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# Insulin Induced Edema: A Rare Effect of a Common Medication

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## Introduction

- Edema is a rare complication seen in both Type 1 and Type 2 Diabetics after initiation or increase of insulin therapy.
- Insulin induced edema is diagnosed in the absence of renal, liver, and cardiac disease.
- We present the case of a 75 year-old female presenting with generalized edema after initiation of insulin glargine.

## Case Description

A 75 year old female with Type 2 Diabetes, Hypertension, and Chronic Kidney Disease presented to the clinic for generalized edema. She endorsed associated nausea, but denied chest pain, shortness of breath, and orthopnea. It began after the initiation of insulin glargine for uncontrolled hyperglycemia. Initially, she developed profound swelling in her legs to the thighs. It progressed in two months to involve her upper extremities and torso. She gained 29 pounds in this time. Notably, her previously uncontrolled hypertension improved, allowing discontinuation of many of her anti-hypertensives.

Venous duplex ultrasound of her upper and lower extremities showed no superficial or deep vein thrombosis. Computed tomography of pancreas was unremarkable.

Renal and liver function testing was normal aside from stable chronic kidney disease and hypoalbuminemia with an albumin of 2. Urine studies showed normal albumin to creatinine ratio and slight proteinuria with urinary protein excretion of 187mg over 24 hours. She had elevated thyroid stimulating hormone of 10.58 but normal free levels, and normal cortisol levels.

BNP was normal at 41. She underwent a trans-thoracic echocardiogram which showed an ejection fraction of 67%, with normal diastolic function, high-normal pulmonary artery pressure of 36, and small pericardial and pleural effusions. She was given escalating doses of furosemide therapy, without improvement of her edema.

Her blood sugar improved with dietary restriction, and her insulin requirements gradually decreased and was discontinued. One month later, her edema had resolved. She lost 26 pounds and became increasingly hypertensive, necessitating up-titration of therapy. She was diagnosed with insulin-induced edema.

## Laboratory Values

**Table 1. Liver Profile after initiation of insulin glargine**

ALT	13 IU/L
AST	15 IU/L
Albumin	2.1 g/dL
Total Protein	4.3 g/dL
Total Bilirubin	0.1 mg/dL
Alkaline Phosphatase	60 IU/L

**Table 2. Endocrine studies following initiation of insulin glargine**

TSH	10.58 uIU/mL
T4	0.73 ng/dL
ACTH	29 pg/mL
Cortisol	17 ug/dL

**Table 3. Urine Studies after initiation of insulin glargine**

Urine Microalbumin, Random	2.60 mg/dL
Urine Creatinine, Random	115 mg/dL
Albumin/Creatinine	22.6 mg/g
24 Hour Urine Protein	187 mg/24hrs

## Discussion

Insulin induced edema is often overlooked in the setting of edema in patients new to insulin, with only a few cases reported in literature. The pathologic mechanism for edema is unclear. Insulin has been posited to reduce renal sodium excretion and increase albumin excretion. However, our patient showed no hyponatremia and had no evidence of excessive urinary albumin or protein excretion. Commonly treated with diuresis and salt restriction, insulin edema usually resolves with time. Our patient did not respond to diuretic therapy. Interestingly, her uncontrolled hypertension resolved with insulin and immediately returned on stopping therapy. This phenomenon may suggest an alternative pathologic mechanism, such as the release of vasoactive mediators, which has been alternatively proposed in the literature.

## Conclusion

- Diagnosis of insulin edema should be one of exclusion, with other causes of generalized edema including renal, liver, and cardiac disease ruled out.
- The timing of insulin initiation and resolution of edema on insulin cessation supports the diagnosis.
- Most patients respond to diuretic therapy, but some do not, as illustrated in this case.

## References

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