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METFORMIN-INDUCED LACTIC ACIDOSIS (MALA): A CASE REPORT

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Abstract:

Background: *Metformin is a first-line oral hypoglycemic agent widely used in type 2 diabetes mellitus. Although generally safe, it can rarely cause metformin-induced lactic acidosis (MALA), a serious and potentially fatal complication, particularly in patients with renal impairment.*

Case Presentation: *A 62-year-old male with a history of type 2 diabetes mellitus and chronic kidney disease presented with altered sensorium, breathlessness, and generalized weakness. Laboratory investigations revealed severe metabolic acidosis (pH 7.08), elevated serum lactate (12.5 mmol/L), and impaired renal function (serum creatinine 3.2 mg/dL). A detailed medication history revealed long-term metformin use. Other causes of lactic acidosis were excluded, leading to a diagnosis of MALA.*

Management and Outcome: *The patient was managed with immediate discontinuation of metformin, supportive care, and hemodialysis, resulting in normalization of metabolic parameters and clinical recovery.*

Conclusion: ***E****arly recognition and prompt intervention are crucial in reducing morbidity and mortality associated with MALA.*

Keywords: *Metformin, Lactic Acidosis, Type 2 Diabetes Mellitus, Renal Failure, Adverse Drug Reaction*

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INTRODUCTION:

The medical community uses Metformin as the primary oral diabetes treatment for type 2 diabetes because it demonstrates effective performance and maintains safety standards and provides heart health advantages. The medication operates by decreasing liver glucose production and increasing insulin sensitivity. The drug maintains high safety standards but can lead to serious adverse effects which occur in rare instances, with lactic acidosis being the most important side effect. Metformin-associated lactic acidosis shows three main symptoms which include high blood lactate levels and low blood pH and high anion gap metabolic acidosis. Although the incidence is low, the condition is associated with significant morbidity and mortality, particularly when diagnosis and treatment are delayed.[1,2,3]

People who already have risk factors that prevent them from removing drugs from their bodies and lead to excess lactate production are the ones who develop metformin-induced lactic acidosis. The primary risk factor for metformin renal excretion remains intact because patients with renal dysfunction constitute the highest risk group. The additional risk factors for this condition include hepatic impairment sepsis hypoxia advanced age and conditions that reduce blood flow to tissues. The process of metformin accumulation in the body causes mitochondrial respiration to stop which increases anaerobic metabolism and produces more lactate. The clinical presentation of the disease shows nonspecific symptoms which include nausea vomiting abdominal discomfort dyspnea and altered mental status that may prevent doctors from diagnosing the condition on time.[4,5]

The early detection and immediate treatment of MALA present essential requirements for achieving better results in patient care. The diagnostic process starts with clinical suspicion, which laboratory results validate through their demonstration of severe metabolic acidosis and elevated lactate levels and metformin usage history. The treatment approach requires immediate Metformin cessation when patients need medical care and doctors provide supportive treatment while they restore acid-base balance and patients with extreme illness receive renal replacement therapy. Hemodialysis functions as an essential method for eliminating drug buildup from the body while restoring normal metabolic functions. The case report presents MALA case study which shows actual patient symptoms and medical testing difficulties and successful treatment methods while demonstrating how doctors should select patients for metformin treatment and monitor them throughout their therapy.[6,7,8]

CASE PRESENTATION:

Patient Information : A 62-year-old male presented to the emergency department with complaints of altered sensorium, generalized weakness, and shortness of breath for one day. The symptoms were acute in onset and progressively worsening. There was no history of fever, chest pain, seizures, or trauma.

Chief Complaints

- Altered mental status – 1 day
- Generalized weakness – 2 days
- Breathlessness – 1 day
- Nausea and multiple episodes of vomiting

History of Present Illness

The patient was apparently asymptomatic until two days prior to admission, when he developed generalized fatigue and malaise. This was followed by nausea and repeated episodes of vomiting. Within 24 hours, he developed progressive breathlessness and confusion, eventually leading to decreased responsiveness. There was no history suggestive of infection such as fever, cough, or urinary symptoms. No history of toxin ingestion, alcohol consumption, or recent hospitalization was reported.

Past Medical History

- Type 2 Diabetes Mellitus for 10 years
- Hypertension for 8 years
- Chronic Kidney Disease (Stage 3), diagnosed 2 years ago

No prior history of cardiovascular disease, liver disease, or respiratory illness was noted.

Medication History

- Metformin 1000 mg twice daily (for 8 years)
- Amlodipine 5 mg once daily
- Atorvastatin 10 mg once daily

The patient reported good adherence to medications. No recent dose adjustments were made. There was no history of use of nephrotoxic drugs or contrast agents.

Personal and Social History

- Non-smoker
- Non-alcoholic
- Diet: Mixed diet
- No history of substance abuse

Family History

No significant family history of metabolic disorders, renal disease, or cardiovascular illness.

General Physical Examination

- Patient was drowsy and disoriented
- Glasgow Coma Scale (GCS): 11/15 (E3 V3 M5)
- Built: Moderately nourished

- Hydration: Mild dehydration present

Vital Signs:

- Blood Pressure: 90/60 mmHg
- Pulse Rate: 110 beats per minute (tachycardia)
- Respiratory Rate: 28 breaths/min (tachypnea)
- Temperature: Afebrile
- Oxygen Saturation: 92% on room air

Systemic Examination

Cardiovascular System

- Tachycardia present
- Normal heart sounds (S1, S2 heard)
- No murmurs or added sounds

Respiratory System

- Tachypnea with deep breathing (suggestive of metabolic acidosis compensation)
- Bilateral air entry present
- No added sounds such as wheeze or crepitations

Central Nervous System

- Altered sensorium
- No focal neurological deficits
- Pupils equal and reactive to light

Abdomen

- Soft, non-tender
- No organomegaly
- Bowel sounds present

Laboratory Investigations

1. Complete Blood Count (CBC)

Parameter	Value	Normal Range	Interpretation
Hemoglobin (Hb)	12.4 g/dL	13–17 g/dL	Mildly decreased
Total Leukocyte Count (TLC)	8,900 cells/mm³	4,000–11,000	Normal
Neutrophils	72%	40–75%	Normal
Lymphocytes	22%	20–40%	Normal
Eosinophils	3%	1–6%	Normal
Monocytes	3%	2–8%	Normal
Platelet Count	2.1 lakh/mm³	1.5–4 lakh	Normal
Packed Cell Volume (PCV)	37%	40–50%	Slightly low

2. Serum Biochemistry

Parameter	Value	Normal Range	Interpretation
Blood Glucose (Random)	140 mg/dL	70–140 mg/dL	Normal
Blood Urea	68 mg/dL	15–40 mg/dL	Elevated
Serum Creatinine	3.2 mg/dL	0.6–1.2 mg/dL	Significantly elevated
Sodium (Na^+)	138 mEq/L	135–145 mEq/L	Normal
Potassium (K^+)	5.6 mEq/L	3.5–5.0 mEq/L	Mild hyperkalemia
Chloride (Cl^-)	102 mEq/L	98–106 mEq/L	Normal
Serum Lactate	12.5 mmol/L	<2 mmol/L	Markedly elevated
Serum Bicarbonate (HCO_3^-)	10 mmol/L	22–28 mmol/L	Severely decreased
Anion Gap	26 mEq/L	8–16 mEq/L	Elevated

3. Arterial Blood Gas (ABG) Analysis

Parameter	Value	Normal Range	Interpretation
pH	7.08	7.35–7.45	Severe acidosis
pCO_2	28 mmHg	35–45 mmHg	Compensatory decrease
pO_2	82 mmHg	80–100 mmHg	Normal
HCO_3^-	10 mmol/L	22–28 mmol/L	Markedly decreased
Base Excess	-15 mEq/L	-2 to +2	Severe metabolic acidosis
Lactate	12.5 mmol/L	<2 mmol/L	Critically elevated

4. Liver Function Tests (LFTs)

Parameter	Value	Normal Range	Interpretation
Total Bilirubin	0.8 mg/dL	0.3–1.2 mg/dL	Normal
Direct Bilirubin	0.2 mg/dL	<0.3 mg/dL	Normal
AST (SGOT)	32 IU/L	10–40 IU/L	Normal

ALT (SGPT)	28 IU/L	7–56 IU/L	Normal
Alkaline Phosphatase	90 IU/L	44–147 IU/L	Normal
Total Protein	6.8 g/dL	6–8 g/dL	Normal
Albumin	3.6 g/dL	3.5–5 g/dL	Normal

5. Urinalysis

Parameter	Result	Interpretation
Color	Pale yellow	Normal
Appearance	Clear	Normal
pH	5.5	Slightly acidic
Specific Gravity	1.015	Normal
Protein	Trace	Mild proteinuria
Glucose	Negative	Normal
Ketones	Negative	Normal
RBCs	0–2 /HPF	Normal
WBCs	1–2 /HPF	Normal
Casts	Absent	Normal

6. Electrocardiogram (ECG)

Findings:

- Sinus tachycardia (Heart rate ~110 bpm)
- No ST-segment elevation or depression
- No arrhythmias detected
- No peaked T waves despite mild hyperkalemia

7. Chest X-ray

Findings:

- Bilateral lung fields clear
- No signs of consolidation, edema, or effusion
- Cardiac silhouette normal
- No radiological evidence of pulmonary pathology

FINAL DIAGNOSIS

Based on the clinical examination and investigations, the patient demonstrated features of severe metabolic derangement, including altered sensorium, tachypnea, hypotension, and generalized weakness. Arterial blood gas analysis showed marked metabolic acidosis with a pH of 7.08 and significantly reduced bicarbonate levels (10 mmol/L). Serum lactate levels were critically elevated (12.5 mmol/L), and the anion gap was increased (26 mEq/L), confirming high anion gap lactic acidosis. Renal function tests revealed elevated serum creatinine (3.2 mg/dL) and blood urea, indicating impaired renal function and reduced drug clearance. Blood glucose levels were within normal limits, and ketone bodies were absent, ruling out diabetic ketoacidosis, while normal liver function tests excluded hepatic causes. There was no evidence of sepsis or hypoxia clinically or radiologically. A detailed drug history revealed prolonged use of Metformin, and in the presence of renal impairment, this strongly suggested drug accumulation, confirming the diagnosis of metformin-induced lactic acidosis (MALA).

TREATMENT AND CLINICAL COURSE (DAY-WISE)

Day 1 (Admission and Initial Stabilization):

The patient was admitted to the intensive care unit with severe metabolic acidosis and altered sensorium. Metformin was immediately discontinued. Initial management focused on airway stabilization, oxygen supplementation, and aggressive intravenous fluid resuscitation to correct hypotension and dehydration. Sodium bicarbonate infusion was initiated due to severe acidemia (pH <7.1). Continuous cardiac monitoring was started in view of hyperkalemia and risk of arrhythmias. Broad supportive care including electrolyte correction and monitoring of urine output was ensured. Nephrology consultation was obtained promptly, and the patient was prepared for urgent renal replacement therapy considering worsening acidosis and renal impairment.

Day 2 (Definitive Management):

On the second day, the patient underwent the first session of hemodialysis to enhance removal of accumulated drug and correct metabolic acidosis. Supportive care with intravenous fluids and electrolyte management was continued. Serial arterial blood gas analysis showed mild improvement in pH and bicarbonate levels, although lactate remained elevated. The patient's mental status remained altered but hemodynamically stable. Insulin therapy was initiated using a sliding scale to maintain optimal

glycemic control, as oral antidiabetic agents were withheld. Strict input-output monitoring and renal parameters were assessed periodically to evaluate response to therapy and guide further management decisions.

Day 3 (Ongoing Monitoring and Second Dialysis):
Due to persistently elevated lactate levels and incomplete correction of acidosis, a second session of hemodialysis was performed. Post-dialysis, significant improvement in metabolic parameters was observed, including gradual normalization of arterial pH and reduction in lactate concentration. The patient showed improvement in sensorium, responding to verbal commands. Hemodynamic status stabilized with improved blood pressure and reduced tachycardia. Oxygen supplementation was continued at a lower flow rate. Laboratory investigations indicated partial recovery of renal function. Supportive care, including electrolyte balance and fluid management, was continued along with close monitoring for any complications or recurrence of acidosis.

Day 4 (Clinical Improvement):
By the fourth day, the patient demonstrated marked clinical improvement. Arterial blood gas parameters approached near-normal levels, with significant correction of acidosis. Serum lactate levels showed a downward trend, and renal function tests indicated gradual recovery. The patient was conscious, oriented, and able to maintain adequate oral intake. Intravenous fluids were tapered, and electrolyte levels were stabilized. Oxygen therapy was discontinued as saturation improved on room air. No further indications for dialysis were noted. The patient was closely monitored for stability, and emphasis was placed on gradual mobilization and nutritional support to enhance recovery.

Day 5 (Recovery Phase):
On the fifth day, the patient maintained stable vital signs with complete resolution of metabolic acidosis. Laboratory parameters, including serum lactate and renal function tests, were near normal. The patient was fully conscious, cooperative, and ambulatory with minimal assistance. Subcutaneous insulin therapy was continued to maintain glycemic control, and dietary counseling was initiated. No new symptoms or complications were observed. The patient was shifted from the intensive care unit to the general ward for further observation. Education regarding medication adherence and avoidance of contraindicated drugs was initiated as part of discharge planning.

Day 6–7 (Discharge and Follow-up Planning):
During the final days of hospitalization, the patient showed sustained clinical and biochemical stability. Renal parameters improved further, and acid-base balance remained normal without recurrence of symptoms. The patient was transitioned completely to insulin therapy, and Metformin was permanently discontinued. Detailed counseling was provided regarding diabetes management, renal function monitoring, and warning signs of metabolic complications. The patient and caregivers were educated about the importance of regular follow-up. The patient was discharged in stable condition with advice for follow-up after one week and periodic monitoring thereafter.

Discharge Laboratory Values

Parameter	Value at Discharge	Normal Range	Interpretation
pH (ABG)	7.36	7.35–7.45	Normal
pCO_2	38 mmHg	35–45 mmHg	Normal
HCO_3^-	23 mmol/L	22–28 mmol/L	Normal
Serum Lactate	1.8 mmol/L	<2 mmol/L	Normalized
Serum Creatinine	1.4 mg/dL	0.6–1.2 mg/dL	Improved
Blood Urea	38 mg/dL	15–40 mg/dL	Near normal
Sodium (Na^+)	139 mEq/L	135–145 mEq/L	Normal
Potassium (K^+)	4.3 mEq/L	3.5–5.0 mEq/L	Normal
Chloride (Cl^-)	104 mEq/L	98–106 mEq/L	Normal
Blood Glucose (Random)	128 mg/dL	70–140 mg/dL	Controlled
Hemoglobin (Hb)	12.8 g/dL	13–17 g/dL	Slightly low
Total Leukocyte Count	7,800 cells/mm^3	4,000–11,000	Normal
Platelet Count	2.3 lakh/mm^3	1.5–4 lakh	Normal
AST (SGOT)	30 IU/L	10–40 IU/L	Normal
ALT (SGPT)	26 IU/L	7–56 IU/L	Normal
Total Bilirubin	0.7 mg/dL	0.3–1.2 mg/dL	Normal
Urinalysis	Normal	—	No abnormalities

DISCHARGE PLAN

The patient was discharged in a clinically stable condition with complete resolution of metabolic acidosis and significant improvement in renal function. Metformin was permanently discontinued in view of the adverse event. The patient was advised to continue insulin therapy for glycemic control, along with regular monitoring of blood glucose levels. Periodic assessment of renal function was strongly recommended to prevent recurrence. Lifestyle modifications including dietary regulation, adequate hydration, and adherence to medications were emphasized. The patient and caregivers were educated regarding early warning signs such as fatigue, breathlessness, and altered sensorium. A follow-up visit was scheduled after one week, with subsequent regular reviews.

DISCHARGE MEDICATIONS

Drug Name	Dose	Frequency	Indication
Human Insulin (Regular + NPH)	10 units (morning), 6 units (evening)	Subcutaneous, twice daily	Glycemic control
Amlodipine	5 mg	Once daily	Hypertension
Atorvastatin	10 mg	Once daily (night)	Dyslipidemia
Pantoprazole	40 mg	Once daily (before food)	Gastric protection
Multivitamin supplement	1 tablet	Once daily	Nutritional support

OUTCOME

The patient showed significant clinical and biochemical improvement following prompt management, including discontinuation of Metformin and initiation of hemodialysis. Metabolic acidosis resolved, and serum lactate levels normalized. Renal function improved substantially, and the patient regained normal mental status. He was discharged in stable condition on insulin therapy, with no recurrence of symptoms during the hospital stay.

PHARMACIST INTERVENTIONS

The clinical pharmacist played a key role in identifying Metformin as the probable cause of lactic acidosis by reviewing the patient's medication history and renal status. The pharmacist recommended immediate discontinuation, guided dose adjustments, monitored drug therapy, and assisted in initiating insulin therapy. Patient counseling on medication safety, adherence, and recognition of warning signs was also provided.

DISCUSSION:

In the present case, a 62-year-old male with chronic kidney disease on long-term Metformin therapy presented with severe metabolic derangement. The patient had arterial pH of 7.08, bicarbonate of 10 mmol/L, serum lactate of 12.5 mmol/L, and an anion gap of 26 mEq/L, confirming high anion gap metabolic acidosis. Renal parameters were significantly elevated (serum creatinine 3.2 mg/dL, blood urea 68 mg/dL), indicating impaired drug clearance. The absence of infection, normal liver function tests, and normal blood glucose with negative ketones helped exclude other causes, supporting the diagnosis of metformin-induced lactic acidosis (MALA), consistent with findings reported in previous case studies.[9]

The clinical features observed in this patient, including altered sensorium, tachypnea (28 breaths/min), hypotension (90/60 mmHg), and tachycardia (110 bpm), are typical of severe lactic acidosis. Similar presentations have been described in earlier literature, where patients with MALA often exhibit nonspecific symptoms that rapidly progress to critical illness. Studies have shown that lactate levels >10 mmol/L and pH <7.1 are associated with severe disease and require urgent intervention. In this case, early arterial blood gas analysis and lactate estimation played a crucial role in timely diagnosis, aligning with published evidence emphasizing rapid biochemical assessment.[10]

Management of this patient involved immediate discontinuation of Metformin, intravenous fluid resuscitation, sodium bicarbonate infusion, and two sessions of hemodialysis. Post-treatment, there was a significant improvement, with lactate levels reducing to 1.8 mmol/L, pH normalizing to 7.36, and serum creatinine improving to 1.4 mg/dL at discharge. These outcomes are comparable to previous reports where early initiation of hemodialysis resulted in rapid correction of acidosis and improved survival. Literature supports that dialysis enhances metformin clearance and corrects acid-base imbalance effectively, especially in patients with renal impairment.[11]

Compared to previously reported cases, this patient had a favorable outcome despite severe initial

presentation. Studies report mortality rates ranging from 20% to 50%, particularly in cases with delayed diagnosis or associated sepsis. In contrast, this case demonstrated complete recovery within one week due to early recognition and prompt multidisciplinary management. The absence of hepatic dysfunction and timely dialysis contributed significantly to recovery. This case highlights the importance of regular renal monitoring and cautious use of Metformin, especially in patients with underlying kidney disease, to prevent such life-threatening complications.[12]

CONCLUSION:

This case highlights metformin-induced lactic acidosis as a rare but serious complication, especially in patients with underlying renal impairment. The patient presented with severe metabolic acidosis (pH 7.08), markedly elevated lactate levels (12.5 mmol/L), and impaired renal function (serum creatinine 3.2 mg/dL), which were key indicators for diagnosis. Early identification of these abnormalities, along with a detailed drug history of Metformin use, enabled prompt diagnosis. Immediate discontinuation of the drug, supportive care, and timely hemodialysis resulted in complete clinical and biochemical recovery. This case underscores the importance of cautious prescribing, regular monitoring of renal function, and early intervention in high-risk patients to prevent life-threatening complications and improve overall patient outcomes.

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