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Case Report

Internal Medicine Section

Troponin I Assay Interference due to Paraproteinaemia: A Diagnostic Challenge in Multiple Myeloma: A Case Report

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ABSTRACT

Cardiac troponins are among the most reliable biomarkers for diagnosing acute myocardial infarction. However, in certain clinical situations, analytical interferences can result in misleading or uninterpretable results, creating confusion in diagnosis and management. One such rare cause of interference is paraproteinaemia associated with plasma cell disorders such as multiple myeloma. A 60-year-old man with no known comorbidities presented with exertional retrosternal chest pain and heartburn of three months' duration. Clinical evaluation revealed pallor and biochemical findings of anaemia, renal dysfunction, and hyperproteinaemia. Electrocardiography showed ischaemic changes, but serial Troponin I assays repeatedly displayed "error" messages, raising the suspicion of assay interference. Further investigations demonstrated a monoclonal spike on serum protein electrophoresis, and bone marrow examination confirmed multiple myeloma. Despite aggressive multidisciplinary management, the patient developed septic shock, disseminated intravascular coagulation, and multiorgan failure and succumbed during the hospital stay. This case highlights a rare but important cause of analytical interference in Troponin I estimation due to paraproteinaemia. It emphasises the need for clinicians to interpret laboratory results in correlation with the clinical picture and to maintain close coordination with laboratory teams whenever results appear inconsistent. Early recognition of such assay interferences can help avoid misdiagnosis and unnecessary interventions in critically ill patients.

Keywords: Biological assay interference, Critical care, Electrocardiography, Immunoglobulins, Monoclonal, Renal insufficiency, Sepsis

CASE REPORT

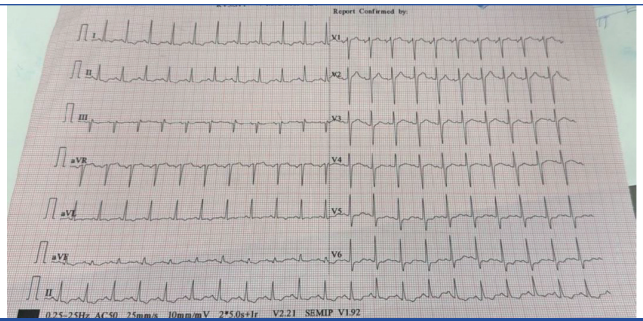
A 60-year-old man with no known comorbidities presented to the General Medicine outpatient department with complaints of retrosternal chest pain accompanied by heartburn for three months. The pain was non-radiating and exertional, typically worsening when he walked briskly or climbed stairs, and easing with rest. There was no history of diabetes, hypertension, or coronary artery disease.

On examination, the patient appeared pale and had digital clubbing. Cardiovascular and respiratory examinations did not reveal signs of heart failure, and there was no skeletal tenderness. Initial laboratory investigations revealed severe anaemia, renal dysfunction, and hyperproteinaemia, as summarised in [Table/Fig-1].

His Electrocardiogram (ECG) showed ST-segment depression in leads V5-V6, raising suspicion of acute coronary syndrome [Table/Fig-2].

Parameter	Result	Reference Range
Haemoglobin (g/dL)	4.6	13-17
Total leukocyte count (/cu.mm)	5890	4000-11000
Platelets (/cu.mm)	1,56,000	150000-450000
Vitamin B12 (pg/mL)	44	120-914
Urea (mg/dL)	36	17-43
Creatinine (mg/dL)	2.1	0.7-1.3
Sodium (mmol/L)	135	136-145
Potassium (mmol/L)	4.8	3.5-5.1
Chloride (mmol/L)	107	98-107
Bicarbonate (mmol/L)	22	21-31
Calcium (mg/dL)	9.1	8.8-10.6
Magnesium (mg/dL)	1.8	1.8-2.6
Phosphorus (mg/dL)	3.8	2.5-4.5
Total bilirubin (mg/dL)	1.5	0.7-1.3
Direct bilirubin (mg/dL)	0.6	≤0.3
AST (SGOT) (IU/L)	19	≤35
ALT (SGPT) (IU/L)	10	≤45
ALP (IU/L)	33	30-120
Total protein (g/dL)	14.2	6.6-8.3
Albumin (g/dL)	1.7	3.5-5.2
Globulin (g/dL)	12.5	2.5-3.0

[Table/Fig-1]: Laboratory parameters of the patient at presentation.
AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase.



[Table/Fig-2]: Electrocardiogram at presentation showing ST-segment depression in leads V5-V6, suggestive of ischaemic changes.

However, serial Troponin I assays repeatedly returned "error" messages, raising the possibility of analytical interference. Troponin I estimation was performed using the Abbott ARCHITECT i1000SR Chemiluminescent Microparticle Immunoassay (CMIA) platform, which employs a two-site sandwich immunoassay principle.

Further evaluation was undertaken in view of unexplained anaemia, renal impairment, and elevated total protein. Urine Bence Jones protein was positive, and serum protein electrophoresis revealed hypoalbuminaemia (serum albumin 2.1 g/dL) with a discrete Monoclonal (M) band in the gamma region, consistent with a plasma cell dyscrasia [Table/Fig-3].



[Table/Fig-3]: Serum protein electrophoresis showing hypoalbuminaemia and a discrete monoclonal band in the gamma region, suggestive of monoclonal gammopathy.

With persistent assay errors, paraproteinaemia-induced interference in the Troponin I assay was strongly suspected, a phenomenon reported in plasma cell disorders but considered rare and under-recognised. A two-dimensional echocardiogram was attempted, but image quality was limited due to a poor acoustic window. The patient was advised inpatient admission for coronary angiography and bone marrow biopsy; however, he left against medical advice on the third day of evaluation.

He re-presented nearly two weeks later in a critically ill state with acute breathlessness (mMRC grade III-IV), fever, and vomiting. Repeat ECG continued to show ischaemic changes, and echocardiography revealed global hypokinesia with a left ventricular ejection fraction of ~30%. Troponin I assays again yielded uninterpretable "error" results. His condition rapidly worsened, with hypotension (blood pressure: 80/60 mmHg) and respiratory failure necessitating vasopressor support, endotracheal intubation, and invasive mechanical ventilation in the Intensive Care Unit (ICU). Progressive renal dysfunction with oliguria (<125 mL/day) required initiation of Sustained Low-Efficiency Dialysis (SLED).

During the ICU stay, he developed coagulopathy with Disseminated Intravascular Coagulation (DIC), requiring multiple transfusions, including 3 units of packed red cells and 6 units of fresh frozen plasma. Broad-spectrum antibiotics were commenced for sepsis, and inotropic support was escalated as per ICU protocol. Following partial correction of coagulopathy, a bone marrow biopsy was performed a few days later, which confirmed the diagnosis of multiple myeloma. In view of his unstable clinical status with ongoing septic shock, chemotherapy was deferred, and supportive management continued.

Despite coordinated care involving critical care specialists, nephrologists, haematologists, and oncologists, the patient's condition continued to deteriorate. He developed refractory septic and cardiogenic shock with multiorgan failure, unresponsive to maximal supportive measures including renal replacement therapy, vasopressors, and mechanical ventilation. He succumbed after six days in the ICU.

Wherein paraproteinaemia-induced analytical interference in the Troponin I assay masked the confirmation of myocardial injury, contributing to delayed decision-making. It underscores the need to correlate laboratory results with the clinical picture and to suspect assay interference when results remain incongruent, especially in plasma cell disorders.

DISCUSSION

Cardiac troponins, particularly Troponin I, are widely regarded as the gold standard biomarkers for diagnosing acute myocardial infarction because of their high sensitivity and specificity [1,2]. However, in clinical practice, misleading results may occur due to analytical interferences, which complicate diagnosis and management, especially in critically ill patients [3,4]. In the present case, electrocardiographic evidence of ischaemia and echocardiographic global hypokinesia with reduced ejection fraction supported the clinical suspicion of myocardial injury, yet serial Troponin I assays repeatedly generated "error" outputs rather than measurable values. The subsequent demonstration of marked paraproteinaemia and confirmed multiple myeloma strongly suggested paraproteinaemia-induced interference with the Troponin I immunoassay, which prevented biochemical confirmation of myocardial necrosis and complicated clinical decision-making.

Several case reports have described troponin assay interference in the setting of plasma-cell dyscrasias. A similar case has been described in which a patient with multiple myeloma presented with chest discomfort and persistently elevated Troponin I levels despite normal coronary angiography and unremarkable echocardiography; subsequent evaluation demonstrated that paraproteinaemia was responsible for the falsely elevated troponin values [5]. Another report documented an unexpected rise in Troponin I in a patient with multiple myeloma, where an extensive cardiac work-up failed to reveal ischaemia, and interference from monoclonal immunoglobulins was identified as the most plausible cause [6]. In contrast to these reports of spuriously raised values, this patient exhibited persistent assay failure with repeated "error" messages, highlighting that paraproteinaemia can cause not only false-positive elevations but also complete disruption of assay function, thereby masking true myocardial injury.

Beyond multiple myeloma-specific reports, numerous publications have emphasised that cardiac troponin immunoassays are inherently vulnerable to interference from endogenous antibodies (heterophilic antibodies, rheumatoid factor), macrotroponin complexes, and other serum proteins [7-9]. Such interferences may cause falsely elevated or depressed values, inter-assay discrepancies, or non-linear results on dilution testing. The IFCC Committee on Clinical Applications of Cardiac Biomarkers has issued recommendations on recognising and managing antibody-mediated interferences, including considering alternative assay platforms, repeating tests with different methodologies, and performing dilution or blocking studies when results are incongruent with the clinical picture [4,10]. Within this broader framework, paraproteinaemia represents a relatively rare but clinically important subset of interferences, particularly relevant in patients with monoclonal gammopathies such as multiple myeloma. Paraprotein-related assay interference is not restricted to cardiac biomarkers. Multiple reports have documented factitious biochemical abnormalities in multiple myeloma, with paraproteins affecting measurements of electrolytes, bilirubin, bicarbonate, and various hormones and drugs, often through precipitation, turbidity, or non-specific binding to assay antibodies [11,12].

These observations underscore a common mechanistic theme: high concentrations of monoclonal immunoglobulins may sterically hinder antigen-antibody interactions, form immune complexes, or interfere with detection systems in immunoassays, leading to spurious results across a range of analytes [13]. This case aligns with this pattern, in that marked paraproteinaemia coexisted with analytical failure of the Troponin I assay, while other clinical and imaging findings strongly suggested myocardial dysfunction. In the present patient, rapid clinical deterioration with septic shock, DIC, renal failure, and multiorgan dysfunction limited the ability to perform confirmatory

laboratory maneuvers such as measurement of Troponin T on an alternative platform, serial dilution studies, deproteinisation, or Polyethylene Glycol (PEG) precipitation to formally demonstrate paraprotein interference. Even so, the clear mismatch between the repeated Troponin I assay errors, the very high level of paraproteins, and the ECG and echocardiography findings strongly suggests that paraproteinaemia was the most likely reason for the test interference. As noted in other reported cases, such unrecognised assay interference can delay or complicate diagnosis and may also affect decisions regarding invasive procedures, including coronary angiography [5,6].

Overall, this case reinforces several key messages for clinicians. First, cardiac troponin results should never be interpreted in isolation but must be correlated with symptoms, ECG changes, imaging findings, and the broader clinical context. Second, persistent troponin results that are incongruent with the clinical scenario, whether unexpectedly high, low, or, as in this case, repeatedly yielding "error," should prompt a high index of suspicion for analytical interference, especially in patients with known or suspected plasma-cell dyscrasias. Third, early communication between clinicians and the laboratory, along with the use of alternative assay platforms or biomarkers, can help unmask such interferences and avoid misdiagnosis or unnecessary interventions. By adding to the limited literature on paraproteinaemia-related Troponin I assay interference, this case emphasises the need for heightened awareness of these rare but significant analytical pitfalls in the critical care setting.

CONCLUSION(S)

This case highlights the importance of recognising paraproteinaemia as a rare but significant cause of analytical interference in Troponin I assays. Clinicians should maintain a high index of suspicion when troponin results are incongruent with clinical findings, particularly in patients with plasma-cell dyscrasias such as multiple myeloma. Failure to identify such interference may delay diagnosis, complicate clinical decision-making, and influence the timing of essential interventions. Timely collaboration between clinicians and laboratory teams, along with the use of alternative biomarkers or assay platforms, can help clarify ambiguous results. Awareness of this analytical pitfall is crucial for preventing misdiagnosis and optimising outcomes in critically ill patients.

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