51 y.o. female with hands swelling and tightness

Endorama, 01/10/2012,
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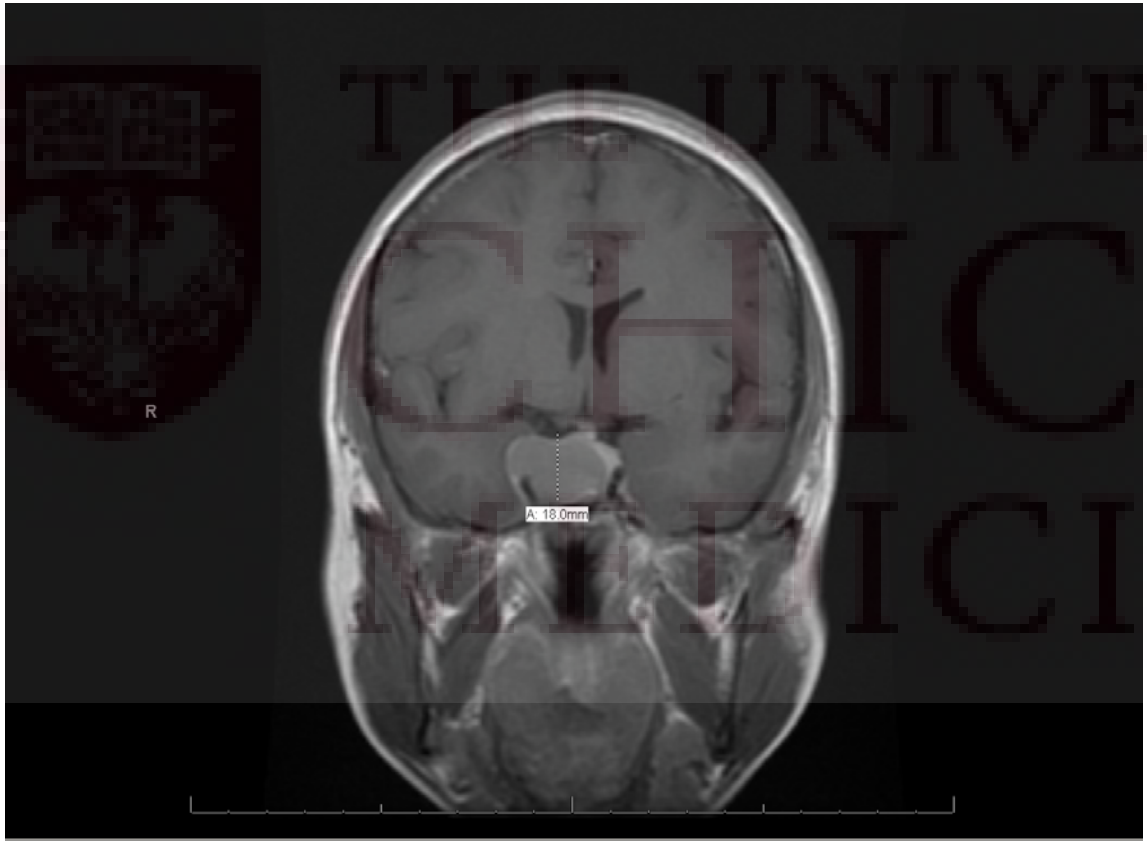
History of past illness:

- In 2005 the patient presented at the age of 44 y.o. with 3 months of morning stiffness in her hands, left more than right.
- She also noticed that 3 years prior to that her menstrual cycles became irregular 6-8 cycles per year for 1 year and then ceased completely. She attributed that to the menopause.
- Her PCP ordered MRI of C-spine and MRI of her head to evaluate for radicular type of pain.

MRI of the head and spine:



- **1. Minimal degenerative changes of the cervical spine with some questionable narrowing of the left neural foramen at C5-C6 and C6-C7 by bony degenerative changes. This would be better evaluated by CT scan or CT myelography.**
- **2. Sellar mass 1.8 cm in craniocaudal dimension, 2.3 cm in lateral dimension and approximately 2.0 cm in AP dimension partially encasing right internal carotid artery. Differential diagnosis including pituitary macroadenoma or less likely a meningioma.**

Labs:

- ACTH 14 (5 to 43 pg/mL)
- Cortisol 11.5 (8AM 6.8 to 26 mcg/dL)
- Estradiol 2 (30-400 pg/mL)
- LH 0.9 (Female adult range: 0.5-12.8 mIU/mL, except cycle peak range: 13.8-72 mIU/mL)
- FSH 11 (Female adult range: 0.6-13.3mIU/mL)
- IGF1 563 (90 - 360 ng/mL)
- Prolactin 149 (0 - 20 ng/mL)

75 g glucose tolerance test:

Elapsed Time (min):	0	30	60	120
Growth Hormone, Stimulated	7.8	6.0	5.8	4.2
Glucose	96	162	168	141

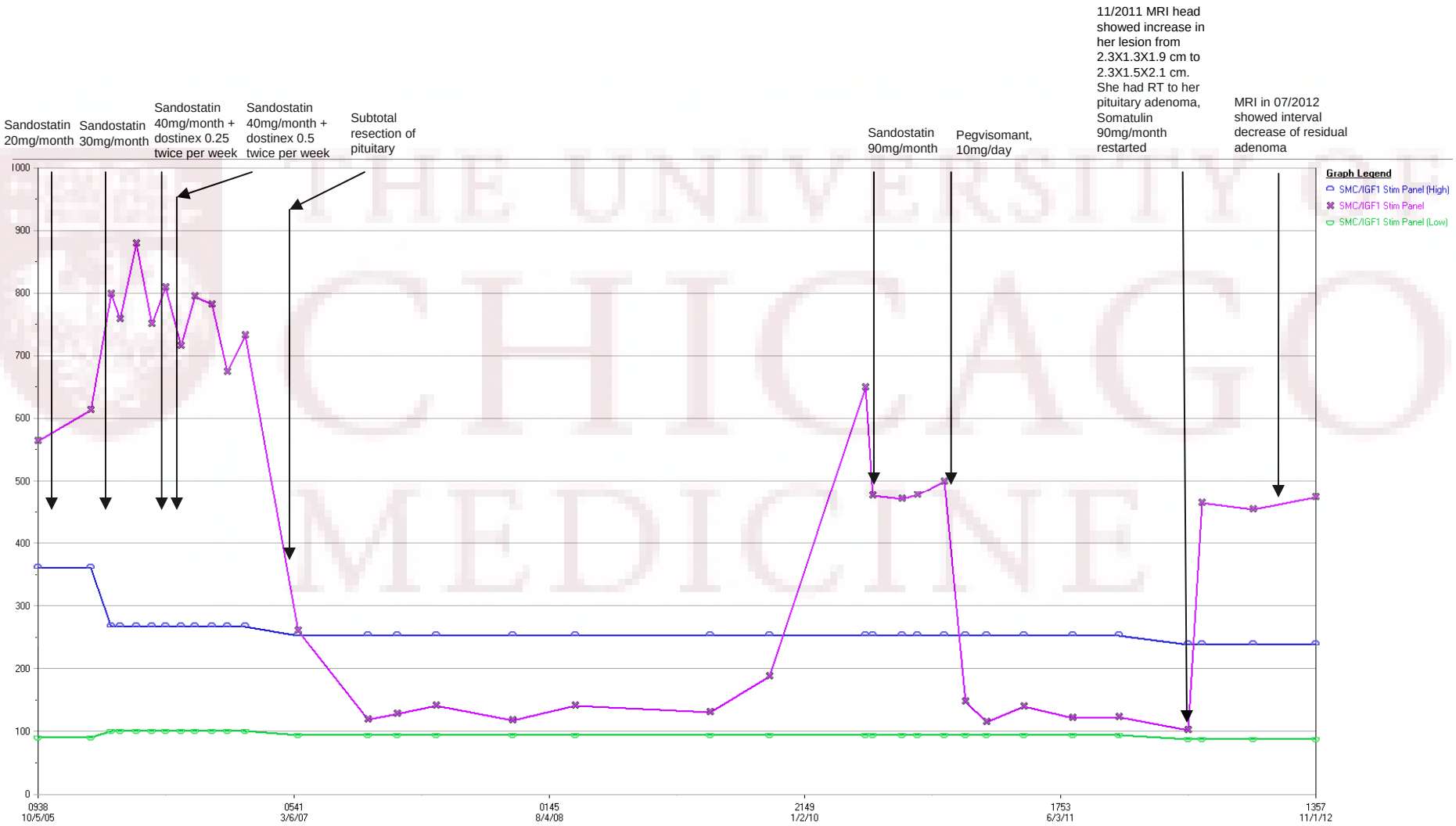
History of past illness:

- Acromegaly was confirmed by glucose tolerance test
- Due to anatomical location of the adenoma and the patient was started on a trial of medications

History of past illness:

- The patient was started on Sandostatin 20mg/month in 12/2005
- Increased to 30mg/month in 02/2006
- Increased to 40mg/month in 05/2006
- Dostinex 0.25mg twice a week added in 05/2006
- Dostinex increased to 0.5mg twice a week in 06/2006
- Subtotal resection of adenoma 12/2006
- Biochemically relapsed and restarted on Sandostatin 90mg/month in 06/2010
- Changed to Pegvisomant 10mg/day in 11/2010
- Adenoma increased in size on the MRI from 11/2011. She received RT with 52Gy and Pegvisomant was discontinued
- Somatuline 90mg/month restarted in 11/2011
- 07/2012 MRI showed interval decrease in size of her pituitary macroadenoma

Changes of IGF1 levels with a time and a course of treatment



Past medical history:

- Acromegaly
- Panhypopituitarism
- Glaucoma
- Cataract
- Osteoporosis

- Medications: hydrocortisone 10/5, levothyroxine 50mcg/day, zometa 2mg/year, somatulin 90mg/month, cosopt ophthalmic drops BID.

- Family history: asthma (father), dementia (mother), MI (father at the age of 75). No history of cancer, pituitary tumors, diabetes, thyroid problems in her family.

- Social history: works as a librarian, has 2 children, does not smoke, drink or use any illegal drugs.

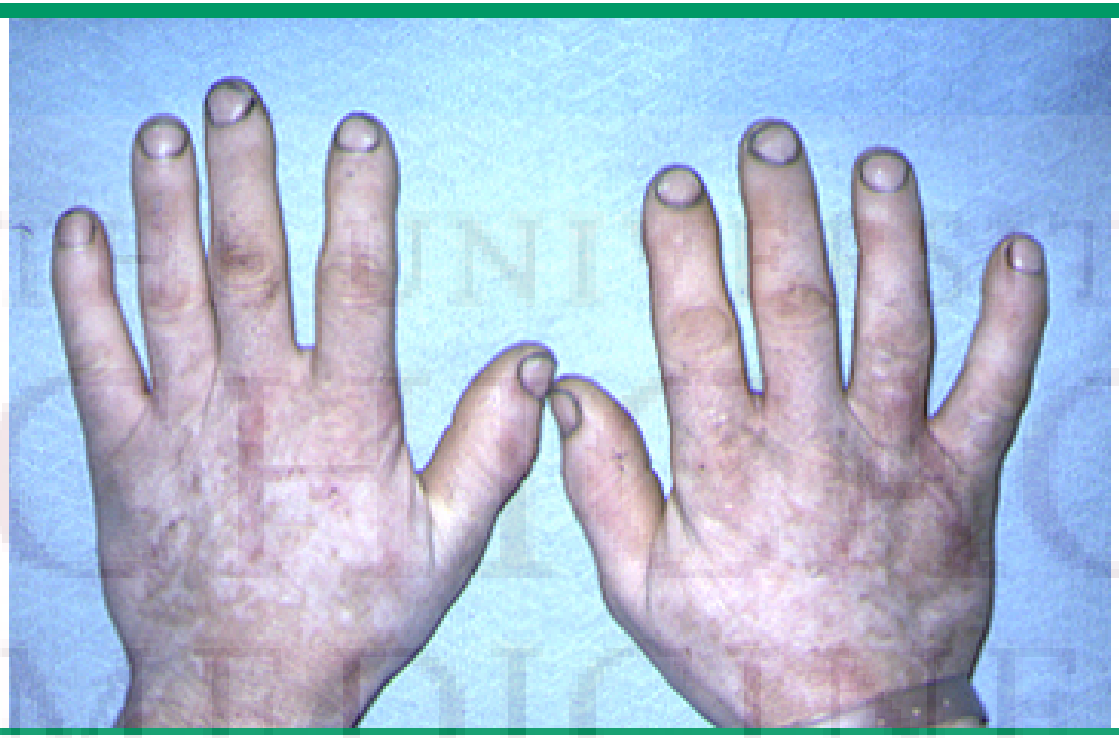
Review of systems:

- Constitutional: No fevers. No weight loss. **+Fatigue.**
- HEENT: No vision changes. No hoarseness. Neck: No neck swelling or pain.
- Cardiovascular: No chest pain. No palpitations.
- Respiratory: No dyspnea. No orthopnea.
- Gastrointestinal: No diarrhea. No constipation.
- Musculoskeletal: No muscle pain. No LE edema. **Hands swelling and tightness, that got worse in the last 6 months. She could not wear her wedding ring anymore.**
- Genitourinary: **+Amenorrhea since 2004.**
- Skin: No rash. No skin changes. No hair loss.
- Neurologic: No tremor. No headache. No weakness.
- Psychiatric: No depression. No anxiety. Endo: No polyuria. No polydypsia.

Physical exam:

- Head: Normocephalic and atraumatic.
- Mouth/Throat: Oropharynx is clear and moist. No oropharyngeal exudate. No macroglosia.
- Eyes: EOM are normal. Pupils are equal, round, and reactive to light. No scleral icterus.
- Neck: Normal range of motion. Neck supple. No JVD present**.** No tracheal deviation present. No thyromegaly present.
- Cardiovascular: Regularly heart rate and rhythm, normal heart sounds and intact distal pulses. No friction rub. No murmur heard.
- Pulmonary/Chest: Bilateral crackles. Moderate respiratory distress. No wheezes. No rales. No tenderness.
- Abdominal: Soft. Bowel sounds are normal. No distension and no mass. There is no tenderness. There is no rebound and no guarding. Swollen abdominal wall. No stretch marks.
- Musculoskeletal: Normal range of motion. No cervical adenopathy. **Enlarged, swollen hands.**
- Neurological: She is alert and oriented to person, place, and time. No cranial nerve deficit. Normal muscle tone. Coordination normal. Brisk reflexes in upper and lower extremities. No LE edema.
- Skin: **Skin thickening.** Skin is warm. Not diaphoretic. No erythema. No pallor.
- Psychiatric: normal mood and affect, behavior is normal. Judgment and thought content normal.
- Vitals: BP 102/62, pulse 72, respirations 20, height 149.9 cm (4' 11"), weight 45.088 kg (99 lb 6.4 oz).

Hands in acromegaly



Swelling of the hands in a patient with acromegaly, which resulted in an increase in glove size and the need to remove rings.

Courtesy of Verna Wright, MD, FRCP.

Labs:

141	103	16	114
4.0	29	0.8	

Ca 8.5 (8.4 - 10.2 mg/dL)

IGF1 473 (87 - 238 ng/mL)

GH 4.6 (0 - 4.2 ng/mL)

TSH 0.05 (0.30-4.00 mcU/mL)

Free T4 1.25 (0.9-1.7 ng/dL)

Total T3 102 (80-195 ng/dL)

- What is a persistent or recurrent acromegaly?
- How recurrent acromegaly should be managed?

The definition of ,,cure,, according to Cortina criteria:

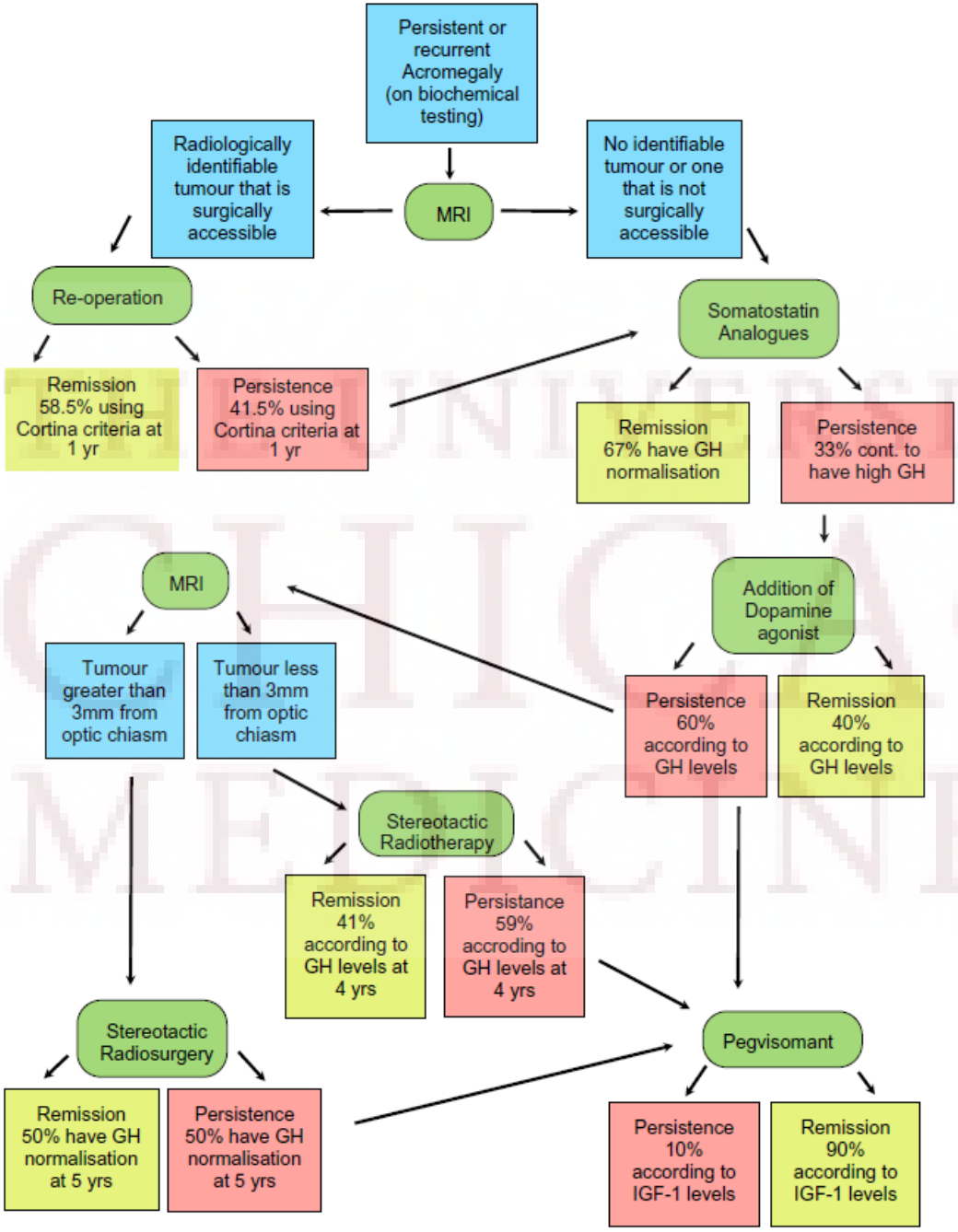
- Basal GH levels below 2.5 µg/L
- Supression of GH levels to 1 µg/L during OGTT
- IGF-1 level that is normal for age and gender.

- Persistent acromegaly: initial treatment of acromegaly failed to lead to remission (,,cure,,).

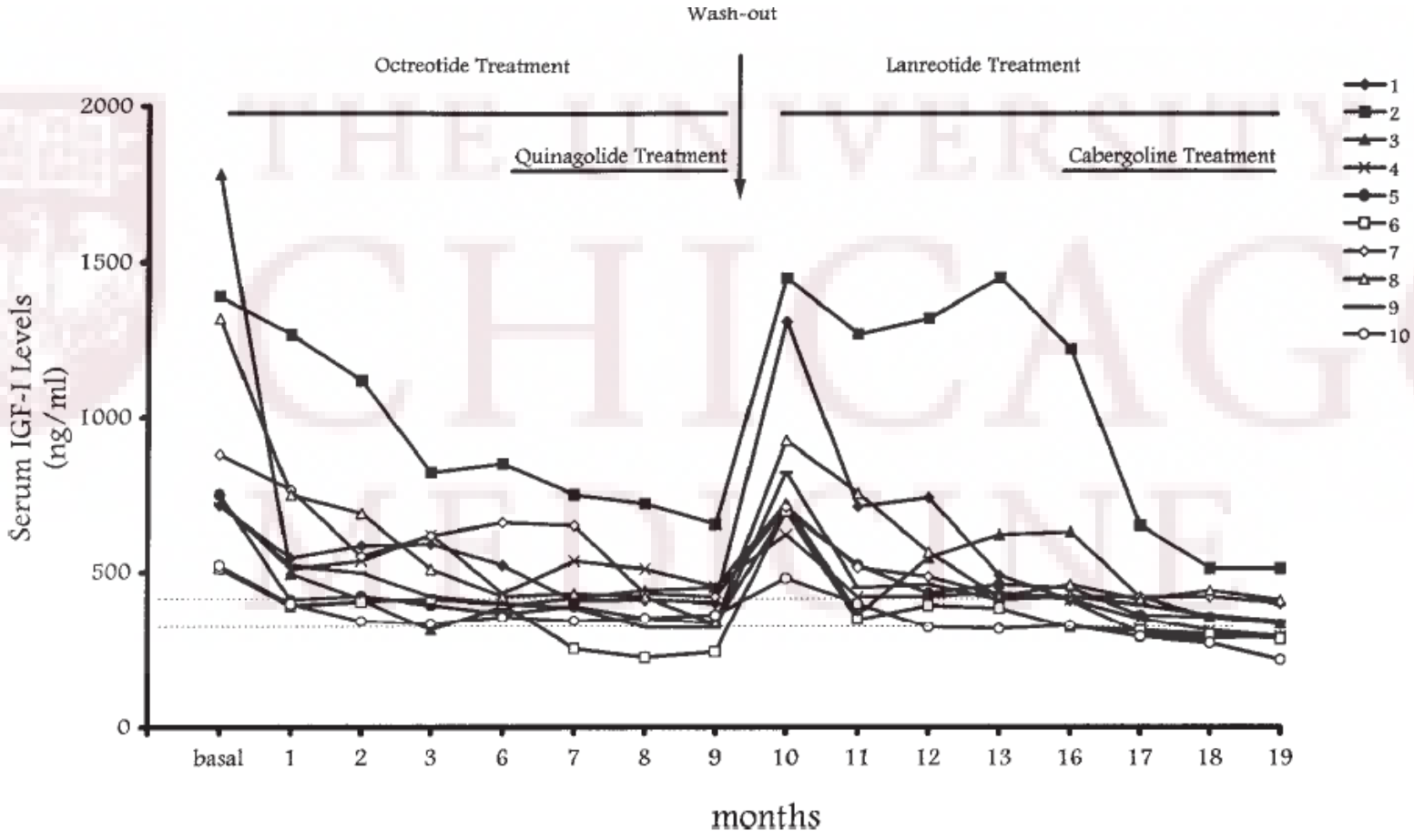
- Recurrent acromegaly: relapse into GH hypersecretion.

Treatment options for persistent or recurrent acromegaly

- Repeat surgery
- Radiotherapy (total of 40Gy to 54Gy delivered in fractionated doses 5 times per week over 5 weeks)
- Medical therapy (somatostatin analogues (octreotide, lanreotide, pasireotide), dopamine agonists (bromocriptine, carbegoline, quinagolide), somatostatin analogues + dopamine agonists, growth hormone receptor antagonists (pegvisomant))

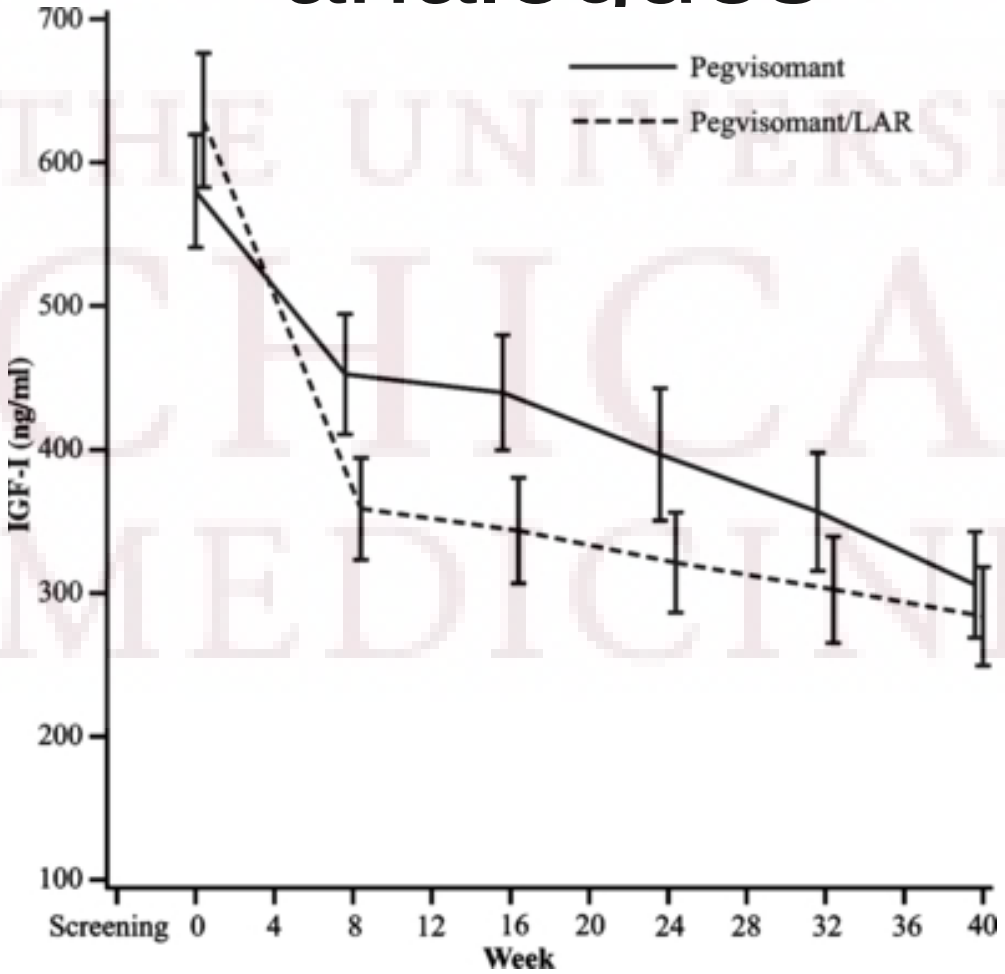

Persistent or recurrent Acromegaly (on biochemical testing)
MRI
Radiologically identifiable tumour that is surgically accessible
No identifiable tumour or one that is not surgically accessible
Re-operation
Remission 58.5% using Cortina criteria at 1 yr
Persistence 41.5% using Cortina criteria at 1 yr
Somatostatin Analogues
Remission 67% have GH normalisation
Persistence 33% cont. to have high GH
Addition of Dopamine agonist
Persistence 60% according to GH levels
Remission 40% according to GH levels
MRI
Tumour greater than 3mm from optic chiasm
Tumour less than 3mm from optic chiasm
Stereotactic Radiotherapy
Remission 41% according to GH levels at 4 yrs
Persistance 59% accroding to GH levels at 4 yrs
Stereotactic Radiosurgery
Remission 50% have GH normalisation at 5 yrs
Persistence 50% have GH normalisation at 5 yrs
Pegvisomant
Persistence 10% according to IGF-1 levels
Remission 90% according to IGF-1 levels

Somatostatin analogues + dopamine agonists



Marzullo P, Ferone D, Di Somma C, Pivonello R, Filippella M, Lombardi G, Colao A. Efficacy of combined treatment with lanreotide and cabergoline in selected therapy-resistant acromegalic patients. Pituitary. 1999;1(2):115-20

Growth hormone receptor antagonists+somatostatin analogues



Trainer PJ, Ezzat S, D'Souza GA, Layton G, Strasburger CJ. A randomized, controlled, multicentre trial comparing pegvisomant alone with combination therapy of pegvisomant and long-acting octreotide in patients with acromegaly. Clin Endocrinol (Oxf). 2009 Oct;71(4):549-57

- The patient was started on Somatulin 60mg/month and Dostinex 1mg/ twice a week with a plan to follow up on IGF1 levels in 3 months.

Take home points:

- Persistence (43%) or recurrence (2–3%) of GH hypersecretion after surgery remains a problem
- It is important to understand the current criteria for cure of acromegaly in order to determine which patients require secondary treatment following surgery
- Medical therapy is the way of the future in the treatment of persistent or recurrent acromegaly

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