A patient with severe metformin-associated lactic acidosis beats all the odds

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Abstract

Metformin-associated lactic acidosis (MALA) generally occurs in the context of renal dysfunction, either due to

- *chronic kidney disease (CKD)* or
- *acute kidney injury (AKI)*

leading to impaired metformin elimination.

Progressive accumulation inhibits *mitochondrial respiration* mainly in the liver, prompting a gradual, but steady increase in serum lactate levels.

Case presentation

A 56-year old patient presented to our Emergency Department with an **acute confusional state**, **disorientation**, **extreme fatigue**, **tachypnea**, **nausea**, **vomiting** and **anuria**.

She had a seven-day history of nausea, vomiting, abdominal pain and fatigue that had progressively worsened three days prior to admission.

Her past medical history was significant for *arterial hypertension*, *type II diabetes mellitus*, *peripheral artery disease* and a *total hip arthroplasty*.

She had been prescribed daily ***rectal indomethacin*** for pain management that she had used regularly in the past month, along with ***lercanidipine*** and ***irbesartan + hydrochlorothiazide*** for her blood pressure, ***cilostazol*** for her peripheral artery disease and ***metformin*** for her diabetes.

	On admission (Pre-hemodialysis)	Post-hemodialysis	Following CRRT
Urea	245	74	41
Creatinine	10.9	3	1.5
ABG			
pH	6.57	6.86	7.39
pCO2	17.9	21.3	29.8
BE	-36.6	-28.3	-6.2
K	8.04	5.45	4.9
Lactate	16.29	7	1.4

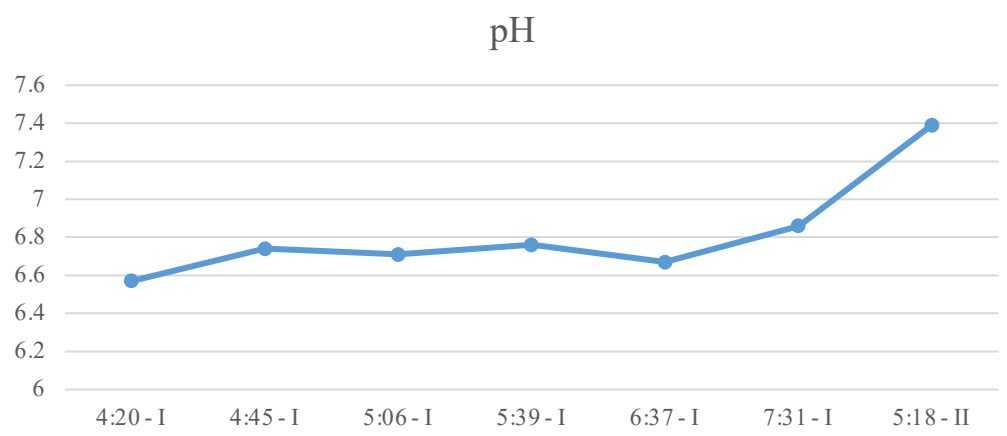

Figure 1. Blood pH levels during the first hours of admission. I - Day 1 and II - Day 2

Case presentation

She was diagnosed with **NSAID-induced acute kidney injury (AKI) and metformin-associated lactic acidosis (MALA).**

The patient was admitted to the ICU and she was started on *intravenous fluid therapy, diuretics, sodium bicarbonate* and *insulin* to manage the profound metabolic acidosis and two hours following her admission in the ICU, she underwent an urgent hemodialysis session.

At the end of the session both her clinical and laboratory parameters had improved with l*actate levels* dropping at *7 mmol/L*.

On her second day in the ICU, she had persistent altered mental status and tachypnea, thus she was placed on assisted ventilation and she underwent an additional session of continuous renal replacement therapy (CRRT) over 30 hours, to remove metformin and replete bicarbonates.

Following CRRT, her clinical condition and laboratory biomarkers significantly improved, she was weaned from mechanical ventilation and her urine output progressively increased on her third day of her ICU stay.

She was transferred to the ward **on her fourth day** of admission. On discharge, her serum *creatinine levels* were *1.3 mg/dL*.

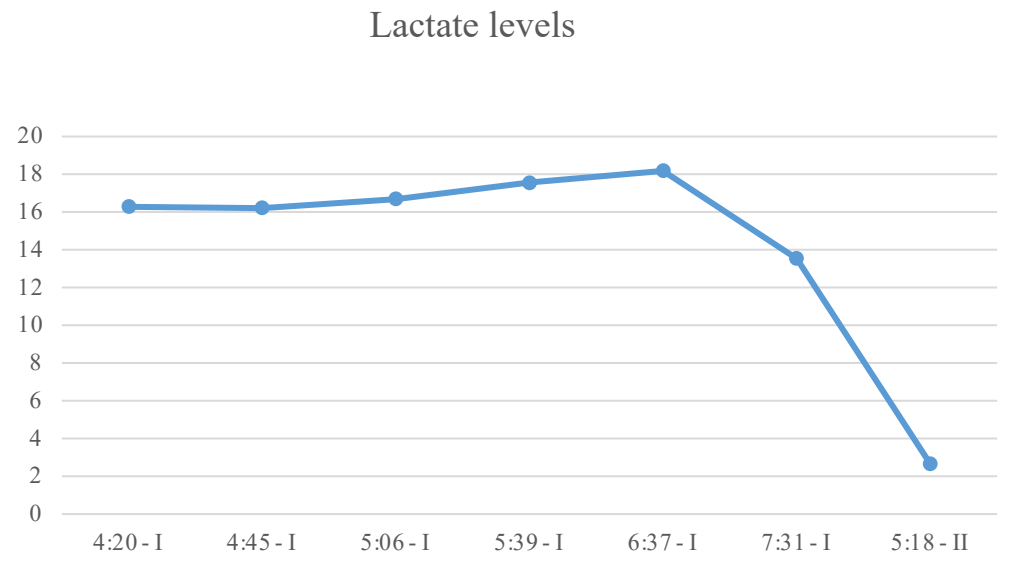

Figure 2. Serum lactate levels during the first hours of admission. I - Day 1 and II - Day 2

Conclusions

Reported cases of severe metformin-associated lactic acidosis (MALA) with **profoundly low blood pH levels (pH<6.8)**, as in the case of our patient, are exceedingly rare and represent rapidly deteriorating, life-threatening conditions.

A high index of clinical suspicion in patients on metformin, with risk factors for AKI is paramount in establishing a timely diagnosis and early initiation of renal replacement therapy, preventing fatal outcomes.