# 18 year old with Kearns Sayre Syndrome

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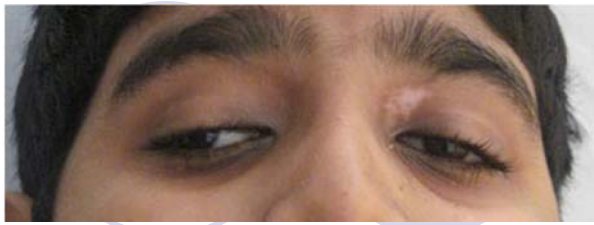
Endorama

6/28/12

# History of Present Illness

- Consulted for “possible endocrinopathies associated with Kearns Sayre Syndrome” in an 18 year old woman admitted for cardiogenic shock.

# Kearns Sayre Syndrome

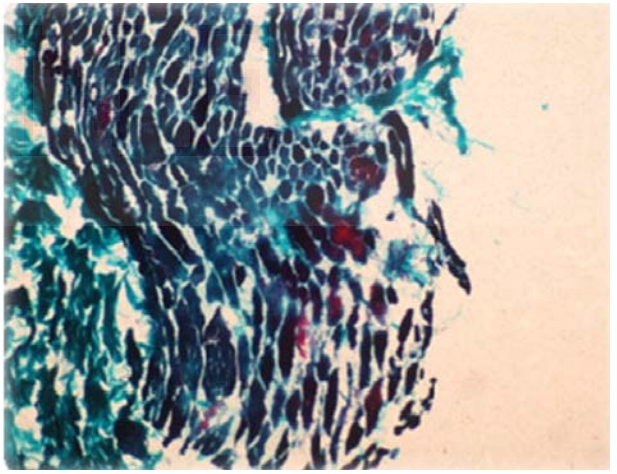


- Rare mitochondrial myopathy due to large-scale heteroplasmic deletions of mitochondrial DNA.
  - Usually spontaneous
  - No predilection for race or sex
  - No known risk factors
- Characterized by a triad of:
  - Chronic progressive external opthalmoplegia
  - Cardiac conduction abnormalities
  - Bilateral pigmentary retinopathy
- Additional features include myopathy, skeletal muscle weakness, exercise intolerance, bulbar symptoms (dysarthria, dystonia, dysphagia, facial weakness, deafness), cerebellar ataxia, dementia, proximal tubular acidosis, cataracts, and various endocrinopathies.
- Presents before age 20.

Phadeke et al. Indian J Pediatr. 2012 May;79(5):650-4.

# Kearns Sayre Syndrome

- Laboratory features:  normal or moderately elevated CK, elevated lactate and pyruvate
- Histology features:  red ragged fibers and large irregularly shaped mitochondria on muscle biospy.
- Radiographic features:  basal ganglia calcification on CT, spongiform encephalopathy on CT/MRI.
- No disease-modifying therapy.
  - Coenzyme Q10 and vitamin supplements.
- Death is common in 3rd and 4th decades of life.



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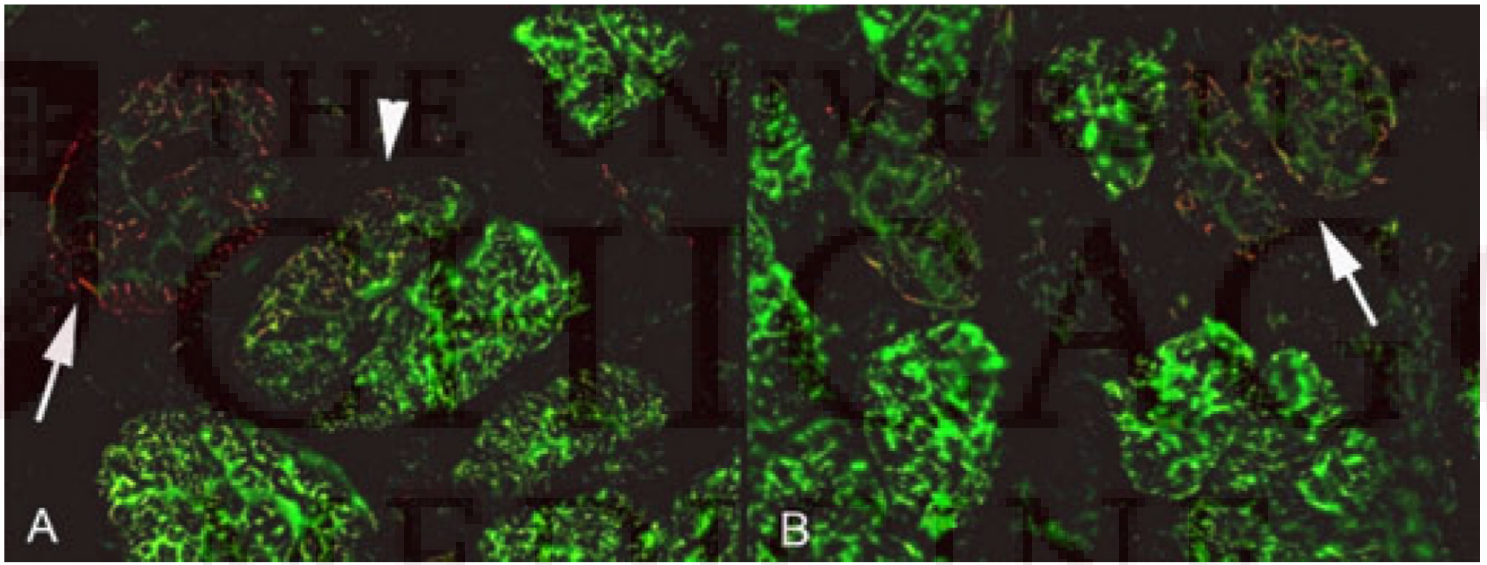
# Kearns Sayre Syndrome




Immunofluorescence for complex IV-I (A) and complex IV-IV (B) of the electron transport chain. Muscle fibers with total (arrows) or partial (arrow heads) deficiency.

Homan et al. Congest Heart Fail. 2011 Mar-Apr;17(2):102-4.

# History of Present Illness

- 18 year old AA woman with known history of Kearns-Sayre Syndrome diagnosed 5 years ago who was transferred from OSH with cardiogenic shock on multiple pressor support and balloon pump here for advanced care.
  - Initially presented to the OSH ER with 3 weeks of worsening generalized weakness, fatigue, and gait imbalance.
  - ROS also positive for generalized fever/chills, cough, dyspnea, diminished appetite, nausea, 5-7 lb recent weight loss.
  - Has often had generalized muscle weakness with KSS but never generalized fatigue.  No history of cardiac complications from KSS.
    - Prior TTE (4/15/09) normal LV/RV, trivial MR and TR

# History of Present Illness

- Recently seen as outpatient 3 weeks ago for sore throat, was strep negative and was felt to have GERD and started on Pepcid.
  - Labs were notable for elevated CK 3626 (baseline 1000s), elevated AST/ALT and Cr 0.5.
- On presentation to OSH pt was afebrile, HR 122, BP 98/62, and RR 20s. During the hospitalization her BP continued to trend downward and was started on dobutamine, milrinone, amiodarone, furosemide, and heparin gtts.
  - Initial labs at the OSH were notable CK 7725
  - TTE: LVEF: 10-15%
- Placed on ECMO.
- Underwent heart transplant.

# Past Medical History

- Past Medical History:
  - Kearns Sayre Syndrome
    - Diagnosed 5 years ago
    - Initially presented with fatigue and muscle weakness
    - Had ptosis eyelid surgery in 2010.
  - Osgood-Schlatter Disease
  - Asthma
  - Recurrent otits media
- Medications:
  - Leucovorin 5 mg BID
  - Levocarnitine 330 mg TID
  - Loratidine 10 mg QD
  - Pepcid 20 mg BID
  - Vit D3
  - Systane Ultra eyedrops
- Allergies:  Augmentin

- Social History:
  - Went to her senior prom
  - College student at Bradley University, majoring in graphic design
  - Lives with her parents
  - No tobacco, etoh, recreational drug use
- Family History:
  - Mother: thyroid problem; history of congestive heart failure
  - Father: DM, HTN

# Admission Physical Exam

- **VITALS:** Temp 97F, BP 93/53, HR 119, RR 20, 96%, 51 kg
- **GEN:** NAD, lethargic/somnolent, minimal verbal response reactive to verbal commands and answers questions appropriately
- **NEURO:** CN II-XII intact. Pupils 3 mm and sluggishly reactive to light**,** intact gag
- **HEENT:** Normocephalic, atraumatic, no gross craniofacial abnormalities, pupils sluggish to light, trachea midline, no cervical/submandibular/supraclavicular lymphadenopathy, no thyromegaly, mucous membranes dry and erythematous, no notable petechiae
- **CV:** irregularly irregular, tachycardic, pounding chest wall, no murmurs/rubs/gallops appreciated, JVP to ear lobe.
- **PULM:** minimal crackles at bases bilaterally. Respirations nonlabored. No wheezing/rubs
- **GI:** Soft, non-tender, non-distended, no rebounding, + guarding, no hepatomegaly, no splenomegaly, normal bowel sounds present.
- **GU:** No suprapubic or costovertebral angle tenderness.
- **SKIN:** No signs of peripheral edema. Extremities cold to touch. Petechial, non blanching rash to anterior chest
- **EXT:** <1sec capillary refill in upper extremities and lower extremities bilaterally.
- **DEVICES:** balloon pump to right femoral groin. Right subclavian 4LC.

Consulted for “possible associated endocrinopathies.”

# KSS and associated endocrine abnormalities

- Short stature: 85/226 (38%)
- Male hypogonadism: 26/123 (21%)
- Female hypogonadism: 18/102 (18%)
- Diabetes mellitus: 29/226 (13%)
  - Insulin-dependent: 14 cases
- Hypoparathyroidism: 14/226 (7%)
- Bone or tooth abnormalities: 13/226 (6%)
- Thyroid disease: 7/226 (3%)
- Hyperaldosteronism: 7/226 (3%)
- Hypomagnesemia: 8/226 (4%)

- Adrenal insufficiency: 4 case reports

Harvey et al. Clin Endocrinol (Oxf). 1992 Jul;37(1):97-103.
Sanaker et al. Acta Neurol Scand Suppl. 2007;187:64-7.

# Variability in KSS

**Table 1.** Proportion of the different recombinant forms of mtDNA in ten tissues from the KSS patient (on molecular basis)

| Tissue | %Normal | %Duplication | %Deletion | %Deletion dimer |
|---|---|---|---|---|
| Cerebral cortex | 58 | 3 | 18 | 19 |
| Cerebellum | 67 | 10 | 15 | 8 |
| Heart | 87 | 6 | 7 | < 1 |
| Muscle 1 | 80 | 10 | < 1 | 9 |
| Muscle 2 | 52 | 1 | 3 | 44 |
| Liver | 34 | 1 | 62 | 2 |
| Kidney | 30 | 16 | 36 | 18 |
| Pituitary | 55 | 11 | 23 | 11 |
| Pancreas | 59 | 10 | 39 | 3 |
| Ovary | 84 | 8 | 3 | 5 |
| Spleen | 65 | 7 | 18 | 9 |

All these samples were taken at post-mortem except muscle 1 which was a biopsy taken 10 years prior to death

Poulton et al. Diabetologia. 1995 Jul;38(7):868-71.

# Possible mechanisms of associated endocrinopathies

- Defective hormone production or secretion of hormone from deficiency of cellular metabolism.
- Hypothalamic damage
  - Spongiform degeneration of the brain
- Autoimmunity
  - Coincidental v. causally linked
  - Deficiency of cellular metabolism may lead to destruction of endocrine cells, abnormal presentation of autoantigens, production of autoantibodies, and secondary autoimmune endocrinopathy

Phadeke et al. Indian J Pediatr. 2012 May;79(5):650-4.
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# Status at time of consult

- Medications:
  - Dobutamine gtt
  - Dopamine gtt
  - Heparin gtt
  - Methylprednisolone 100 mg q8 hr
  - Mycophenolate 750 mg q12 hr
  - Cefepime 1 gm q12 hr
  - Vancomycin 1 gm q 24 hr
  - Ganciclovir 5mg/kg q24 hr
  - Famotidine 20 mg qhs
  - Duoneb nebulizer q4 hr
  - Ascorbic acid 500 mg TID
  - Ferrous sulfate 300 mg TID
- D5NS at 40 cc/hr
- PRNs:
  - Magnesium
  - Potassium
  - Morphine
  - Zofran
  - Benadryl
- Physical Exam:
  - Intubated
  - Anasarca, chemosis
  - Unable to elicit DTRs
  - No Chvestok's sign.

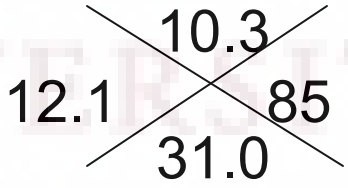
# Admission labs

137 103 30 / 113
3.8 17 2.2

Ca 8.1, Phos 2.8, Mg 1.9

Total protein 6.1, alb 3.4
Prealbumin 11 (21-41)
Tbili 1.6, alk phos 49
AST 282, ALT 205
LDH 1159
Lactic acid 5.6

CK 1459, CK MB 27.1,
Trop T 0.14



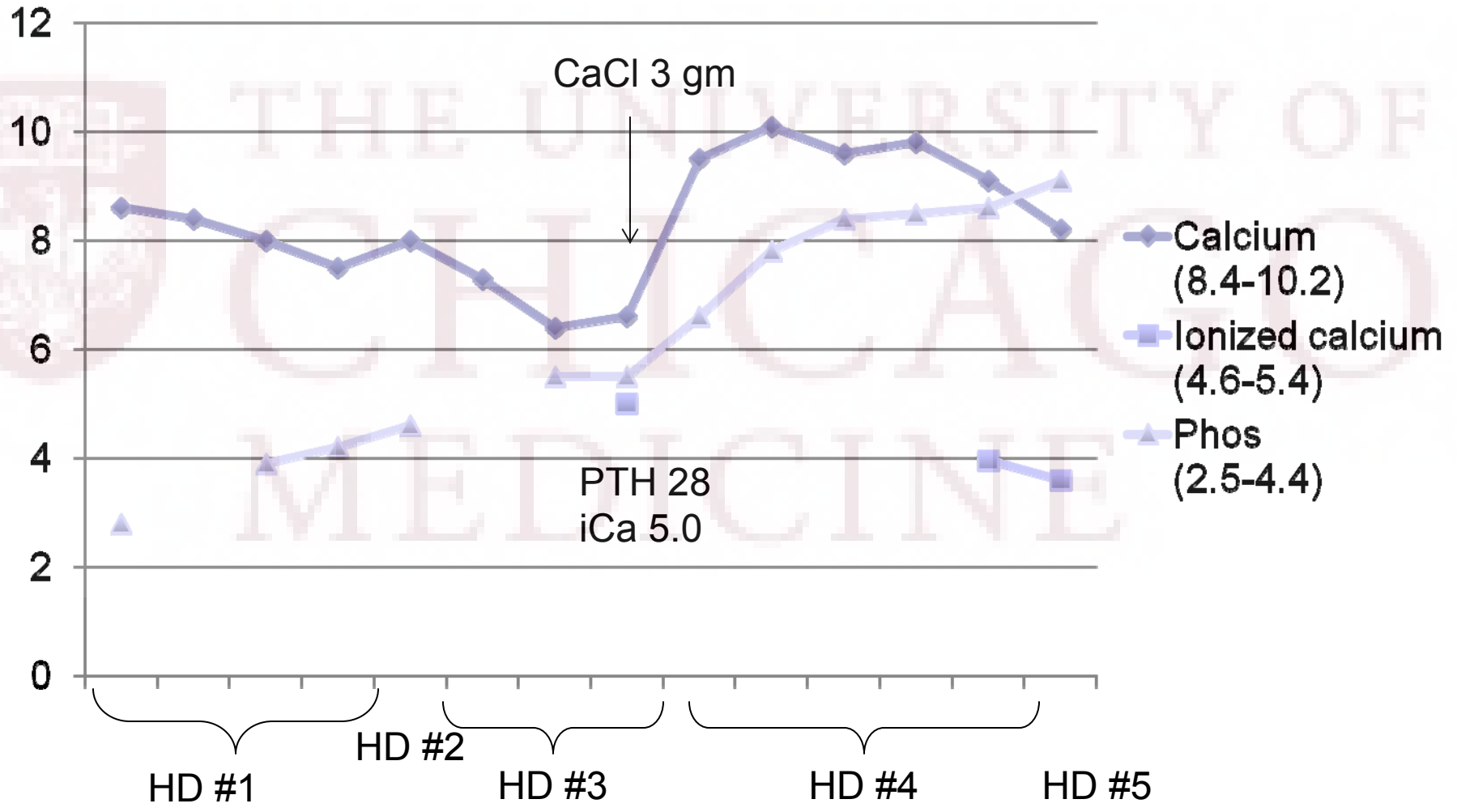

78N, 12L, 10 M

PT 17.9, PTT 51.2, INR 1.6

# Endocrine labs

- Outpatient clinic visit, 2 weeks prior to presentation:
  - TSH 1.234
  - Ca 9.1
  - Alb 4.1
  - Alk phos 47
- Admission:
  - Ca 8.1 (corr 8.6)
  - Phos 2.8
- Glucose: 67-194
  - On high dose steroids, continuous tube feeds
- HgbA1c 5.7%
- TFTs:
  - TSH 3.05
  - T4 6.6 (5.0-11.6)
  - T3 52 (80-195)
  - fT3 129 (230-420)
  - rT3 1547 (160-353)

# Calcium Trend



# Assessment and Plan:

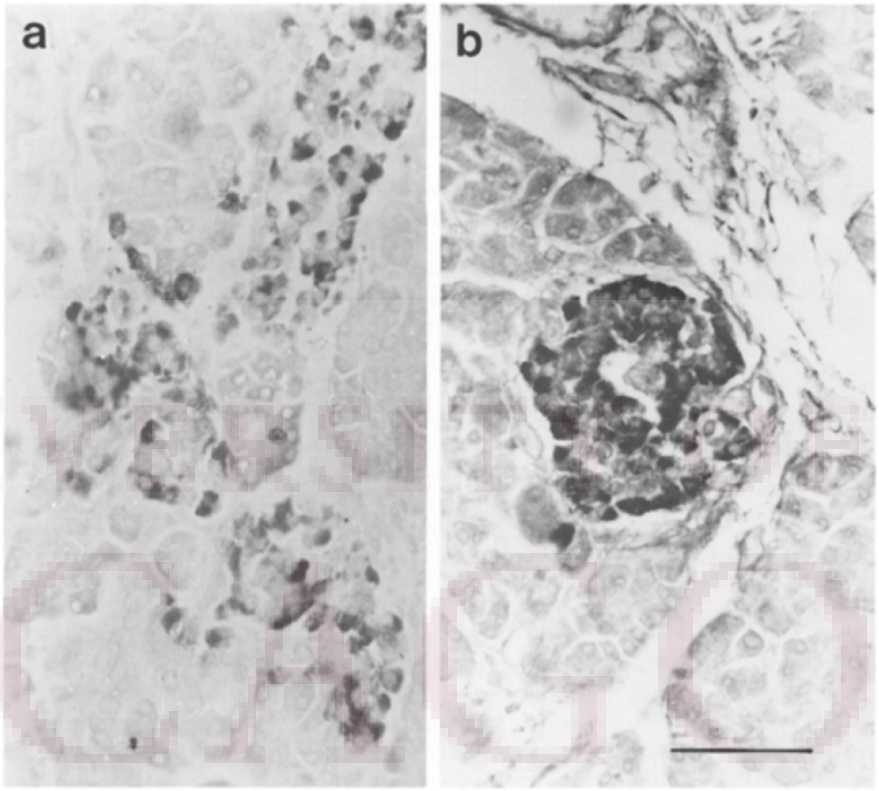
- Hypoparathyroidism:  Likely previously had mild hypoparathyroidism that was compensated and this was unmasked by blood transfusions and ECMO. Low alk phos is also c/w hypoparathyroidism.
  - Recommended monitoring total and ionized calcium q8 hours and IV calcium gtt for repletion.
- Steroid-induced hyperglycemia:
  - Low dose NISS q 4 hours→insulin gtt
- Thyroid function:  sick euthyroid and amiodarone use
- Gonads:  seemed to have been intact given regular menses
- Adrenal:  on high dose steroids
- Growth hormone:  5’2”

# KSS and Hypoparathyroidism

- May be presenting feature:
  - 10/14 cases presented with tetany.
- Associated with more severe disease.
- Unclear etiology—no reports have shown evidence of dietary, malabsorption, vitamin D disorders, or autoimmune mechanism
  - May be partially related to hypomagnesemia
- Autopsy of 2 cases:
  - Absent parathyroid glands
  - One parathyroid gland identified

Harvey et al. Clinical Endo. 1992 37:97-104.
Katsanos et al. Am J Nephrol. 2001 Mar-Apr;21(2):150-3.

# KSS and Diabetes




- Diabetes associated with mtDNA rearrangements commonly present with insulin-dependent diabetes at a young age with eventual complete loss of β cell function.
- Impaired insulin secretion is likely related to lack of ATP to close potassium channels in the β cell membrane.
- No evidence of autoimmune etiology.

Harvey et al. Clinical Endo. 1992 37:97-104.
Poulton et al. Diabetologia. 1995 Jul;38(7):868-71.

# Back to the patient

- Started on CVVH.
- Noted to have anisocoric sluggish pupils and persistent unresponsiveness.
- CT head showed ICH/IVH/SAH with associated cerebral edema, midline shift, brainstem compression and herniation through Foramen Magnum.

# References


- Harvey et al. Clin Endocrinol (Oxf). 1992 Jul;37(1):97-103.
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