

## Asthenia with Bilateral Pedal Edema and Swelling in the Hands of an Elderly Man with Metformin Use

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### Abstract

Diabetes mellitus is a common noncommunicable disease forming the highest burden worldwide [1]. Metformin is the drug of choice in Type 2 Diabetes Mellitus (T2DM). Metformin has different pharmacokinetics in different individual. Some patients tolerate the medication well, and some have symptoms so severe which warrants treatment discontinuation. Our patient started with asthenia and bilateral swelling of the lower extremities and hands 1.5 months after starting metformin treatment for noninsulin-dependent diabetes mellitus. We are reporting this case as a rare presentation of metformin induced bilateral lower limb and hand swelling associated with asthenia which resolved after discontinuation of metformin.

**Keywords:** Asthenia; Bilateral Pedal Edema; Metformin

### Background

Our main aim of publishing this case report is to acknowledge about the effects of metformin in elderly. It can help in preventing aggressive and costly investigations after ruling out common causes. In the case of an elderly diabetic patient on metformin therapy presenting with swollen extremities, providers should consider the possibility of metformin-induced swelling once common causes such as deep vein thrombosis, congestive heart failure and nephropathy have been ruled out.

Such clinical presentation has not been reported in literature.

### Case Presentation

Our patient is a 90-year-old male with a history of hypertension and recently diagnosed Type 2 Diabetes Mellitus who presented with generalized weakness and bilateral swelling of the lower limbs which progressed over one month. During the visit, his daughters were relating symptoms to the start of his treatment with the drug Metformin. Patient denied any medication use other than the recently started metformin. The patient was denying any chest pain, shortness of breath, palpitations, or generalized weakness. His daughters reported that initially he was able to walk and perform his activities of daily living, but over the past month, his weakness worsened, and he was not able to stand from his chair. On examination, his vitals were stable. He was not orthostatic. He was hard of hearing which was age-related. Head and neck examination were normal with no jugular-venous distension. Respiratory exam was normal. Abdominal examination was normal with no organomegaly. Edema was present in the hands and lower extremities up to the knees. There was no lymphadenopathy noted.

**Investigations**

His labs were normal except for a haemoglobin of 11.9 (Table 1 and 2). The red blood cells appeared normocytic and normochromic on a peripheral blood smear. His urinalysis was normal and his Vitamin B12 was borderline normal. BNP was within normal range. Doppler ultrasounds of the vessels in his lower limbs were negative for deep vein thromboses. Echocardiogram was normal with an ejection fraction of 60%.

	Measure	Unit	Reference Range
Lipase	22	U/L	12 - 51
HDL Cholesterol	37	mg/dL	>/= 61
LDL Direct	122.1	mg/dL	</= 100
Sodium	135	mmol/L	136 - 145
EGFR	80		>/= 60
Potassium	3.8	mmol/L	3.4 - 5.1
Chloride	98	mmol/L	98 - 107
CO2	27	mmol/L	20 - 31
Glucose	133	mg/dL	74 - 106
Creatinine	0.9	mg/dL	0.7 - 1.3
Urea Nitrogen	25	mg/dL	9 - 20
Amylase	50	U/L	30 - 118
Free T4	1.33	ng/dL	0.8 - 1.80
Calcium	10.0	mg/dL	8.7 - 10.4
TSH	4.85	mIU/mL	0.4 - 5.5
Magnesium	1.8	mg/dL	1.3 - 2.7
Anion Gap	10.0	meq/L	7 - 16
Cholesterol	172	mg/dL	</= 199
Triglyceride	99	mg/dL	</= 149
Protein, total	8.3	g/dL	5.7 - 8.2
Albumin	4.0	g/dL	3.4 - 4.8
Total Bilirubin	0.8	mg/dL	0.3 - 1.2
Alkaline Phosphatase	65	U/L	46 - 116
AST	23	U/L	14 - 59
ALT	19	U/L	10 - 60
Creatinine Kinase	65	U/L	38 - 174

**Table 1:** Comprehensive Metabolic Panel of our patient prior to metformin therapy.

	Measure	Unit	Reference Range
White Blood Cell count	13.01	thou/uL	12 - 51
Red Blood Cell Count	4.52	mil/uL	>/= 61
Hemoglobin	11.9	g/dL	</= 100
Hematocrit	38.3	%	136 - 145
Mean Cellular Volume	84.7	fL	>/= 60
Mean Cellular Hemoglobin	26.3	pg	
Mean corpuscular hemoglobin concentration	31.1	g/dL	3.4 - 5.1
Red Blood Cell Distribution width	44.4	fL	98 - 107
Platelets	326	thou/uL	20 - 31
% Neutrophils	68.1	mg/dL	74 - 106
% lymphocytes	17.0		
% Monocytes	12.2	mg/dL	0.7 - 1.3
% Eosinophils	1.7	mg/dL	9 - 20
% Basophils	0.5	U/L	30 - 118
% Immunoglobulin	0.5	ng/dL	0.8 - 1.80
Absolute Neutrophil Count	8.86	mg/dL	8.7 - 10.4
Absolute Lymphocyte Count	2.21	mIU/ mL	0.4 - 5.5
Absolute Monocyte Count	1.59	mg/dL	1.3 - 2.7
Absolute Eosinophil Count	0.22	meq/L	7 - 16
Absolute Basophil Count	0.07	mg/dL	</= 199
Absolute Immunoglobulin count	0.06	mg/dL	</= 149

**Table 2:** Complete Blood Count of our patient prior to metformin therapy.

### Differential diagnosis

- Congestive cardiac failure
- Acute renal failure
- Diabetic nephropathy with proteinuria
- Metformin induced drug toxicity

### Treatment

We removed metformin from the patient's medication regimen and his swelling of the hands and pedal edema improved.

### Outcome and follow-up

Bilateral extremity swelling completely resolved a couple of weeks after discontinuation of the medication. The patient is being followed in our department of internal medicine and is doing well after removal of metformin from his treatment regimen. His diabetes is currently only being managed with strict diabetic diet.

## Discussion and Conclusion

Metformin is a biguanide that is principally used as an oral antidiabetic medication. It is very effective in controlling the blood sugar in patients with mild diabetes. Its major effect is to decrease hepatic glucose output by inhibiting gluconeogenesis [2-4]. Metformin increases insulin-mediated glucose utilization in peripheral tissues mostly in muscles and liver, particularly after meals. It reduces serum free fatty acid concentrations, thereby reducing gluconeogenesis.

Metformin is recommended by both the American Diabetes Association and the European Association for the Study of Diabetes as first-line oral therapy for T2DM [5].

The most common side effects of metformin are gastrointestinal, including a metallic taste in the mouth, mild anorexia, nausea, abdominal discomfort, and soft bowel movements or diarrhoea [1,6]. Extremity swelling was not been reported as such so far. For this reason, we did extensive workup in our patient. His labs and imaging proved to be normal.

Asthenia is a side effect commonly reported in elderly patients on metformin [7].

Metformin as an individual agent leading to bilateral pedal edema and hand swelling is very uncommon. Our patient started with bilateral pedal edema and bilateral swelling of hands with worsening asthenia and he had a gross subjective and objective improvement in his next clinic visit after we stopped his metformin. We did not start him on diuretics.

Our main aim of publishing this case report is to acknowledge such an adverse effect to metformin therapy exists as it can help in preventing aggressive and costly investigations after ruling out common causes. Elderly diabetic patients on metformin therapy presenting with swollen extremities, providers should consider the differential of metformin-induced swelling. After common causes, such as deep vein thrombosis or congestive heart failure or nephropathy, have been ruled out metformin induced worsening edema should be considered.

## Learning Points/Take Home Messages

- Metformin can present as swelling in extremities.
- Metformin can cause asthenia.

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