60 year old Gentleman with significant proximal muscle weakness and newly diagnosed DM and HTN.

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First year Fellow
Endorama 10/10/2013

HPI

- 60 year old male with no significant PMH, presented to our clinic significant proximal muscle weakness.
- Doing well -> 2 months ago. Start c/o proximal muscle weakness, and worsening LE edema. Tried on Lasix for 2 week without benefit.
- Initially went to OSH and found to have very low K 1.6, BG 275, Dx with DM and HTN (BP 160/95).
- Muscle spasm worsened and start c/o increasing skin bruising. Admitted again to the hospital and endocrinology service was consulted
- Prior to this past 2 months he was ambulating without assistance and is currently requiring a wheelchair

- **PMH: recently diagnosed DM and HTN**
- **Past Surgical History: Non**
- **Social History: Denied smoking, alcohol or illicit drugs.**

Current Medications:

✓Spironolactone 25 mg po daily.
✓KCL 20 mEq TID
✓Lantus 25 units daily.
✓Flomax 0.4 mg po daily.
✓Prilosec 20 mg po daily.
✓Fluconazole 200 mg TID
✓Norvasc 10 mg po daily.

ROS

- **Constitutional:** generalized weakness **mainly proximal muscle.**
- **HENT:** No blurred vision, No sore throat, no VF problem
- **Neck:** No neck swelling, difficulty swallowing
- **Cardio/pulm:** No CP, no palpitation, no orthopnea or PND. **LE swelling**
- **GI:** No N/V/D, no constipation, **mild epigastric discomfort**, no melena or hematochezia
- **GU:** Negative
- **Skin: bruising ,** but no hyperpigmentation, no rash
- **MSK: generalized body ache,** No specific joint pain/swelling, **Neuro:** no numbness, no tingling, CN intact

On Examination

- **Vitals: BP 107/70 | Pulse 73, no fever, RR 15, BMI 34.36 kg/m2**

- **General: awake alert, sitting in a wheelchair, looks sick and tired.**
- **HEENT: normocephalic non traumatic, no plethora, no supraclavicular fullness or buffalo hump.**
- **Neck: supple, no LN enlargement, no thyromegaly, no JVD.**
- **CVS/Pulm: clear equal air entry no added sounds, S1 + S2, no murmur.**
- **Abd: soft lax, no organomegaly, audible bowel sounds.**
- **Skin: warm, no rash, no darkening, bruise in his legs bilateral.**
- **Neuro: CN intact, sensation normal , decrease proximal muscle power 3/5**
- **Psych: normal mood, and affect**

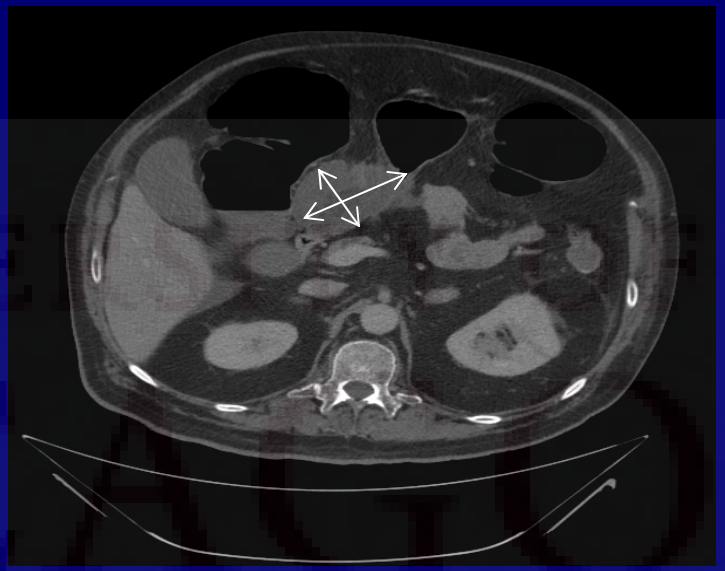
OSH Labs

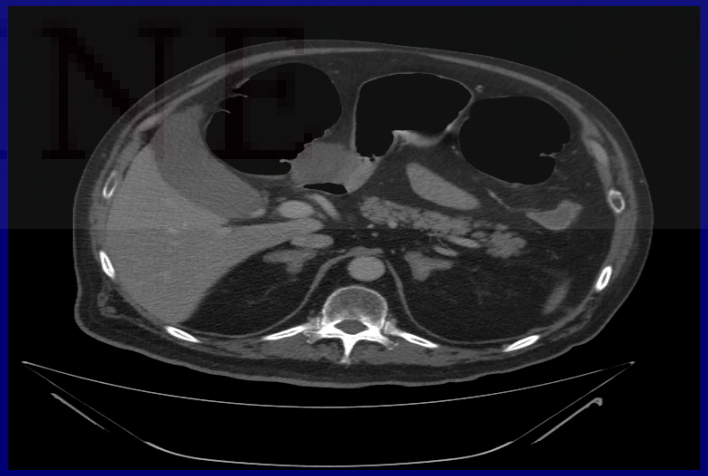
Test	Result	Test	Result
K	1.6	Renin	0.07 (2.9-10.8)
BG	275	Aldo	4 ng/dl (<21)
Bicarb	30	24hr UFC	3720
8 AM Cortisol	105	24hr U Cr	2179
ACTH	625		

Test	8 am Cortisol	ACTH	
LDDST 1 mg dex	93.7	450	
HDDST 8 mg dex	97.5		

OSH Radiological studies

- ✓ **CT chest: no acute chest pathology.**
- ✓ **CT Abdomen/Pelvis: Nonspecific stranding of the mesenteric fat/Omentum about the gastroepiploic artery w/single enlarged LN measuring up to 18 mm. Adrenal glands hyperplasia.**
- ✓ **MRI brain: pituitary stalk is midline, pituitary homogeneous w/no significant enhancement.**
- ✓ **Repeated CT Abd in a few days (b/c abdominal pain) showed low density soft tissue lesion extending from the anterior gastric antral surface of the anterior duodenum to the peripancreatic region. measures 7.4 x 5.4 cm at the anterior gastric surface. The adrenals are diffusely thickened bilaterally.**
- ✓ **EUS: Mass seen on CT abdomen was biopsied via EUS, consistent with pancreatic pseudocyst.**

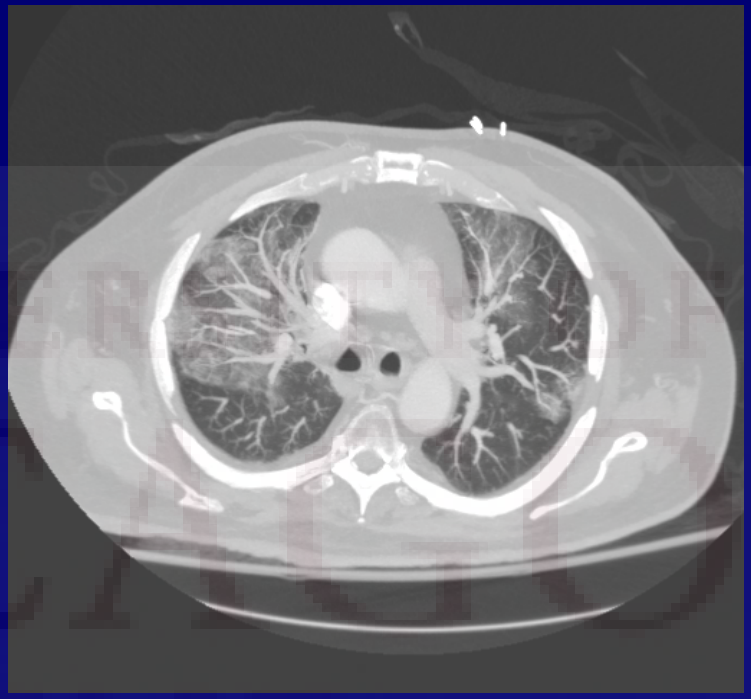




CT scan abdomen > enlarged adrenal glands B/L

OSH images continue

- ✓ **Repeated CT chest with contrast: patchy bilateral ground glass infiltrate mainly Rt upper lobe**
- ✓ **PET scan: irregular 3x4 cm hyper metabolic area at the upper lobe of the Rt lung.**
- ✓ **He was started on Fluconazole 200 mg TID x 1 wk (end of July til ~ 8/5) and we saw him on 8/7.**



Admission Labs at UCMC

Hb	13.3
WBC	8.6
Glucose	123
Hb A1c	8.2
K	4.4
Carbon dioxide	24
BG	189
BUN/Cr	21/0.9
Cortisol 8 pm	18.8
ACTH 8pm	997.0 (RR <52)
T3	87
FT4	0.86 (0.9-1.7)
TSH	1.8

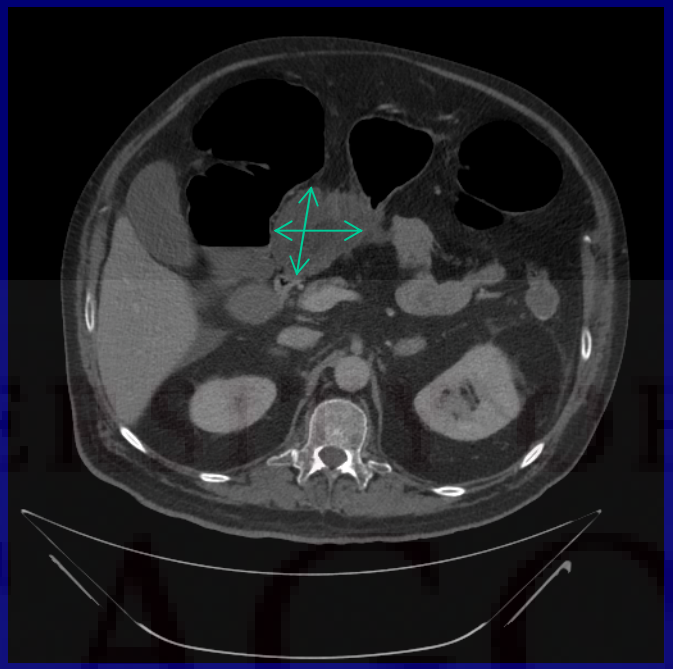
CRH Stim Test

Time/Test	Baseline	15 min	30 min	60 min	90 min	120 min	240 min
Cortisol	38.3	38	38.3	37.3	35.9	33.2	31.2
ACTH	261	280	289	250	219	207	197

Imaging studies at UCMC

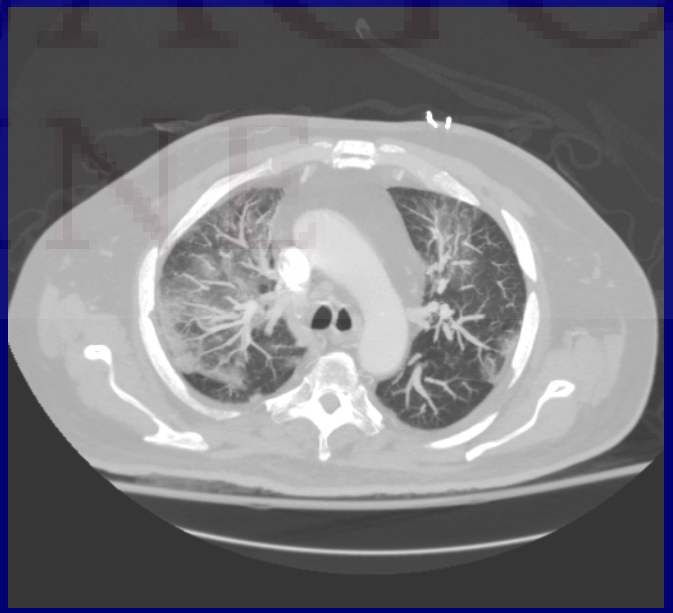
❖ CT chest/Abd:

- ➢ Mild upper lobe ground glass opacity compatible with infection or edema on this limited
- ➢ Mesenteric mass abutting the lesser curvature of the stomach 7.4 x 5.4cm



❖ EUS:

- ➢ lesion was cyctic, 70 cc fluid aspirated, cytology non diagnostic. **Culture grew MSSA (treated with 5 days of Amoxicillin)**



❖ Octreotide scan:

➢ Normal physiologic radiotracer distribution is seen in the spleen, kidneys, liver, bowel and bladder. There is no abnormal focus of activity to indicate an Octreotide avid lesion. No abnormal radiotracer uptake is seen in the patient's known mesenteric masses.

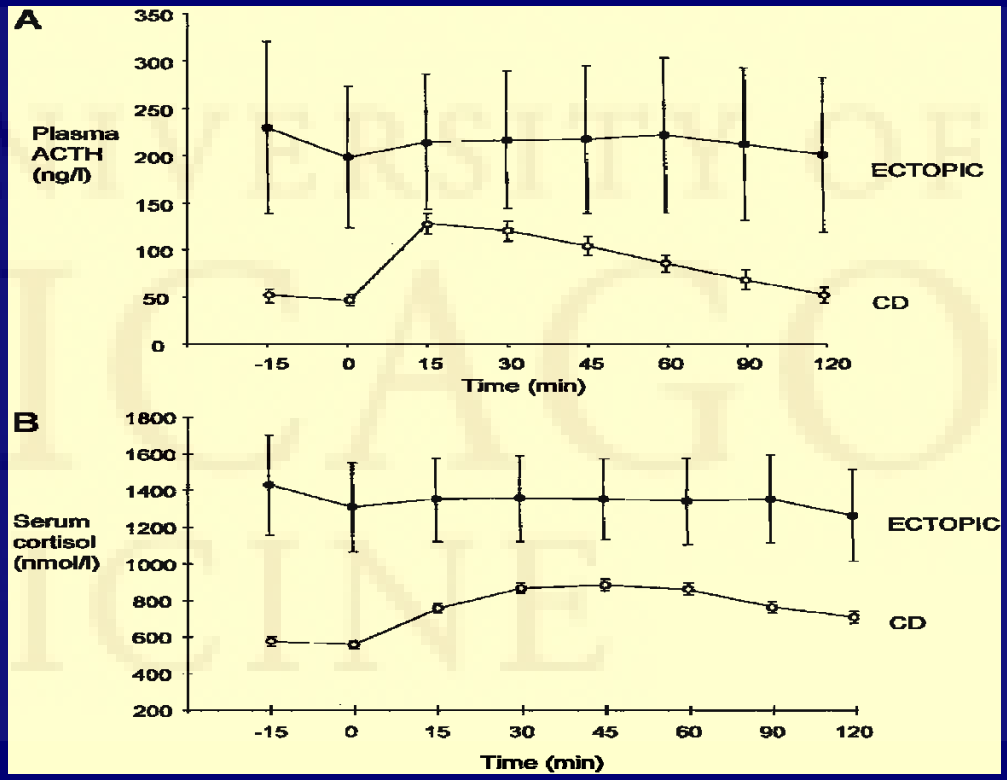
Clinical Qs

- Effectiveness of CRH-stim test in evaluation of ACTH dependent Cushing.
- Sensitivity of Octreotide scan.
- Recurrence rate of EAS after surgery
- Survival/prognosis of different causes of EAS.

CRH stim Test in the Differential Diagnosis of ACTH-Dependent Cushing's Syndrome

Randomized control study

- ✓115 pts with ACTH dependent Cushing
- ✓101 with CD (78 females; mean age, 40 yr)
- ✓14 with EC (7 females; mean age, 46 yr)
- ✓The response to hCRH was also studied in 30 normal with no clinical evidence of CS



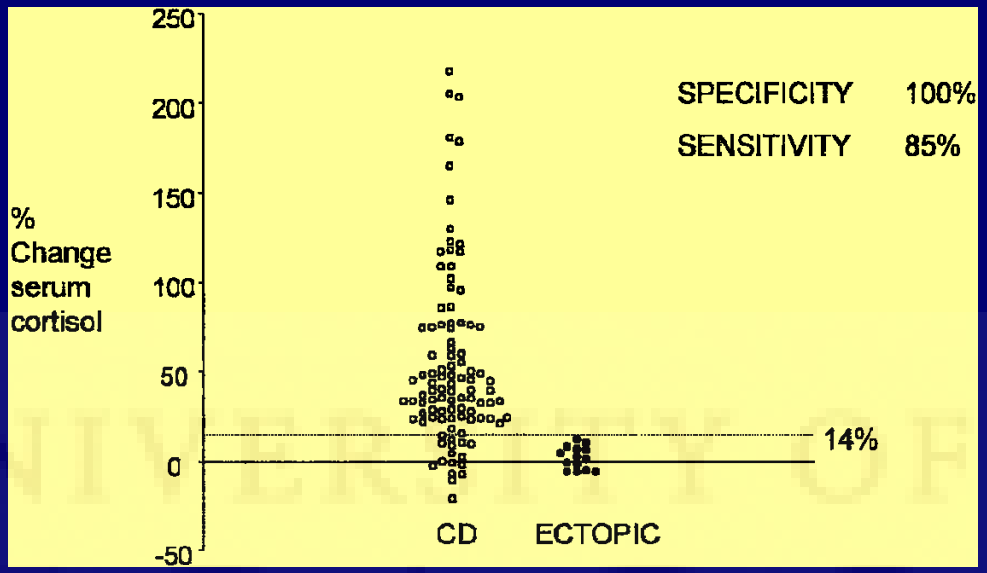
Mean (SEM) plasma ACTH (A) and serum cortisol (B) responses to hCRH (100 mcg iv) in the pt with CD and EC

J. NEWELL-PRICE, D. G. MORRIS, W. M. DRAKE, M. KORBONITS, J. P. MONSON, G. M. BESSER, AND A. B. GROSSMAN

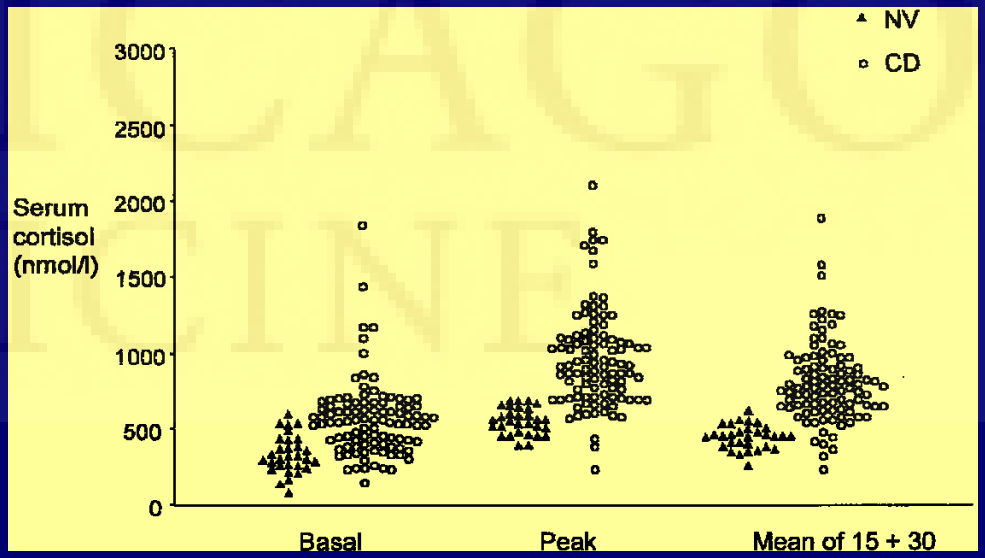
Department of Endocrinology, St. Bartholomew's Hospital, London EC1A 7BE, United Kingdom 2002

Continue

- Percentage change in serum cortisol from mean basal at 15, 30 min to meal value 15, 30 min after administration of hCRH in 100 patients with CD and 14 patients with EC



- Basal, peak and mean 15,30 min serum cortisol value in response to 100 mcg iv hCRH in **NV vs CD**



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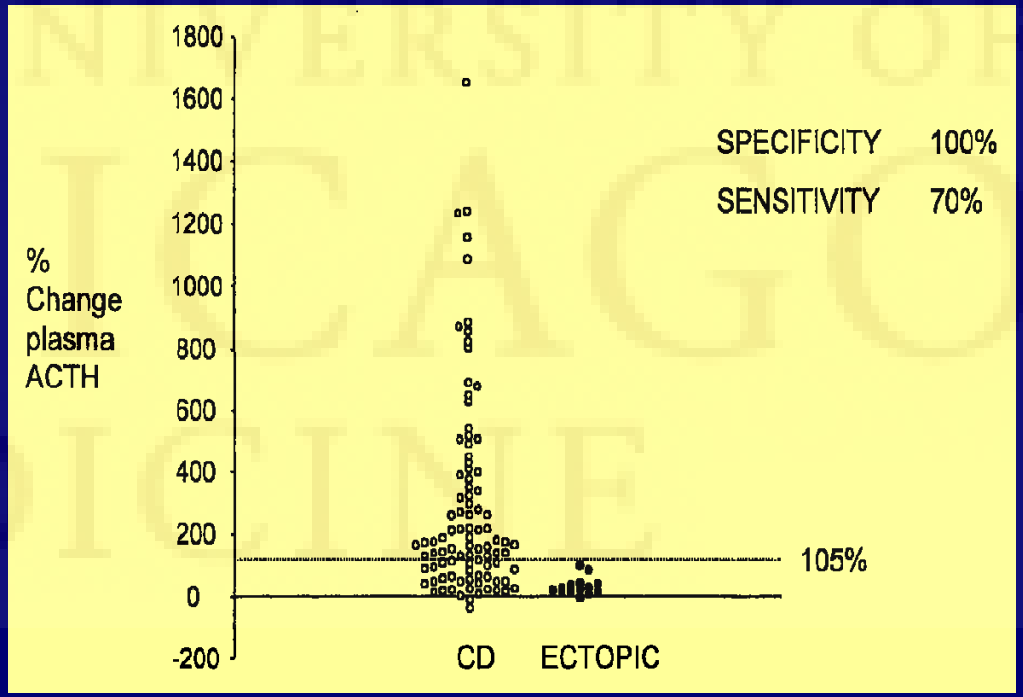
Percentage change in plasma ACTH from a mean basal at 15 and 0 min to the maximum value after the administration of hCRH (100 mcg iv)

- 94 patients with CD and 14 patients with the EC.



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After CRH stim-test

- Increase ACTH > 50% or cortisol >20 % have sensitivity of 85-90% and specificity of 95% of Cushing disease.
- Increase ACTH >100% or cortisol >50% has 100% sensitivity for Cushing disease.
- The sensitivity and specificity of **HDDS** in diagnosis of Pituitary dependent CD are 81% and 67.1% respectively.

Sensitivity and specificity of Octreotide scan

Comparison of Somatostatin Analog and Meta-Iodobenzylguanidine Radionuclides in the Diagnosis and Localization of Neuroendocrine Tumors

- Retrospectively analysis of 54 patients with a variety of neuroendocrine tumors of whom 46 patients had metastatic disease
- All patient had undergone imaging with both [^{123}I]MIBG and [^{111}In] pentetreotide scintigraphy

Result:

➢**MIBG** has been shown to have a more than 90% sensitivity and very high specificity for the diagnosis of adrenomedullary tumors, but a sensitivity of only 30–70% in detecting other neuroendocrine tumors.

➢**Radiolabeled Octreotide** has been shown to have a detection rate of 80–91% for all neuroendocrine tumors, *but is less specific*.

G. KALTSAS, and His Colleagues, Departments of Endocrinology (G.K., M.K., E.Z., J.J.M., P.J.J., S.L.C., J.P.M., G.M.B., A.B.G.), Diagnostic Radiology (R.R.), and Nuclear Medicine (R.F., K.E.B.), St. Bartholomew's Hospital, UK

Recurrence rate after the surgery

- Retrospectively reviewed the records of patients with EAS admitted to the NIH Clinical Center from 1983 through 2004.
- Median duration of follow-up was 26 months (range, 0–226 months)
- Number of Cases 86
- Occult source of EAS (n = 17)

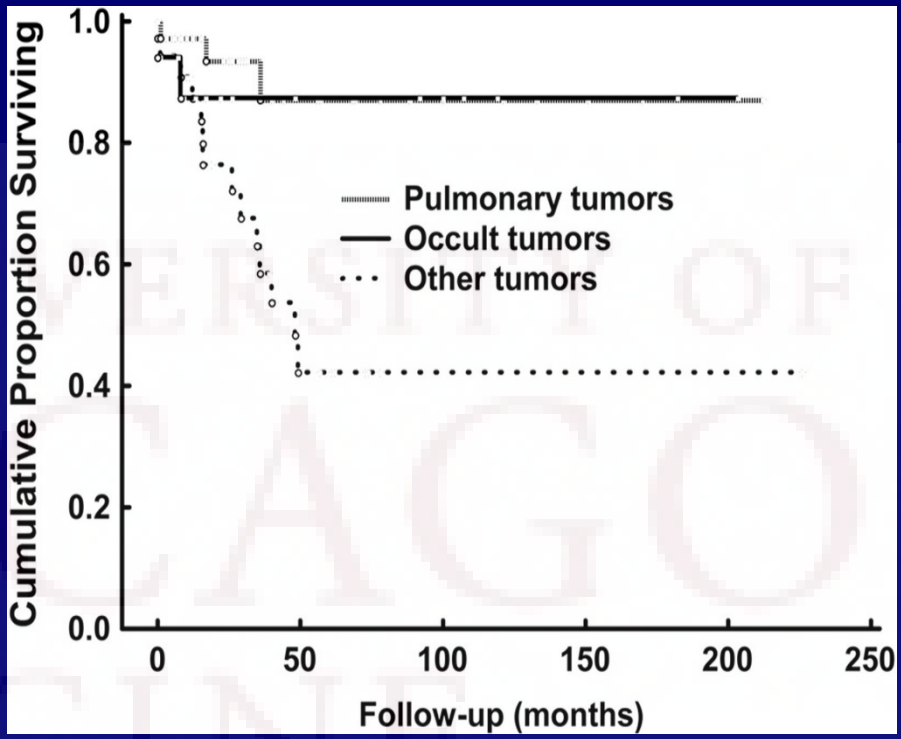
- ✓ **Three out of 29 patients with typical pulmonary carcinoids (no lymph node involvement, and no radiotherapy) relapsed in 128 months after surgery.**
- ✓ **One out 6 patients with atypical pulmonary carcinoid (positive lymph nodes, and no radiotherapy) relapsed after 48 months.**
- ✓ **One out of 13 patients with neuroendocrine tumor of the carotid sheath and postoperative radiotherapy relapsed after 120 months.**
- ✓ **All five patients are alive.**

Ioannis Ilias, David J. Torpy, Karel Pacak, Nancy Mullen, Robert A. Wesley, and Lynnette K. Nieman, 2005, National Institutes of Health
The Journal of Clinical Endocrinology & Metabolism 2005, 90(8):4955–4962

Survival of patient with EAS

- Eighteen patients are known to be deceased.

1) Three of 35 with pulmonary carcinoid
2) Two of five with thymic carcinoid
3) Four of six with gastrinoma
4) Two of 13 with neuroendocrine tumor
5) Two of two with medullary thyroid cancer
6) One of five with pheochromocytoma
7) Three of three with small cell lung cancer
8) One of 17 with occult tumor.



- Patients with an unknown/occult source of EAS survived longer, compared with those with an identified tumor, particularly during the later phase of follow-up.
- Among patients with an identified tumor, those with pulmonary ACTH-secreting tumors (excluding small cell lung cancer) survived longest.
- In general Unknown cause of elevated ACTH- 65% 5 year survival, 55% 10 year survival

Ilias I et al. JCEM 2005;90:4955-4962

Back to our patient

- ✓ Giving the fact that sever Hypercortisolism is a life-threatening Endocrinopathy, he underwent laparoscopic bilateral adrenalectomy on 8/13.
- ✓ Surgical pathology showed Rt Bilateral Adrenal hyperplasia (Rt 29.8 gm and Lt 22.5 gm)
- ✓ 24 hrs after surgery start c/o SOB, CTA chest negative for PE. SOB Improved by overnight BiPAP.
- ✓ Discharge on physiological dose of Hydrocortisone (20 mg QAM and 10 mg QPM) + 0.1 mg Fludrocortisone.
- ✓ Scheduled for repeating CT abdomen along with CT scan Guided biopsy on 11/3rd .

Summary

- CRH-Stim test is an excellent test for evaluation of patient with ACTH dependent Cushing.
- ✓ Increase ACTH > 50% or cortisol >20 % have sensitivity of 85-90% and specificity of 95% of Cushing disease.
- ✓ Increase ACTH >100% or cortisol >50% has 100% sensitivity for Cushing disease.
- Ectopic ACTH of unknown origin represent about 12% of Ectopic ACTH Secretion
- In general Unknown cause of elevated ACTH- 65% 5 year survival, 55% 10 year survival

References

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- Ilias L, Torpy DJ, Pacak K, Mullen N, Wesley RA, Nieman LK. Cushing's syndrome due to ectopic ACTH secretion. Twenty years' experience at National Institute of Health. *J Clin Endocrinol Metab* 2005; *90* : 4955-62.
- Harrison's principles of internal medicine.
- Up to date

Thank you