstructs the three-dimensional electromechanical map that is represented by color-coding (*e.g.* violet: normal, red: severely impaired). Voltage mapping enables the prediction of recovery in regional and global left ventricular function. In our patient, local shortening mapping detected globally depressed cardiac function (**Figs. 1−C, D**) and voltage mapping showed irreversibly damaged, non-viable myocardium (**Fig. 3**).

Somatostatin, a cyclic tetradecapeptide, lowers GH secretion or its response, and returns IGF-I level to normal with resultant improvement of cardiac manifestations in acromegalic patients[5]. Reduction in the level of GH to below 2.5 ng/m*l*, and inhibition of IGF-I reduces cardiovascular mortality and morbidity in acromegaly[1]. However, limited improvement or little effect can be expected in patients with late-stage acromegalic cardiomyopathy[2], because cardiac remodeling due to prolonged elevated IGF-I-induced interstitial fibrosis is already present and is irreversible. Under such severe conditions, sudden death associated with life-threatening arrhythmias, or heart failure, can occur. Clinicians should be aware of the relationship between hormonal disorders and cardiovascular complications, as illustrated by the present case.

Diagnosis: Late-stage acromegalic cardiomyopathy

Key Words: Diagnostic techniques (NOGA system); Cardiomyopathies, other; Hormones (growth); Growth factor (IGF-Ⅰ); Systole (systolic dysfunction)

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Fig. 1 Investigations using catheterization of the heart
A, *B*: Left ventriculograms showing marked dilation of the ventricle.
End-diastolic volume: 435 m*l*; End-systolic volume: 362 m*l*.
C, *D*: NOGA local shortening mapping of regional contractility. The violet zone depicts ≥ 12% of contractility (normal). The red zone indicates ≤ 6% of contractility (severely impaired).
A, *C*: Right anterior oblique view. *B*, *D*: Left anterior oblique view.
RA = right atrium; LA = left atrium.

Fig. 2 Chest and cranial imaging
A: Chest radiograph in 1991 showing a cardiothoracic ratio of 43%.
B: Chest radiograph in 1994 showing a cardiothoracic ratio of 53%.
C: Chest radiograph in 2000 showing a cardiothoracic ratio of 68%.
D: Cranial radiograph showing an intact sella turcica.
E: T_1-magnetic resonance image revealing high intensity areas on both sides of the pituitary (*thin arrow*).
F: Rapid enhanced T_2-magnetic resonance image revealing a persistent low intensity lesion (4 mm) on the right side of the pituitary (*thick arrow*).

Fig. 3 NOGA local voltage mapping of regional viability
The violet zone depicts normal voltage values (≥ 15 mV). The red zone indicates severely impaired voltage values (≤ 5 mV).
A: Right anterior oblique view. *B*: Left anterior oblique view.