A 56-YEAR OLD MALE WITH HEADACHES AND VOMITING

HISTORY OF THE PRESENT ILLNESS

56-year old male, with complicated medical history, including extensive cardiac disease and chronic kidney disease, presenting with:

One month history of low grade, tension-type headache; acute worsening with sudden-onset "smashing" right-sided temporal headache on the night prior to admission.

Headaches associated with nausea and recurrent emesis. No relief with Tylenol #3 or NSAIDS.

No precipitating trauma.

No associated vision changes, confusion, lethargy, rhinorrhea, or aura.

PAST MEDICAL & SURGICAL HISTORY

Non-Ischemic Dilated Cardiomyopathy
Orthotopic Heart Transplant 2005, complicated by cardiac allograft vasculopathy
Re-transplant March 2013; s/p biV-AICD

- Mycophenolate mofetil
- Tacrolimus
- Predisone 5 mg

Chronic Kidney Disease
LECT-2 amyloidosis

Anemia

- Erythropoietin
- Cyanocobalamin
- Folate
- Ferrous sulfate

Hypertension

- Diet-controlled after transplant

Dyslipidemia

- Pravastatin

Barrett's Esophagus

- Esomeprazole

Depression

- Citalopram

SOCIAL AND FAMILY HISTORY

Lives between US and Mexico
US Citizen since 2007

Lives with wife

Quit tobacco in 2004
No etoh or illicit drug use

Father died in 70s; Cause unknown

Mother alive, healthy, in late 80's

4 brothers, 4 sisters.
1 brother with heart failure, CVA

4 grown children (all with advanced professional degrees) living in Mexico

REVIEW OF SYSTEMS

Constitutional: Denies fevers, chills, hot or cold intolerance. Reports fatigue, 20 pound weight loss (since transplant 6 mos. ago).

HEENT: Denies vision changes including blurriness, loss of peripheral vision or double vision, tinnitus, rhinorrhea, trouble swallowing, neck pain or goiter. Worsening headaches, right molar dental caries worsening headache.

Cardiovascular: Denies chest pain, palpitations or racing heart, syncope, lower extremity edema. No signs of dizziness with position changes.

Respiratory: Denies difficulty breathing or shortness of breath, cough, or wheezing.

Gastrointestinal: Denies changes in appetite, abdominal pain. Nausea, vomiting, and constipation.

Genitourinary: Denies urinary incontinence, frequency, dysuria, burning with urination. No erectile dysfunction or change in libido.

Musculoskeletal: Diffuse arthralgias and occasional joint swelling in his arms. No changes in shoe, ring finger size.

Neurological: Denies tremors, numbness, tingling, weakness.

Skin: Denies diaphoresis, new rash, changes in hair or nails. New frontal acne.

Psychiatric/Behavioral: Reports mood is depressed and feeling anxious. Wife reports he has been more "nervous."

PHYSICAL EXAMINATION

BP 129/83 **P** 92 **T** 36.6 **R** 81 **O2** 96% RA **Wt** 77.5 kg **Ht** 170.2 cm

GENERAL: Oriented to person, place, and time. Well-developed, well-nourished. No acute distress. **Tired appearing.**
HEENT: EOMI. Oropharynx clear. No frontal bossing or macroglossia is evident. There are no gross visual field deficits to confrontation.
NECK: Supple. Thyroid soft. There is no apparent goiter or thyromegaly. No acanthosis nigricans or skin tags are noted.
CV: Regular rate and rhythm. No murmurs, rubs, or gallops are appreciated. No JVD.
RESP: Good respiratory effort, clear to auscultation bilaterally with no wheezes or rales.
ABD: Soft, non-tender, non-distended. Normal bowel sounds present. No hepatosplenomegaly is appreciated. There are no violacieous striae.
GENITOURINARY: No galactorrhea expressed from nipples bilaterally.
MSK: Normal range of motion. No edema. 2+ distal peripheral pulses.
NEURO: No tremors. Normal gait. Normal reflexes with no change in relaxation phase.
SKIN: Skin is warm and dry. **Frontal acne is present.**
PSYCH: Normal mood and affect. Behavior, thought content appear normal.

DIAGNOSTIC EVALUATION

Glucose	105
Sodium	140
Potassium	4.2
Chloride	101
CO2	23
Anion Gap	16
BUN	50
Creatinine	2.3
GFR	30
Calcium	10.0
Albumin	4.1
Total Protein	6.1
T bili	0.5
Alk Phos	29
AST	21
ALT	11

WBC	6.3
HGB	14.2
HCT	43.2
PLT	180

TSH	1.37

CSF Analysis	Total cell count 25 RBC 25 Glucose 75 Protein 44 Bacterial, Fungal, HSV, CMV, JCV, Cryptococcal, AFB cultures Negative

DIAGNOSTIC EVALUATION OF HEADACHES - CT HEAD WO

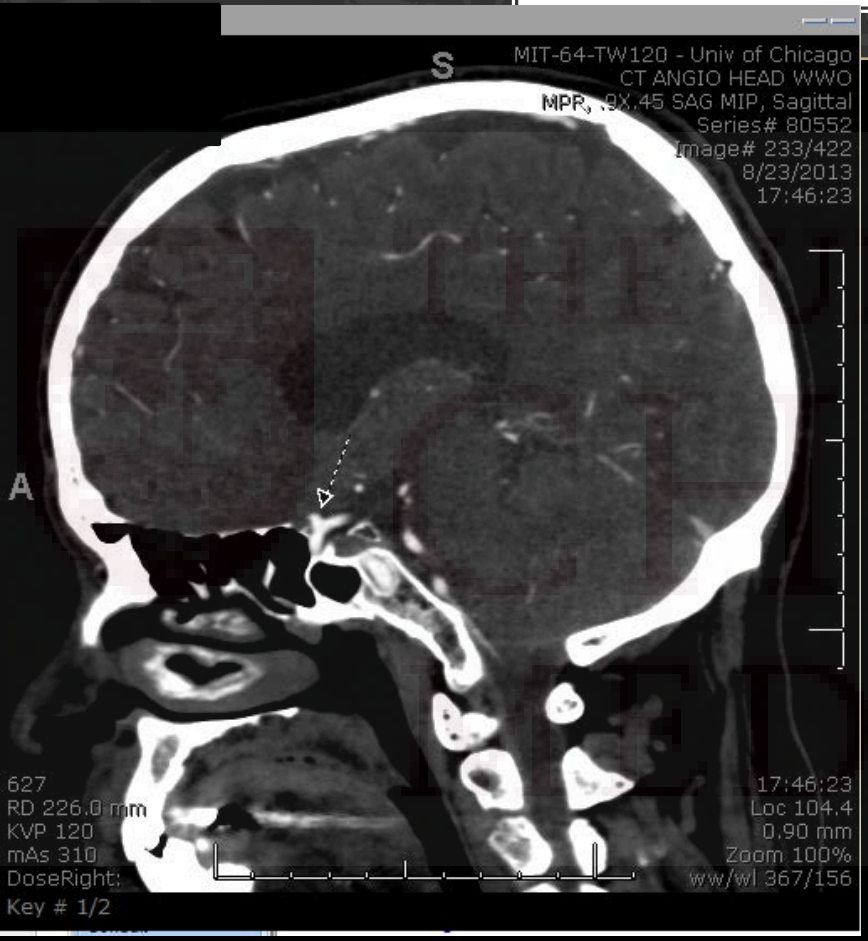
Soft tissue density is demonstrated extending from the left cavernous sinus region into the left sella turcica.

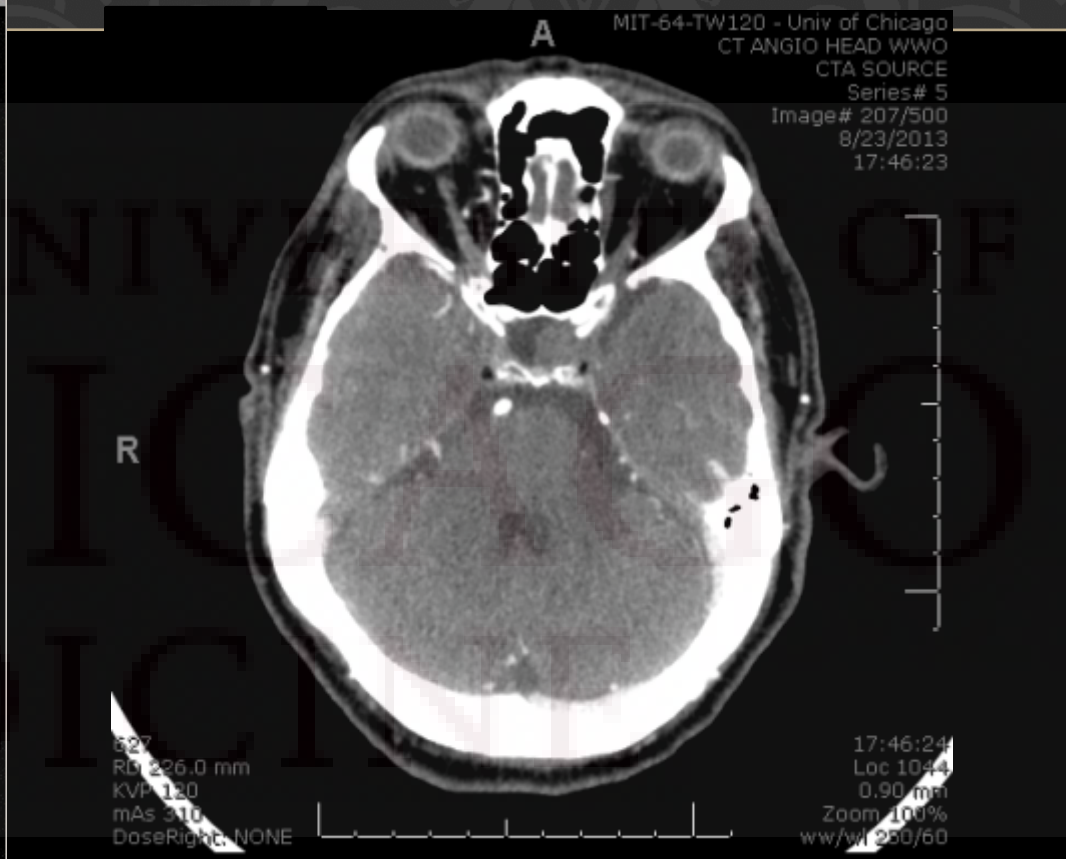
Ddx includes tortuous cavernous portion of internal carotid artery, meningioma, carotid a. aneurysm, or less likely pituitary adenoma.

Further eval with MRI brain/pituitary and MRA wwo is recommended.

Mild small vessel ischemic changes.

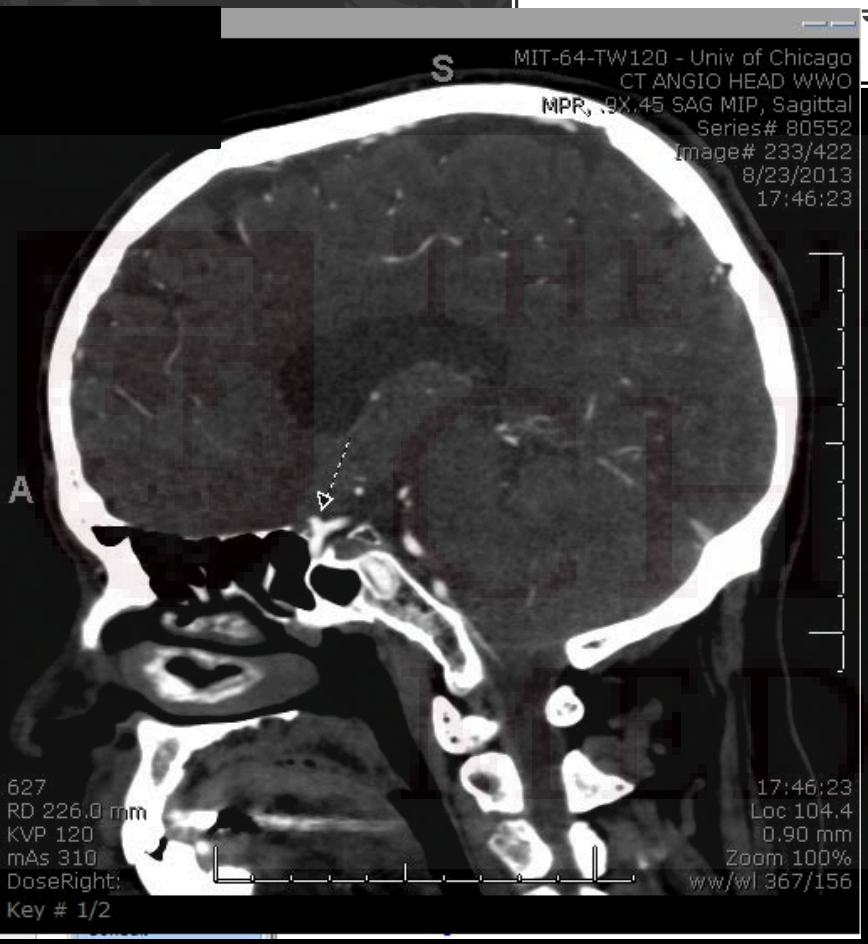
CT ANGIO HEAD WWO

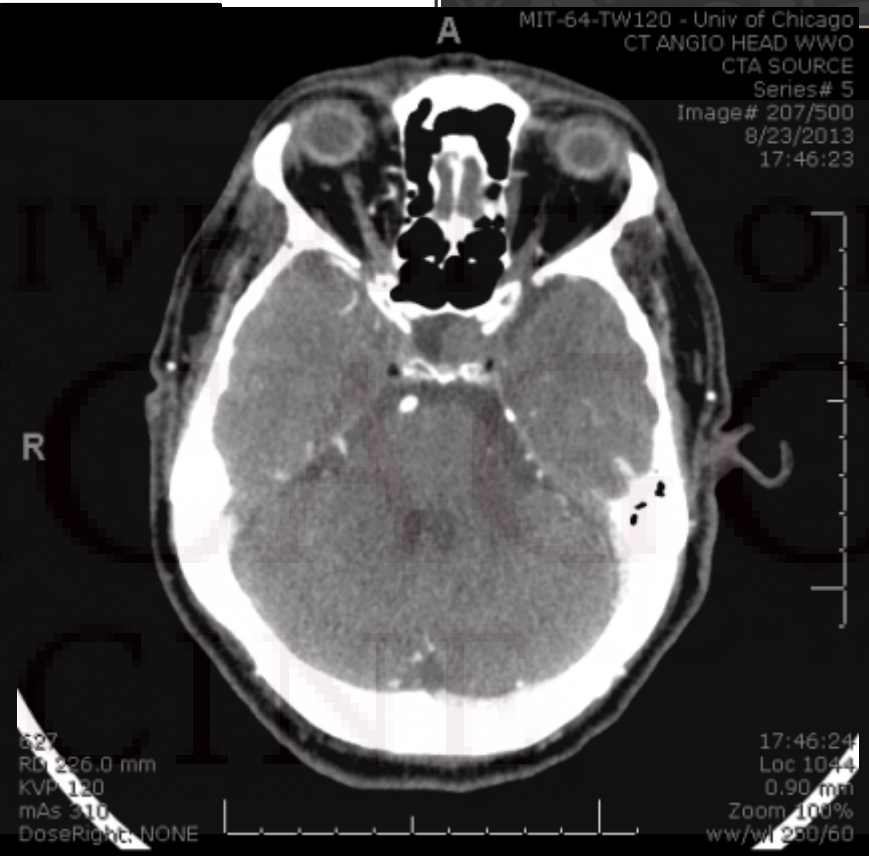




Redemonstration of soft tissue lesion occupying left sella and perhaps left cavernous sinus. Lesion may contact the left ICA, but is not vascular or aneurysmal in nature. The native pituitary gland is not clearly distinguished, and so the relationship of the lesion to the pituitary gland cannot be determined. The differential diagnosis would include meningioma or primary lesion of pituitary. MRI remains only adequate modality to better assess this lesion.

CT ANGIO HEAD WWO





The left half of the pituitary is heterogeneous and enlarged in appearance whereas the right half looks like a partial empty sella. It is conceivable that this may represent a microadenoma in the left half of the pituitary possibly associated with empty sella on the right side. An alternative explanation may be there is a different soft tissue mass in the left half of the sella such as a meningioma or another lesion.

BIOCHEMICAL EVALUATION OF PITUITARY AXES

Free Testosterone	97
Total Testosterone	271 Ref Range: 180-800 ng/dL
Sex Hormone Binding Globulin	29 Ref Range: 10-80 nmol/L

FSH	5.1
LH	6.4

Prolactin	14.2 Ref range: 4-15.2 ng/mL

Insulin-Like Growth Factor 1	386 Ref range: 81-225 ng/mL
Insulin-Like Growth Factor Binding Protein 3	6.6 Ref range: 3.4 -6.9
Growth Hormone	1.5 Ref range: 0-4.2ng/mL

TSH	1.37 Ref range: 0.3-4.0 mCu/mL
FT4	1.34 Ref range: 0.9-1.7ng/dL
T3	62 Ref range: 80-95 ng/dL

ELEVATED IGF-1 – WHAT'S NEXT?

Oral Glucose Tolerance Test with Growth Hormone Levels

Initial Inpatient OGTT – 8/28/2013

Time (min)	0	60	120
GH Ref range: 0-4.2 ng/mL	1.5	5.4	3.9

Follow-Up Outpatient OGTT – 9/11/2013

IGF-1	Time (min)	30	60	90	120
464 Ref range: 81-225 ng/mL	GH Ref range: 0-4.2 ng/mL	1.9	3.3	1.4	1.6

DIAGNOSIS OF ACROMEGALY

Random GH < 0.4 μg/L and normal IGF-1 excludes acromegaly

In a normal patient, serum GH should drop to < 1 ng/mL within two hours after ingestion of a glucose load of 75 g.

In an acromegalic patient, post-glucose GH is > 2 ng/mL in > 85% of the time.

Jaffe CA, et al. Regulation of GH secretion in acromegaly: reproducibility of daily GH profiles and attenuated negative feedback by IGF-1. J Clin Endocrinol Metab 2001; 86:4364-4370.

Giustina A, et al. Criteria for cure of acromegaly: a consensus statement. J Clin Endorinol Metab. 2000;85(2):526-529.

Table 1. Clinical Features of Acromegaly.

Local tumor effects
- Pituitary enlargement
- Visual-field defects → Formal testing with no deficits
- Cranial-nerve palsy
- Headache

Somatic systems
- Acral enlargement, including thickness of soft tissue of hands and feet
- Musculoskeletal system
  - Gigantism
  - Prognathism
  - Jaw malocclusion
  - Arthralgias and arthritis
  - Carpal tunnel syndrome
  - Acroparesthesia
  - Proximal myopathy
  - Hypertrophy of frontal bones
- **Skin and gastrointestinal system**
  - Hyperhidrosis
  - Oily texture
  - Skin tags
  - Colon polyps
- **Cardiovascular system**
  - Left ventricular hypertrophy
  - Asymmetric septal hypertrophy
  - Cardiomyopathy → Dilated,Non-Ischemic
  - Hypertension → Post-tx BPs < 130/90
  - Congestive heart failure → NYHA IV
- **Pulmonary system**
  - Sleep disturbances
  - Sleep apnea (central and obstructive)
  - Narcolepsy

Visceromegaly
- Tongue
- Thyroid gland
- Salivary glands
- Liver
- Spleen
- Kidney
- Prostate

Endocrine and metabolic systems
- Reproduction
  - Menstrual abnormalities
  - Galactorrhea
  - Decreased libido, impotence, low levels of sex hormone–binding globulin
- Multiple endocrine neoplasia type 1
  - Hyperparathyroidism
  - Pancreatic islet-cell tumors
- Carbohydrate
  - Impaired glucose tolerance
  - Insulin resistance and hyperinsulinemia
  - Diabetes mellitus → A1c 5.8
- Lipid
  - Hypertriglyceridemia → TG 139
- Mineral
  - Hypercalciuria, increased levels of 25-hydroxyvitamin D_3
  - Urinary hydroxyproline
- Electrolyte
  - Low renin levels
  - Increased aldosterone levels
- Thyroid
  - Low thyroxine-binding–globulin levels
  - Goiter

INITIAL MANAGEMENT OF ACROMEGALY

Transsphenoidal surgery – 1st line for
Intrasellar microadenomas
Noninvasive macroadenomas
Tumors causing compressive symptoms

Surgical removal provides biochemical control with IGF-1 normalization in 75-95% of patients

Contraindications to surgery:
Patient refusal, severe cardiomyopathy or respiratory disease, or lack of skilled surgeon availability

Melmed S, et al. Guidelines for acromegaly management: an update. J Clin Endocrinol Metab. 2009;94(5):1509-1517.

OUR PATIENT'S HEART – SURGICAL CANDIDATE?

ECHO 12/2012 (Pre-Re-Transplant)

Global LV dysfunction
Mild left ventricular hypertrophy, no septal hypertrophy
Left ventricular performance is moderately reduced (EF 34.9%)
Unable to assess diastolic dysfunction due to tachycardia
Right Ventricle normal in size – RV performance is reduced
There is no significant valvular disease

ECHO 4/2013 (Post- Re-Transplant)

Left and right ventricles are normal in size
Moderate left ventricular hypertrophy
Visually estimated LV EF is 65-70%
Mildly reduced RV performance
There is no significant valvular disease.

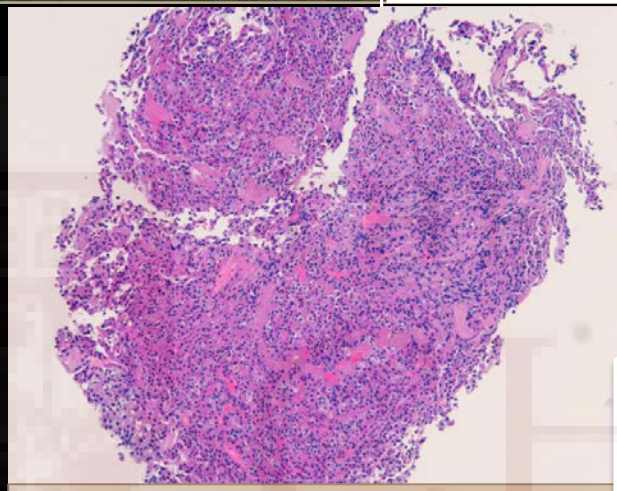
Cardiology assessment: "We discussed the patient at our transplant meeting and agreed that we should proceed with resection. He had his right heart catheterization and biopsy - his hemodynamics are good (just some dehydration). From a cardiac pre-op point of view, he would not need any other testing done."

MANAGEMENT

Patient underwent transsphenoidal resection of piutitary microadenoma on 11/4/2013.

Given his prolonged history of immunosuppression and prednisone therapy for OHT, it was recommended that he receive stress dose steroids peri-operatively.
Post-operatively, he was started on replacement corticosteroids with hydrocortisone 20 mg/10 mg daily.

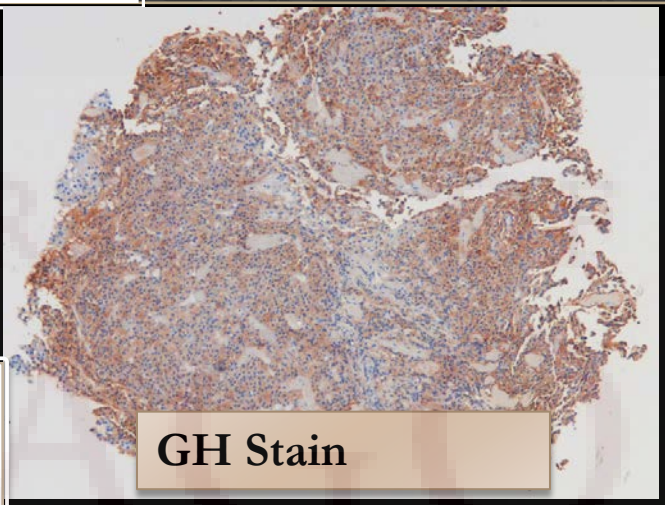
TRANSSPHENOIDAL RESECTION-PATHOLOGY



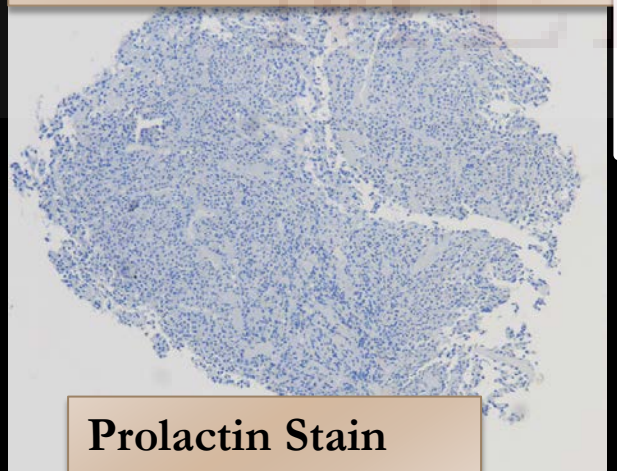
Original H&E
No expression of ACTH, TSH, Prolactin, LH, and FSH.
Patchy staining for GH

Frozen Path
2 soft-tissue adenoma fragments measuring 0.7 and 0.3 cm

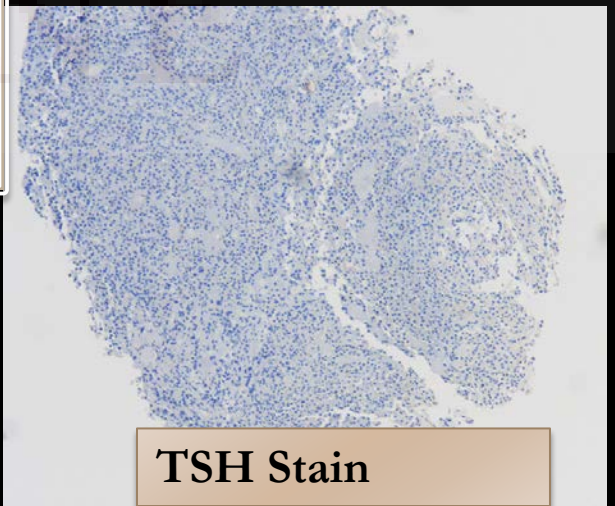
Fresh – multiple fragments from 0.1 to 0.6 cm in size



GH Stain



Prolactin Stain



TSH Stain

POST-OPERATIVE EVALUATION

	11/5/2013 05:14 (POD #1)	11/6/2013 03:41 (POD #2)
Growth Hormone Ref range: (0-4.2 ng/mL)	1.1	1.4
SMC/IGF1 Ref range: 81-225 ng/mL	474	319

	11/6/2013
TSH	1.66

24-hour UOP	1785 mL

With successful surgery, GH levels typically fall to normal within 1-2 hours (depending on level of elevation before surgery). IGF-1 concentrations fall more slowly, from weeks to months.

Feelders RA, et al. Postoperative evaluation of patients with acromegaly: clinical significance and timing of oral glucose tolerance testing and measurement of (free) insulin-like growth factor 1, acid-labile subunit, and growth hormone binding protein levels. J Clin Endocrinol Metab. 2005;90(12):6480.

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  - Goiter

ACROMEGALIC ARTHROPATHY

"Prior GH excess has irreversible, deleterious late effects on the clinical and radiological aspects of joints in patients with long-term cure of acromegaly"

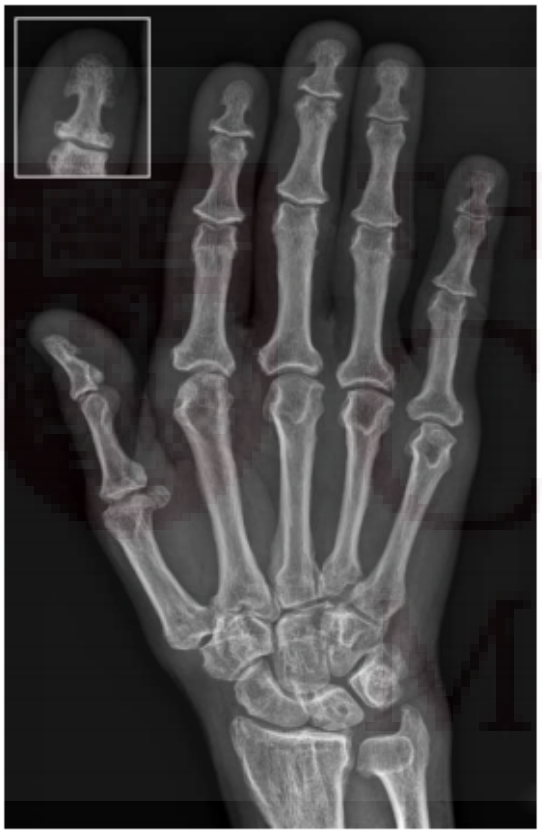

Figure 6 Hand. The main feature of osteoarthritis of the hands in acromegalic patients was the heavy tufting of the phalanges, with the terminal phalanges being spade-like in shape. Other features included degenerative changes in the metacarpophalangeal joints, such as subchondral sclerosis and osteophytosis with the preservation of the joint space resulting from increased cartilage thickness. Thus, this appearance known from active acromegaly persists even during the long-term follow-up.

Table 3 Prevalence of radiological osteoarthritis in acromegalic patients compared with a literature-based reference group.

	Patients (n=89) N (%)	Controls (n=4842) N (%)	Odds ratio	95% CI
Cervical spine	82 (92%)	1921 (40%)	10.5	4.9–22.1
Lumbar spine	78 (88%)	1600 (33%)	20.0	7.2–5.5
DIP	50 (56%)	1375 (28%)	1.7	1.1–2.8
PIP	38 (43%)	482 (10%)	4.2	2.6–6.8
CMC1	54 (61%)	684 (14%)	7.2	4.3–11.4
Hip right	27 (30%)	177 (4%)	6.9	4.1–11.5
Hip left	25 (28%)	155 (3%)	6.8	4.0–11.4
Knee right	34 (38%)	551 (11%)	2.3	1.5–3.8
Knee left	30 (34%)	537 (11%)	2.1	1.3–3.3

Data are shown as n (%). All data were corrected for age and sex using ANCOVA analysis. Controls were reference category. DIP, distal interphalangeal; PIP, proximal interphalangeal; MCP, metacarpophalangeal; CMC1, first carpometacarpal; CI, confidence interval.

99% of patients had radiological osteoarthritis (spine and hip most common and increased at all sites compared to controls)

Wassenaar MJE, et al. High prevalence of arthropathy, according to the definitions of radiological and clinical osteoarthritis, in patients with long-term cure of acromegaly: a case-control study. Eur Jour Endocrinol. 2008; 160:357-365.

POST-OPERATIVE MANAGEMENT

Plan for post-operative MRI and pituitary function testing in 3 months.

Additional imaging studies to be determined by presence or absence of surgical "cure."

Above will determine need for medical therapy with somatostatin analogues.

Patient should also undergo polysomnogram to evaluate for OSA (Prevalence of 25-60%)

Ongoing assessment of co-morbidities including: headaches, hypertension, arthralgias, assessment for diabetes, goiter

Baseline colonoscopy – internal hemorrhoids only

ASSESSING FOR CURE

TABLE 2. Acromegaly treatment outcomes

Outcome	Criteria	Management
Controlled	Nadir GH <1 μg/L Age-sex-normalized IGF-I No clinical activity	Asses GH/IGF-I axis Evaluate pituitary function Periodic MRI No treatment or no change in current treatment
Inadequately controlled	Nadir GH >1 μg/L Elevated IGF-I Clinically inactive	Assess GH/IGF-I axis Evaluate pituitary function Periodic MRI Assess cardiovascular, metabolic, and tumoral comorbidity Weigh treatment benefit or consider new treatment *vs.* low risk of elevated GH
Poor control	Nadir GH >1 μg/L Elevated IGF-I Clinically active	Assess GH/IGF-I axis Evaluate pituitary function Periodic MRI Actively treat or change treatment

Failure to control GH to a normal level is associated with a 3.5 x increased mortality as compared to patients in whom GH is controlled . Mortality in the latter is no different from controls.

Giustina A, et al. Criteria for cure of acromegaly: a consensus statement. J Clin Endorinol Metab. 2000;85(2):526-529.

OPTIONS BEYOND SURGERY

Comparison of treatments for acromegaly

	Surgery		Radiotherapy	Octreotide, lanreotide	Cabergoline	Pegvisomant
	Microadenoma	Macroadenoma				
Normal IGF-1	80-90 percent	40 percent	50 percent at 10 yrs	50 percent	40 percent	95 percent
Adenoma shrinkage	95 percent	70 percent	95 percent	50 percent	No data	Not expected
Advantages	Potential cure reduction	Rapid size reduction			Oral administration	
Disadvantages	Recurrence: 5-10 percent	Regrowth of adenoma	Slow	Injection		Injection
Complications						
Hypopituitarism	Rare	15 percent	50 percent at 10 yrs	None	None	None
Other	Diabetes insipidus, 5 percent	Diabetes insipidus, 10 percent	Neurological deficits	GI symptoms, gallstones	Nausea, lassitude	Elevated liver enzymes

A summary of the advantages, disadvantages, and complications of different treatments of acromegaly.

QUESTION REMAINS?

What caused this patient's cardiomyopathy?

CAUSE OF CARDIOMYOPATHY

Non-Ische

Orthotopic H

by cardiac all

Re-transplan

My

Ta

Pr

Chronic Ki

LECT-2 amy

Anemia

Erythropoietin

Cyanocobalamin

Ferrous sulfate

Growth Hormone-Producing Pituitary Adenoma With Crystal-Like Amyloid Immunohistochemically Positive for Growth Hormone

HIROSHI MORI, MD,* SHINTARO MORI, MD,†‡ YOUICHI SAITOH, MD,† KANAME MORIWAKI, MD,§
SAYOMI IIDA, MD,§ AND KEISHI MATSUMOTO, MD*

Growth hormone (GH)-producing pituitary adenoma from a 50-year-old acromegalic female was studied histochemically, immunohistochemically and electron microscopically. The adenoma was characterized by numerous crystal-like amyloid bodies of 5 to 40 μm in diameter. In the periphery of the crystal-like amyloid, bundles of amyloid fibrils were closely associated with deep invaginations of adenoma cells. The adenoma cells had numerous vesicles and vacuoles filled with amyloid fibrils, some of which were continuous with extracellular space. The crystal-like amyloids, as well as the adenoma cells, were immunohistochemically positive for GH. It might be possible that disorder of hydrolysis of "prohormone," from which GH is elaborated, is responsible for the amyloid production, and that amyloid discharge is accompanied with immunoreactive GH.

Cancer 55:96–102, 1985.

Limitations: Causality is not addressed.

Conclusions: Based on our studies, we posit that LECT2-associated renal amyloidosis represents a unique and perhaps not uncommon disease, especially in Mexican Americans. The pathogenesis, extent, and prognosis remain to be determined.

Am J Kidney Dis 56:1100-1107.

MULTI-DISCIPLINARY THOUGHTS

"We as the transplant team do not have much info on his original diagnosis prior to transplant #1."

Patient had dilated cardiomyopathy – not due to coronary artery disease and likely no known genetic cause. With no other known cause, GH induced heart failure would be high on the list.

Patient had 8 year graft survival, which is not terrible and since vasculopathy and graft failure is the #1 cause of death in heart transplant patients long term, it may have been just the natural history of his graft and he had documented rejection.

However, the conditional half life of a transplanted heart is 13 years. Could a GH producing tumor have accelerated his allograft vasculopathy is a good question?

BMJ Case Reports

Unexpected outcome (positive or negative) including adverse drug reactions

Normalisation of plasma growth hormone levels improved cardiac dysfunction due to acromegalic cardiomyopathy with severe fibrosis

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Summary

A 51-year-old man was referred to the Department of Cardiology in our hospital due to severe congestive heart failure and ventricular arrhythmias in March 2008. He had repeated ventricular tachycardia for years and the left ventricular ejection fraction (EF) was 11% on admission. A myocardial biopsy revealed that over 50% cardiomyocytes were replaced by fibrosis. Due to the typical acromegalic features, he was referred to the endocrinology department and diagnosed as acromegaly. He was treated with octreotide for 8 months followed by trans-sphenoidal surgery. The plasma levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) decreased by octreotide and normalised by surgery after which the cardiac function improved drastically. The current case demonstrates that cardiac dysfunction in acromegaly could be recovered by normalisation of GH and IGF-1 even in the presence of severe fibrosis in the myocardium.

adenomas, 2005, Albert Beckers and GrapiMed, Liege, Belgium.]

ACROMEGALIC CARDIOMYOPATHY

Impaired Structure → Functional Changes

Stage 1 – Hyperkinetic syndrome which can go undetected for years
- Increased contractility and cardiac output
- Increased LV mass, Reduced exercise capacity, normal or mildly abnormal diastolic filling.

Stage 2 – Intermediate stages, most adults diagnosed at this stage
- Concentric cardiac hypertrophy
- Diastolic filling abnormalities at rest
- Impaired cardiac performance at exercise

Stage 3 – Late stage, elderly patients with long disease duration
- Impaired systolic and diastolic performance
- Low cardiac ouptut even at rest
- Can also see cardiac valve disease (mitral and aortic)

Ectopic beats, paroxysmal atrial fibrillation, paroxysmal supraventricular tachycardia, sick sinus syndrome, ventricular tachycardia and bundle branch blocks are also more common than in controls.

Colao A, et al. The heart: an end-organ of GH action. Eur Jour Endocrinol. 2004;151:S93-S101.

WHO GETS ACROMEGALIC CARDIOMYOPATHY?

Table 2 Prevalence of cardiovascular and metabolic complications in patients with acromegaly and in age- and gender-matched controls. Data are present as *n* (%) Hypertension, diastolic blood pressure above 90 mmHg (30); diabetes mellitus, fasting glucose >7 mmol/l (126 mg/dl) at two consecutive measurements or 2 h after the oGTT glucose ≥11.1 mmol/l (200 mg/dl) (23); impaired glucose tolerance (IGT), impaired fasting glucose (IFG) <7 at baseline and between ≥7.7 mmol/l and <11.1 mg/dl 2 h after the oGTT (25); LV hypertrophy (LVH) was considered when LVM indexed for body surface area (LVMi) was ≥135 g/m^2 in men and ≥110 g/m^2 in women (21); diastolic dysfunction was diagnosed by an early-to-late mitral flow velocity ratio (E/A) below 1 while systolic dysfunction was diagnosed by a left ventricular ejection fraction below 50% (21, 22).

				Observed odds ratio		
	Patients	**Controls**	χ^2 *P*	OR	95% CI	Two-sided *P*
Prehypertension	85 (41.5)	136 (33.2)	0.10	1.43	0.99–2.04	0.049
Mild hypertension	43 (21.0)	56 (13.6)	0.003	1.67	1.05–2.66	0.027
Severe hypertension	60 (19.3)	86 (20.9)	<0.0001	1.58	1.04–2.32	0.027
Arrhythmias	14 (6.8)	6 (1.5)	0.013	4.93	1.74–15.9	0.001
IFG and/or IGT	57 (27.8)	52 (12.7)	<0.0001	2.65	1.70–4.13	<0.0001
Diabetes	47 (22.9)	50 (12.2)	0.006	2.14	1.34–3.40	0.0009
Left ventricular hypertrophy	160 (78.0)	41 (10.0)	<0.0001	11.9	7.40–19.5	<0.0001
Diastolic dysfunction	90 (43.9)	40 (9.8)	<0.0001	3.32	2.09–5.31	<0.0001
Systolic dysfunction	54 (26.3)	10 (2.4)	<0.0001	14.2	6.95–32.2	<0.0001

Matta MP, Caron P. Acromegalic cardiomyopathy: a review of the literature. Pituitary. 2003;6:203-207.

Colao A, et al. Determinants of cardiac disease in newly diagnosed patients with acromegaly: results of a 10 year survey study. Eur Jour Endocrinol. 2011;165:713-721.

OUTCOMES

Potentially reversible with:
Control of GH hypersecretion with surgery or somatostatin analogues
More likely when
- patient is < 45 years old
- shorter duration of GH hypersecretion
- maintain control of GH hypersecretion for > 5 years

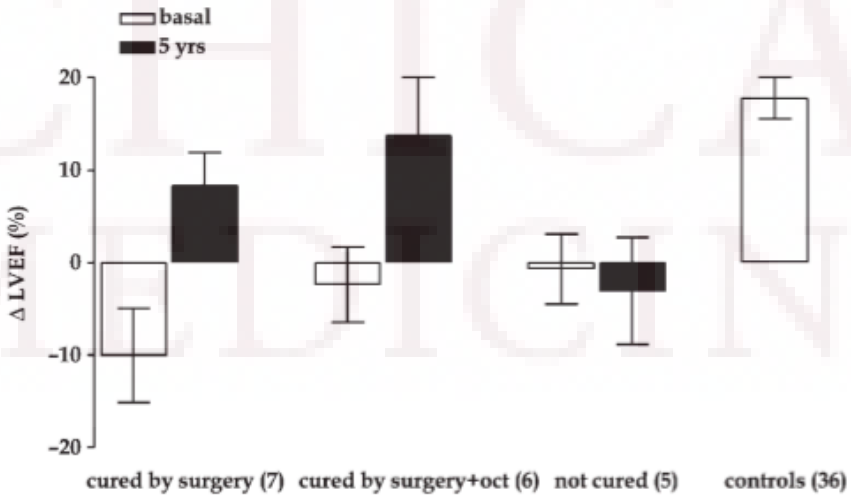

Figure 6 Results of the LVEF changes at peak exercise (normal >5%) (ΔLVEF) in patients with acromegaly before and 5 years after achieving disease controls by surgery, or surgery plus s.c. octreotide (oct) and in those patients not achieving disease control. Data are drawn from reference 56. Values are means±S.E.M.

Colao A, Cuocolo A, Marzullo P, et al. Is the acromegalia cardiomyopathy reversible? Effect of 5 year normalization of growth hormone and insulin-like growth factor-I levels on cardiac performance. J Clin Endocrinol Metab 2001;86:1551-7.

Colao A, et al. The heart: an end-organ of GH action. Eur Jour Endocrinol. 2004;151:S93-S101.

CARDIOMYOPATHY FOLLOWING SURGERY

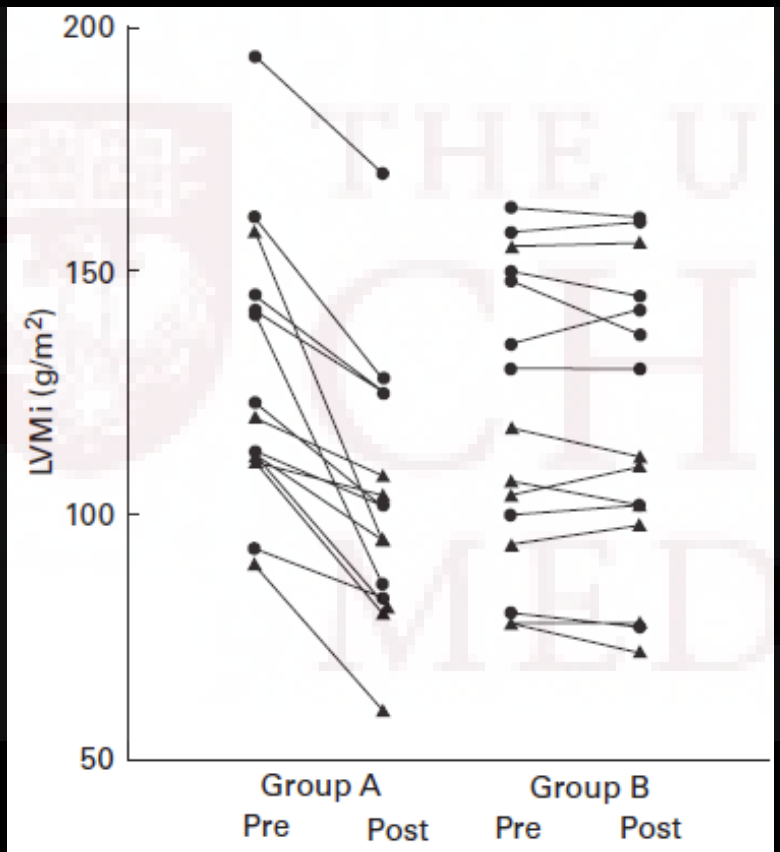

Fig. 1 Pre- and postoperative left ventricular mass index (LVMi) in well controlled (group A) and poorly controlled (group B) acromegalics. ▲, women; ●, men.

30 newly diagnosed acromegalics who underwent transsphenoidal surgery

Group A: 15 patients well-controlled after 6 months of surgery
- Significant decrease in LV mass
- Improvement in diastolic function
- Significant decrease in 24-hour systolic BP

Group B: 15 patients who did not achieve biochemical control after 6 months of surgery
- No significant change in above

Minniti G, et al. Marked improvement in cardiovascular function after successful transsphenoidal surgery in acromegalic patients. Clin Endocrinol. 2001;55:307-313.

CONCLUSIONS

Elevated serum IGF-1, with a Growth Hormone that fails to suppress after OGTT confirms diagnosis of acromegaly.

Surgical resection (transsphenoidal surgery) is first-line treatment for intrasellar microadenomas, noninvasive macroadenomas, and tumors causing compressive symptoms. When surgical control is not achieved, tumor anatomy is unfavorable to surgery, or patient is not a surgical candidate, medical therapies (somatostatin analogues, GHRH antagonists, and dopamine agonists), and radiation therapy can be considered.

Many, but not all, co-morbidities, including diabetes, hypertension, OSA, acromegalic cardiomyopathy may be reversible. Early detection of symptoms, identification of disease, and prompt treatment is imperative to preventing complications and decreasing mortality associated with acromegaly.

EXTRA SLIDES

THE UNIVERSITY OF CHICAGO MEDICINE

OUTCOMES IN ACROMEGALIC PATIENTS WITH CHF

TABLE 2. Cardiovascular characteristics at baseline and during follow-up in nine patients with acromegaly and CHF

Patient no.	Baseline (at time of CHF diagnosis)					Cardiovascular risk factors				Comorbidities	Cardiologic treatments	Follow-up			
	Age	NYHA stage	Echocardiography			HT	CHD	DM	Dyslip.			Duration (yr)	NYHA stage	Last LVEF	Outcome in 2003
			H	D	LVEF										
1	48	III	+	+	20	+	−	−	−	COPD	D, ARA	3	I	55	Still alive
2	42	IV	+	+	11	+	−	−	+	SAS	D, ARA, B	0.3	I	45[a]	Heart transplantation, 1989
3	54	IV	−	+	45	+	−	−	−	hT, AA	D, ACEI, Dig	16	I–II	32	Still alive
4	63	IV	+	+	33	+	−	+	−	COPD	D, ACEI, Dig, A	2	III	38	Still alive
5	58	IV	+	+	29	+	UK	−	−	AA	D, ACEI, A	5	I	16	Deceased–1990 (refractory CHF)
6	28	IV	UK	+	24	+	UK	+	−	−	D, ACEI, Dig	14	II	20	Deceased–1990 (refractory CHF)
7	59	III–IV	−	+	14	−	−	−	−	−	D, ACEI, A	6	II	53	Deceased–1998 (myocardial infarction)
8	47	IV	UK	+	37	+	+	+	+	−	D, ACEI, B	1	II	40	Deceased–2002 (refractory CHF)
9	62	IV	+	−	40	+	−	−	−	hT, SAS COPD	D, ACEI, B, Dig	9	II–III	68	Still alive

Echocardiography: H, ventricular hypertrophy (+, present; −, absent; UK, unknown); D, ventricular dilatation; LVEF, left ventricular ejection fraction (%).
Cardiovascular risks factors: HT, hypertension; CHD, coronary heart disease demonstrated by angiography; DM, diabetes mellitus; Dyslip., dyslipidemia.
Comorbidities: COPD, chronic obstructive pulmonary disease; SAS, sleep apnea syndrome; hT, hyperthyroidism; AA, atrial arrhythmia.
Cardiologic treatments: D, diuretics; ARA, angiotensin receptor antagonists; B, beta-blockers; ACEI, angiotensin-converting enzyme inhibitors; Dig, digitoxine; A, amiodarone.
[a] LVEF after heart transplantation.

TABLE 1. Biochemical levels at the time of diagnosis and at the last visit during follow-up in nine patients with acromegaly and CHF

Patient no.	Sex/age (yr) at diagnosis of acromegaly	Basal hormonal levels		Treatments of acromegaly[a]	Time with good control of GH/IGF hypersecretion (yr)	Hormonal levels at the last visit during follow-up	
		GH	IGF-I			GH	IGF-I
1	M/34	60	900[b]	S, SA	3	0.8	350[b]
2	M/41	3.2	960[b]	S, RT	6	<0.1	280
3	M/43	6.5	690[b]	S, RT, SA	12	0.8	210
4	M/63	12	680[b]	SA	2	4.5	220
5	M/59	264	NA	SA	Partial control	31	370[b]
6	M/38	11	NA	SA	Partial control	3	260
7	F/59	6.9	670[b]	S	5	3	180
8	M/47	39	550[b]	S, SA	No control	45	510[b]
9	M/62	10.2	330[b]	S, SA	8	0.1	111

Upper limit of normal range for IGF-I according to age: 410 μg/liter (30–40 yr), 375 (40–50), 315 (50–60), 285 (60–70), 265 (70–80), 155 (>80).

[a] S, Surgery; SA, somatostatin analogs; RT, radiotherapy.

[b] Supranormal levels of IGF-I; NA, not available.

9/330 (2.7%) of patients with acromegaly had systolic heart failure

TABLE 1. Hormone levels and hemodynamic and functional parameters measured at rest and at peak exercise by equilibrium radionuclide angiography in healthy controls and patients with uncomplicated acromegaly

Parameters	Controls (n = 36)		Patients (n = 18)		*P*
	Range	Mean ± SEM	Range	Mean ± SEM	
Age (yr)	23–60	38.7 ± 1.9	18–65	40.1 ± 2.7	
Serum GH levels (μg/L)[a]	0.1–1.2	0.4 ± 0.03	8–130	43.9 ± 9	0.0001
Plasma IGF-I levels (μg/L)	130–333	230.3 ± 9.2	350–850	600.7 ± 36.4	0.0001
Heart rate (bpm)					
At rest	48–96	73.9 ± 2.0	60–105	79.4 ± 2.9	0.5
During exercise	95–191	140.7 ± 3.5	103–168	135.4 ± 4.7	0.6
Systolic blood pressure (mm Hg)					
At rest	100–135	121.4 ± 1.2	90–150	121.1 ± 3.6	1
During exercise	130–200	165.0 ± 3.1	130–210	175.0 ± 5.6	0.6
Diastolic blood pressure (mm Hg)					
At rest	60–90	79.3 ± 1.2	60–90	76.4 ± 2.4	0.5
During exercise	80–120	100.0 ± 2.2	75–140	97.2 ± 3.3	0.3
Ejection fraction (%)					
At rest	50–78	61.6 ± 1.0	46–76	58.7 ± 1.7	0.4
During exercise	56–95	72.5 ± 1.5	37–75	56.1 ± 2.4	0.001
Δ (%)	0–50.7	17.8 ± 2.2	24–11.1	−4.9 ± 2.6	0.001
PER (EDV/sec)	2.1–5.5	3.6 ± 0.1	2.4–4.5	3.6 ± 0.1	1
PFR (EDV/sec)	1.6–4.1	2.8 ± 0.1	1.2–4.9	3.1 ± 0.2	0.6
PFR (SV/sec)	2.8–6.8	4.5 ± 0.1	2.1–9.7	5.1 ± 0.4	0.7
PFR/PER	0.4–1.1	0.7 ± 0.02	0.4–1.2	0.8 ± 0.05	0.05
Exercise duration	6–12	9.4 ± 0.2	6–8	6.9 ± 0.2	0.001
Exercise potency	75–125	100.0 ± 2.8	50–125	80.0 ± 3.7	0.001

[a] GH values are the mean of a 6-h blood sampling. The normal GH value was ≤2.5 μg/L. The normal IGF-I range in 20- to 30-, 31- to 40-, 41- to 50-, and over-50-yr-old subjects was 110–502, 100–494, 100–303, and 78–258 μg/L, respectively. Normal blood pressure DBP ≤ 90 mm Hg. The normal PFR was ≥2.5 EDV/sec. The normal ejection fraction at rest was >50% and the normal response of the ejection fraction at peak exercise was >5% of resting values.

Bridged with IABP and underwent re-transplant in March 2013. Pathology from transplanted heart showed changes consistent with chronic rejection:

- Coronary artery vasculopathy (chronic rejection).
- Multifocal Quilty lesions involving endocardium, myocardium and epicardium.
- Multifocal patchy fibrosis.

CORONAL DYNAMIC (NO POST CONTRAST CORONAL DONE)