47 Year-Old Man with DKA

Endorama

By Anoopa Koshy, M.D.

HPI

- 47 year-old AA male with a hx of "borderline diabetes," obesity (BMI =38), gout was admitted on 3/26 with fatigue, polyuria, polydipsia, chest discomfort and shortness of breath.
- Symptoms began a month ago and have been worsening week prior to admission
- Presented to the ER with a glucose of 615, anion gap of 20, bicarb of 15, creatinine of 1.3, and a beta-oh butryate of 4.94.
- Told he had borderline diabetes several years ago.
- No DM medications prescribed in the past

HPI

- Has no insurance and does not have a PCP
- Gained 22 lbs in the past year. “I’ve always been heavy”-currently weighs 260 lbs with a BMI of 38.
- Does not watch his diet (drinks regular soda 2L/day, eats fried foods)
- Denies abdominal pain, nausea, vomiting
- Labs returned showing TG>5,550.

PMHX, Fam Hx, Social Hx

Past Medical History

"Borderline Diabetes"

Gout

Hx of hiatal hernia repair

Obesity

Meds: None

Allergies: NKDA

Social Hx

Single, lives alone
Works as a utility worker
Denies smoking, illicit drugs
Drinks 8 pack of beer
2-3 days/week

Family Hx

Sister, Brother-type 2 DM
(dx in 50s, on oral meds)
5 brothers and 5 sisters-healthy
Mother- Type 2 DM (dx in 50s), died of unknown complications in 60s
Father-died at age 50 of MI

Review of Systems

Constitutional: + **fatigue**, negative for fevers/chills

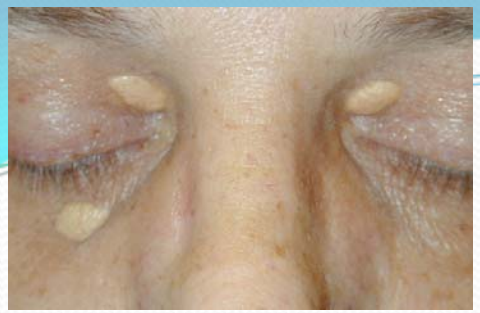
HEENT: + **increased thirst**

Respiratory: + **SOB**

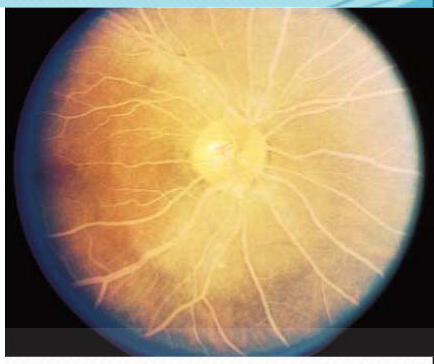
Cardiovascular: **+chest pain**

Gastrointestinal: negative for nausea, vomiting, abdominal pain

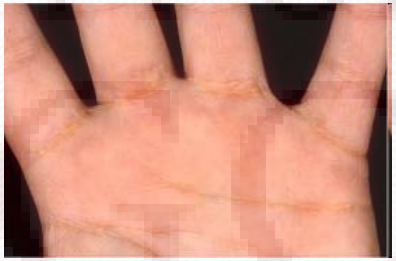
Genitourinary: **+urinary frequency**, **+nocturia**

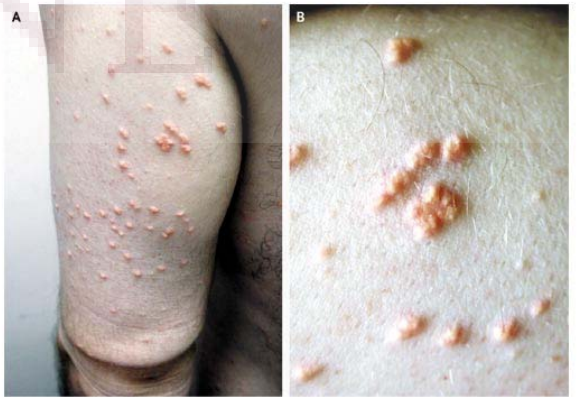


Physical Exam



VS: 97.2^{0}F , HR 84, BP 124/68, RR 19 O2sat95%on RA
weight 117 kg height 5'9" **BMI=38**
General: well-developed, **obese**
Eyes: no xanthelasma, arcus senilis or corneal opacities
Neck: supple, no thyromegaly
Cardiovascular: +S1/S2, no murmurs, rubs or gallops
Pulmonary/Chest: Effort normal, breath sounds normal, CTA b/l
Abdomen: Soft, **+abdominal obesity,** nontender to palpation
Neurological: Alert and oriented x 3 with no focal deficits
Skin: **No palmar or tendinous xanthomas**, **+acanthosis nigricans on back of neck, no striae**





LABS

130 | 95 | 26 / 615
5.1 | 15 | 1.3 \

Ca-10
Mg-2.2
Phos-5.4

AST -23
ALT-30
Alk phos-43

Tbili-0.4
Tprotein-5.7
Albumin 3.9

B-OH butryate-2.94 (<0.3 mmol/L)
HbA1c- 9
Lipase-36 (11-65 U/L)
TSH-1.45 (0.3-4 mcU/ml)
Ft4-1.08 (0.9-1.7 ng/dL)

Total Cholesterol-853 mg/dl
LDL- incalculable
HDL-40 mg/dl
Triglycerides- >5,550 mg/dl

8.1 \ / 188
/37.8\

Hypertriglyceridemia

Fasting Chlyomicronemia

- characterized by triglyceride levels in the 99th percentile in association with creamy plasma supernatant and cloudy infranatant due to increases in chylomicrons and VLDL.

-Clinical manifestations- include hepatosplenomegaly and occasional eruptive xanthomas

Familial hypertriglyceridemia

-autosomal dominant disorder with moderate elevations in seru TG (200-500 mg/dl)

-accompanied by insulin resistance, obesity, hyperglycemia, hypertension, hyperuricemia,

-patients are heterozygous for inactivating mutations of LPL gene and have low serum HDL

-associated with increased coronary risk and is common with patients with premature CHD

Familial Combined Hyperlipidemia

-autosomal disorder caused by overproduction of hepatically-derived apolipoprotein B-100 associated with VLDL.

-associated with clear increase in coronary risk and accounts for 1/3-1/2 of familial causes of CHD

-primary defect is not known but a locus has been identified on chromosome 1q21

Familial dysbetalipoproteinemia

- multifactorial disorder inherited as an autosomal dominant trait.

-characterized by two apo E2 alleles

-premature CHD and xanthomas are common

-physical findings include tuberoeruptive xanthomas and xanthomas of palmar creases

-Additional genetic or acquired factor that increases lipoprotein production or impairs lipoprotein removal is required (ie. Diabetes, hypothyroidism, obesity, or gout)

Secondary Causes of Hypertriglyceridemia

- Obesity
- Diabetes Mellitus
- Nephrotic syndrome
- Hypothyroidism
- Pregnancy
- Estrogen replacement
- Tamoxifen
- Beta-blockers
- Thiazide diuretics
- HIV antiretroviral regimens
- Retinoids
- Immunosuppressive Medications
  -Glucocorticoids
  -Cyclosporine

Hospital Course

- Admitted to the MICU from the ER
- Started on insulin gtt and gemfibrozil 600 mg BID, Anion gap closed and ketones cleared.
- Endocrinology consulted for further evaluation
- Recommended continuing insulin gtt until TG<1500
- Keep patient NPO.
- Recommended switching patient from Gemfibrozil to Fenofibrate due to potential gemfibrozil-statin interaction.

Hypertriglyceridemia in the ABSENCE of Pancreatits

- No guidelines on inpatient management of hypertriglyceridemia (TG>500) in the absence of pancreatitis (not well-studied in the literature and limited data available).
- Acquired disorders such as diabetes mellitus and obesity raise serum triglyceride levels.
- Patients with very high triglycerides are at increased risk of developing pancreatitis.
- Fasting lowers triglycerides.
- Patients will often require combination of triglyceride lowering agents (ie. fibrates, fish oil, nicotinic acid) to reduce triglyceride levels
- It has been suggested that nicotinic acid, which may interfere with glucose control, not be used as a first-line drug for the treatment of hypertriglyceridemia in patients with diabetes

Pharmacologic Treatment

Table 2. Pharmacologic Treatment for Hypertriglyceridemia.

Drug Class	Decrease in Triglycerides (%)	Maintenance Regimen	Contraindications	Side Effects	Selective Decrease in Small, Dense LDL Cholesterol	Selective Increase in HDL_2 Cholesterol
Nicotinic acid	17–26	1500–2000 mg once a day	Hypersensitivity, hepatic dysfunction	Flushing, pruritus, nausea, hepatitis (at higher doses), activation of migraine (rare)	Yes	Yes
Fibrates	18–45	Gemfibrozil, 600 mg twice a day; Fenofibrate, 145 mg once a day	Hypersensitivity, hepatic dysfunction, end-stage renal disease	Myositis, cholelithiasis	Yes	No
Statins	5	Multiple agents	Hypersensitivity, pregnancy, breast-feeding	Myalgia, influenza-like syndrome, rhabdomyolysis (rare), weakness	No	No
Nicotinic acid and statin	36	Same as for individual agents	Same as for individual agents	Same as for individual agents	Yes	Yes

Brunzell JD. Clinical Practice. Hypertriglyceridemia. N Engl J Med. 2007;357(10):1009.

Insulin and Treatment of Hypertriglyceridemia

- IV insulin decreases triglyceride levels by enhancing LPL activity
- More effective than subcutaneous insulin and will lower TG levels faster
- Regular insulin in 5% dextrose at rate of 0.1-0.3 u/kg/hour to maintain bs 150-200 mg/dl
- Fingersticks q4h and TG monitored 12-24 hours
- IV insulin stopped when TG <500

Gemfibrozil-Statin Interactions

- Reported 20 years ago that gemfibrozil can increase the risk of rhabdomyolysis when administered with a statin
- Gemfibrozil and its glucuronide is a potent, metabolism-based inhibitor and inactivator of CYP2C8 and OATP1B1 (organic anion transporting polypeptide 1B1).
- Gemfibrozil has been found to inhibit statin glucuronidation, which may lead to inhibition of statin elimination in vivo
- Gemfibrozil markedly increases the AUC of active simvastatin acid and lovastatin acid
- Rhabdomyolysis occurs 15x more frequently when statins are combined with gemfibrozil than when statins are used with fenofibrate.

Hospital Course Continued…

- Received resistance from Primary Team on NPO status
- MICU team allowed patient to eat (1st meal was hamburger with potato chips) while on insulin gtt
- Recommended diet be switched to low fat, diabetic diet
- Bridged over to Lantus and Novolog
- Transferred to Medicine Floor Service
- Insulin titrated daily; Triglycerides slowly trended down
- Add Lovaza/fish oil (not on formulary)
- Discharged home on Lantus/Novolog regimen, fenofibrate, and fish-oil supplement with follow-up scheduled at Cook County

Lipids Trend

☐ Hide data prior to: 9/5/2010 Use Date Range Wizard

	15 3/26/2012 0118	14 3/26/2012 0605	13 3/26/2012 1401	12 3/26/2012 2100	11 3/27/2012 0200	10 3/27/2012 1152	9 3/28/2012 0718
Cholesterol	853 *	605 *	792 *	787 *	808 *	812 *	855 *
HDL Cholesterol	40 *	35 *	44 *	40 *	36 *	43 *	42
LDL Cholesterol...	Calculation of...	Incalculable *	Incalculable	Incalculable	Calculation of...	Calculation of...	Incalculable
Triglycerides	>5500 *	>2000 *	>5500 *	4160 *	4460 *	4013 *	3667 *

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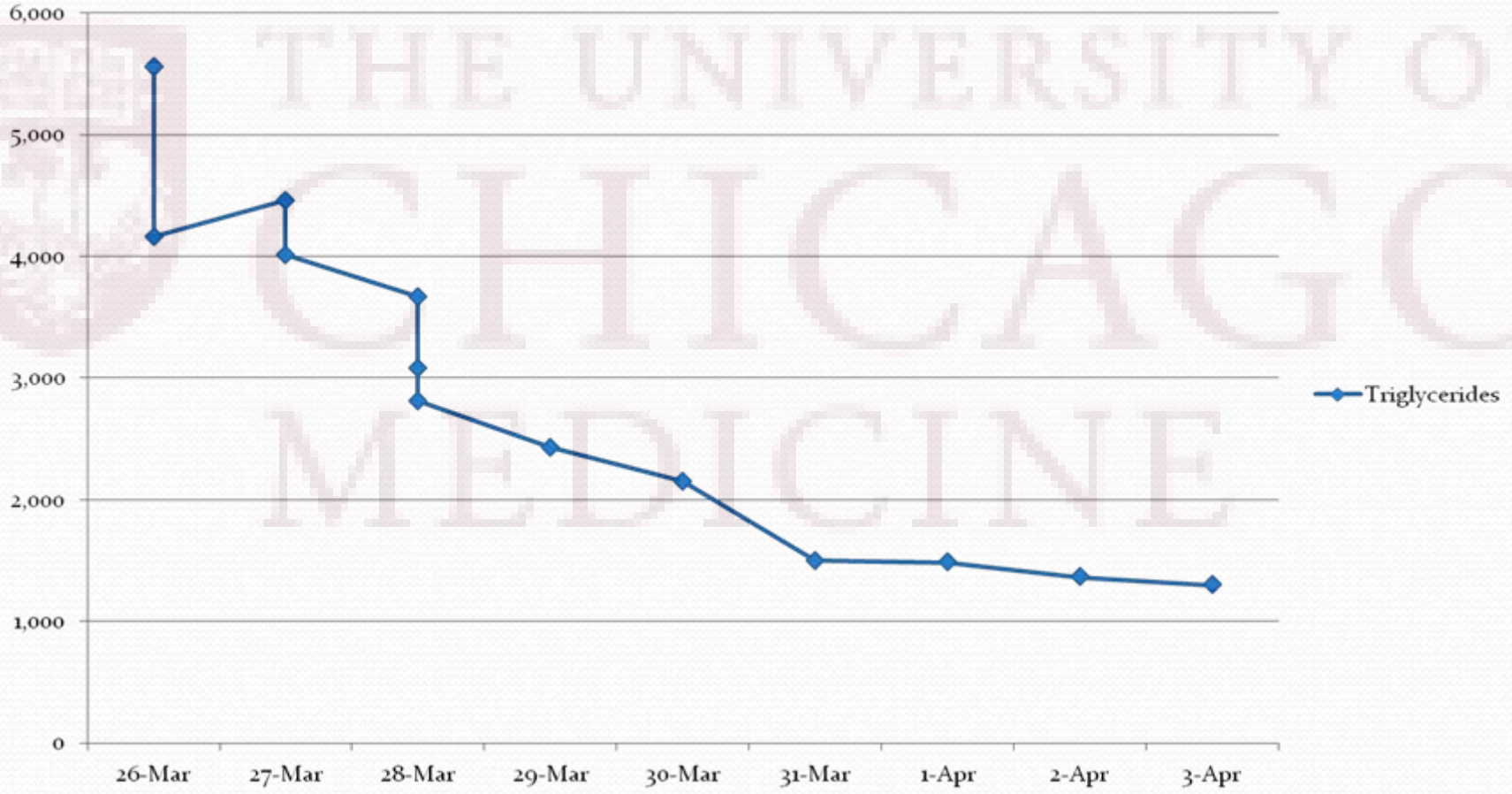
	8 3/28/2012 1208	7 3/28/2012 2015	6 3/29/2012 0200	5 3/30/2012 0432	4 3/31/2012 0412	3 4/1/2012 1022
Cholesterol	787 *	792 *	749 *	684	576	594 *
HDL Cholesterol	39 *	44 *	38 *	33	31	34 *
LDL Cholesterol...	Calculation of...	Calculation of...	Calculation of...	Calculation of...	Calculation of...	Calculation of...
Triglycerides	3080 *	2809 *	2429 *	2153 *	1501 *	1487 *

	2 4/2/2012 0411	1 4/3/2012 0406
Cholesterol	475	428
HDL Cholesterol	31	28
LDL Cholesterol...	Calculation of...	Calculation of...
Triglycerides	1364 *	1299 *

Triglycerides Trend



Take Home Points

1. Treatment of marked hypertriglyceridemia with IV insulin decreases triglyceride levels by enhancing LPL activity and therefore decreases risk of pancreatitis.

2. Gemfibrozil in combination with a statin can result in significant myotoxicity.

3. Patients with marked hypertriglyceridemia will often require combination of triglyceride lowering agents (ie. fibrates, fish oil, nicotinic acid) to reduce triglyceride levels.

References

- 1. Jabbar MA, Zuhri-Yafi MI, Larrea J . Insulin therapy for a non-diabetic patient with severe hypertriglyceridemia. J Am Coll Nutr. 1998;17(5):458.
- 2. Treatment of severe hypertriglyceridemia in nondiabetic patients with insulin. Mikhail N, Trivedi K, Page C, Wali S, Cope D. Am J Emerg Med. 2005;23(3):415.
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