

Diabetes Case Study: Co-morbidity of Nonadherence

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Comorbidity of Diabetes Case Study

- Objective: the learner will discuss an underreported comorbidity of diabetes.
- I have no related conflicts of interest or disclosures.

Case Study: KL

- KL is a 15 year old female diagnosed with Type 1 DM since age 15 months. She is managed on a basal bolus insulin regimen of insulin glargine (Basaglar) and insulin aspart (Novolog).
- Father called angry that KL was having swelling of her bilateral lower extremities .
- She had been seen in the ED the day prior (9/20/18), for "swelling" and was not given any "treatment".

Case Study: KL

- Had DKA admission on 9/7/17 and had admitted to missing insulin for 2 days prior. A1C was 14.4 on 9/7/17.
- Since discharge, reports taking all insulin as prescribed, with much improved glycemic control.
- She returned to the ED on 9/20/18, after she developed swelling in the bilateral lower extremities 1 week after DKA admission.
- Swelling occurred from the feet to the vulva bilaterally and she reported pain in her ankles and pelvis.

Case Study: KL

- Complained of itching of bilateral lower extremities and had taken 2 Benadryl tablets earlier that day.
- She denied taking any other medications except insulin, although she had switched brand of insulin glargine from Lantus to Basaglar recently.
- She reported feeling a little short of breath earlier that day, that had resolved without intervention.
- Had swelling of her face 3 days ago that resolved without intervention.
- On 9/7/18 at DKA admission, wt. 59.7kg, - 3.6kg decrease /7months. BMI normal at 80%.

Next steps?

- What differential diagnoses come to mind?
- What other questions would you ask?
- What labs or studies would you obtain?
- What's your diagnosis?
- What are your concerns for this patient?

Differentials

- Differential diagnoses:
 - Nephrotic syndrome
 - Renal Failure
 - Congestive Heart failure
 - Pleural Effusion
 - Liver Disease
- And....

Test Results

Normal Chest Xray –no pleural effusion

Component Latest Ref Rng & Units	9/20/2017	9/20/2017	9/20/2017
	6:30 PM	8:27 PM	9:12 PM
Glucose, Point- of-Care 70 - 106 mg/dL		29 (LL)	65 (L)

Other labs

Component <i>Latest Ref Rng & Units</i>	9/20/2017
	6:30 PM
Sodium 136 - 145 mmol/L	143
Potassium 3.8 - 5.4 mmol/L	3.3 (L)
Chloride 98 - 106 mmol/L	106
Carbon Dioxide 20 - 26 mmol/L	31 (H)
Urea Nitrogen 7 - 18 mg/dL	7
Creatinine 0.3 - 0.8 mg/dL	0.7
Glucose 70 - 106 mg/dL	34 (LL)
Calcium 8.4 - 10.1 mg/dL	9.1
Total Bilirubin 0.6 - 1.4 mg/dL	0.8
Total Protein 6.2 - 8.1 g/dL	6.4
Albumin 3.7 - 5.6 g/dL	3.7
Alkaline Phosphatase 70 - 230 U/L	77
Aspartate Aminotransferase 10 - 30 U/L	34 (H)
Alanine Aminotransferase 5 - 30 U/L	38 (H)
Magnesium 1.5 - 2.5 mg/dL	2.2
Phosphorus 2.9 - 5.4 mg/dL	3.6

Urine Test Results

Component <i>Latest Ref Rng & Units</i>	9/20/2017
POC Urine Glucose <i>Negative mg/dL</i>	Negative
POC Urine Bilirubin <i>Negative</i>	Negative
POC Urine Ketones <i>Negative mg/dL</i>	Negative
POC Urine Specific Gravity 1.003 - 1.035	1.010
POC Urine Blood <i>Negative</i>	Negative
POC Urine pH 4.8 - 7.8	7.0
POC Urine Protein <i>Negative mg/dL</i>	Negative
POC Urine Urobilinogen 0.2 - 1.0 E.U./dL	0.2
POC Urine Nitrite <i>Negative</i>	Negative
POC Urine Leukocytes <i>Negative</i>	Negative
Urine Pregnancy <i>Negative</i>	Negative

Diagnosis??

- What is the diagnosis?

Diagnosis??

- Insulin Edema

What Is Insulin Edema?

- Rare under-reported complication of insulin therapy.
- Presentation varies from mild peripheral edema to cardiac failure and pleural effusion.
- Although essential for DM, insulin can have adverse effects such as hypoglycemia and weight gain, and rarely generalized or peripheral edema. Also ascites, periorbital and facial edema.
- In pediatrics, insulin edema is reported more often in female pediatric patients, and patients with a low BMI.

When Does Insulin Edema Occur? Which Patients Are Affected?

- Shortly after the initiation, or re-initiation of intensive insulin therapy and resolves eventually, without direct intervention in many cases.
- Reported in **newly** diagnosed T₁DM following initiation of insulin therapy
- T₂DM following the initiation of insulin therapy
- Poorly controlled T₁DM following insulin omission, after insulin is re-initiated.
- **Underweight** patients on large doses of insulin.

So, what is known about Insulin Edema?

- Under reported, complication of insulin therapy.
- Severity is variable, most cases being mild.
- Presents from mild peripheral edema to rarely, cardiac failure and pleural effusion.

Pathophysiology of Insulin Edema: Cause is unclear

- Initial theory-Due to rapid retention of tissue fluid secondary to glycogen deposition
- Possibly due to the loss of albumin from the circulation due to increased transcapillary leakage (but patients with normal albumin levels have been reported)
- Alterations in renal electrolyte transport

Pathophysiology of Insulin Edema

- Intensive fluid resuscitation in an insulin-deficient catabolic state may lead to extravasation of fluid to the subcutaneous tissue, resulting in peripheral edema.
- May be exacerbated by the increased capillary permeability associated with chronic hyperglycemia.
- Transient inappropriate hyperaldosteronism has also been suggested to contribute to the fluid retention.

Other Reported Cases of Insulin Edema

- Reported cases of insulin-induced edema in childhood and adolescence are rare
- Insulin Edema was first reported in 1928
- The first pediatric report dates back to 1979, and then tends to be underreported since
- One reference in 2015, cited 12 pediatric cases described since 1979

One reported case of peripheral edema-11 year old girl



Bas, VN. Et. al. (2010). Insulin Oedema in Newly Diagnosed Type 1 Diabetes Mellitus. J Clin Res Ped Endo 2010;2(1):46-48. DOI: 10.4274/jcrpe.v2i1.46

One reported case of peripheral edema-14 year old girl



Bas, VN. Et. al. (2010). Insulin Oedema in Newly Diagnosed Type 1 Diabetes Mellitus. J Clin Res Ped Endo 2010;2(1):46-48. DOI: 10.4274/jcrpe.v2i1.46

Other Reported Cases of Insulin Edema

- a 19-year-old woman with newly diagnosed Type 1 DM presented with bilateral pleural effusions, ascites and extensive peripheral edema 2 weeks after starting insulin therapy. Significant cardiac disease was excluded, and the massive fluid retention resolved spontaneously with conservative management

• Reported by Lee, P., Kinsella, J., Borkman, M. & Carter, J. (2007). Bilateral pleural effusions, ascites, and facial and peripheral oedema in a 19-year-old woman 2 weeks following commencement of insulin lispro and detemir—an unusual presentation of insulin oedema. *Diabetic Medicine*. Vol 24(11).

Intervention- KL

- NP reviewed this case with Endocrinologist in outpatient clinic and Endo team involved in treating patient in ED the day prior
- Reassured KL's father that this is a known complication of insulin, particularly after episode of insulin omission, and intensive insulin management is resumed
- Insulin edema is self limiting.
- Watch for any signs of shortness of breath, heart racing. Return to ED if this occurs.
- Continue present insulin management.

Outcome of KL's Insulin Edema

- KL returned to clinic on 10/5/17 with an A1C 7.2 (<5.7, goal of <7.5) with most blood sugars in target range since her discharge from DKA admission
- No peripheral edema on P/E
- All edema had resolved without intervention, except elevation of BLE
- Wt. increased to 62.3kg, normal BMI 80%

Conclusion: Comorbidity of Diabetes: Insulin Edema

- Insulin Edema is a rare and underreported side effect of insulin therapy and should be recognized as a potential patient comorbidity.
- This self limiting diagnosis should be considered after excluding renal, cardiac, and hepatic causes of edema in a diabetic child.
- Monitor for shortness of breath, breathing difficulties, or rapid heart rate and refer to ED if this occurs.
- Nurses managing diabetes patients should be aware of the potential for insulin edema, particularly for new onset T1DM, T2 patients starting insulin, or patients resuming intensive glycemic control with insulin, following a period of insulin omission, or in underweight diabetic patients.

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