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Fatal hypercalcaemic crisis and acute kidney injury revealing undiagnosed multiple myeloma in an elderly woman: a case report

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ABSTRACT

Hypercalcaemic crisis is an uncommon initial presentation of multiple myeloma and may rapidly become life-threatening if not recognized promptly. An 83-year-old woman presented with severe hypercalcaemia and acute kidney injury, accompanied by progressive confusion and reduced consciousness. Serum protein electrophoresis revealed a monoclonal immunoglobulin G -lambda spike. The electrocardiography showed a shortened QT interval and Osborn waves. Despite hydration, corticosteroids, and supportive therapy, the patient deteriorated and died within 31 hours. This case underscores the importance of early biochemical evaluation in elderly patients with unexplained hypercalcaemia, as delayed recognition significantly worsens the prognosis.

Introduction

Hypercalcaemia represents a clinically significant metabolic abnormality most frequently encountered in association with primary hyperparathyroidism and malignant disease, which together account for the majority of cases (1). Although relatively uncommon in the general population, its incidence increases substantially with advancing age (2). In the oncological setting, hypercalcaemia often reflects advanced disease burden and carries important prognostic implications.

Multiple myeloma is a plasma cell dyscrasia predominantly affecting older adults and constitutes a leading haematological cause of malignancy-associated hypercalcaemia (3-6). Excessive osteoclastic bone resorption, driven by tumour-related cytokine signaling, results in calcium release and progressive skeletal destruction (7-9). Severe hypercalcaemia may culminate in a hypercalcaemic crisis, a medical emergency characterized by neurological impairment, cardiovascular instability, and renal dysfunction, with mortality rates reported to exceed 50% in the absence of timely treatment (10,11).

Recognition of hypercalcaemia in older adults is frequently delayed because presenting symptoms are non-specific and may be misattributed to ageing or comorbid conditions. Consequently, early biochemical investigation plays a crucial role in identifying reversible causes and preventing catastrophic outcomes.

We report a fatal hypercalcaemic crisis with acute kidney injury as the initial manifestation of previously undiagnosed multiple myeloma in an elderly woman, highlighting the diagnostic challenges and the narrow therapeutic window associated with this presentation.

Case Report

An 83-year-old woman was admitted to the nephrology department with acute kidney injury and progressive deterioration in mental status. According to family members, she had experienced increasing weakness, constipation, back pain, and gait instability over one week, followed by a marked reduction in alertness. For approximately three days before admission, she remained in a stuporous state and was unable to communicate or follow commands. There was no known history of malignancy, and she was not receiving medications known to influence calcium metabolism. Her medical history included arterial hypertension, an ischaemic stroke involving the right middle cerebral artery territory two decades earlier, and a surgically treated lumbar disc herniation.

The patient's regular medications included valsartan/amlodipine 160/80 mg, atenolol 100 mg, corneline 20 mg, atorvastatin 20 mg, pentoxifylline, pantoprazole, and intermittent diazepam. She was not receiving calcium supplements, vitamin D, thiazide diuretics, lithium, or any other medications known to affect calcium metabolism.

On examination, the patient responded only to painful stimuli. Blood pressure, heart rate, and oxygen saturation were within normal limits, and urine output was preserved. Clinical signs of intravascular dehydration were evident, including dry mucous membranes and reduced skin turgor; mild bilateral lower-limb oedema was attributed to hypoalbuminaemia and reduced mobility. Residual neurological deficits from prior cerebrovascular disease included left facial paresis and left-sided hemiparesis. Cardiopulmonary and abdominal examinations revealed no additional abnormalities.

Albumin-corrected calcium, calculated using the standard formula [corrected calcium = measured total calcium+0.02×(40-serum albumin)], was approximately 4.2 mmol/L (16.9 mg/dL), confirming a hypercalcaemic crisis. Laboratory findings were also consistent with acute kidney injury, reflected by elevated urea [31.7 mmol/L (190 mg/dL)] and creatinine [229 µmol/L (2.59 mg/dL)]. The estimated glomerular filtration rate [estimated glomerular filtration rate (eGFR), chronic kidney disease epidemiology collaboration] was 18 mL/min/1.73 m^2, consistent with severe renal impairment. Additional abnormalities included leukocytosis, normocytic anaemia, marked hyperproteinaemia with hypoalbuminaemia, and elevated globulin levels. Immunological testing revealed a marked increase in immunoglobulin G with lambda free light-chain predominance and a suppressed kappa-to-lambda ratio, findings indicative of monoclonal gammopathy. Alkaline phosphatase levels were within the normal range, and urinalysis was negative for Bence-Jones protein. A summary of biochemical and immunological findings is provided in Table 1.

Electrocardiography demonstrated left bundle branch block, significant QT interval shortening, and prominent Osborne (J) waves, consistent with severe hypercalcaemia. Non-contrast computed tomography of the brain showed diffuse cortical atrophy and chronic small-vessel ischaemic changes, without evidence of acute intracranial pathology (Figure 1).

Management included aggressive intravenous administration of isotonic saline and enteral fluid replacement via a nasogastric tube to correct dehydration and enhance renal calcium

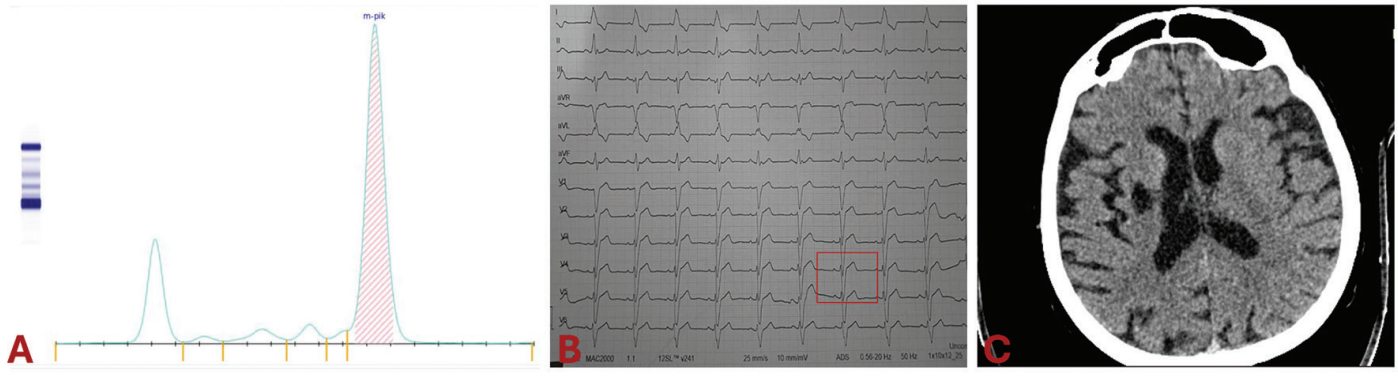

Figure 1. Electrocardiographic, laboratory, and neuroimaging findings in severe hypercalcaemia. (A) Serum protein electrophoresis demonstrating a dominant monoclonal M-spike in the gamma region, consistent with monoclonal gammopathy. (B) Twelve-lead electrocardiogram showing left bundle branch block, marked QT-interval shortening, and prominent Osborne (J) waves (highlighted), characteristic of severe hypercalcaemia. (C) Non-contrast axial brain computed tomography scan demonstrating global cortical atrophy and chronic small-vessel ischemic changes, without evidence of acute intracranial pathology

Table 1. Biochemical and immunological findings in hypercalcaemic crisis at presentation

Parameter	Patient value	Reference range	Clinical interpretation
Inflammatory markers			
C-reactive protein	7.4 mg/L	<5	Mild inflammatory response
Procalcitonin	0.21 ng/mL	<0.5	No evidence of bacterial sepsis
Haematology			
White blood cells	25.5×10^9/L	4-9	Leucocytosis with left shift
Haemoglobin	102 g/L	120-180	Anaemia (CRAB criterion)
Platelets	237×10^9/L	150-450	Normal
Renal and metabolic parameters			
Urea	31.7 mmol/L (190 mg/dL)	2.7-7.8	Acute kidney injury
Creatinine	229 µmol/L (2.59 mg/dL)	45-109	Reduced eGFR
eGFR	18 mL/min/1.73 m^2	>60	Severe renal impairment
Uric acid	787 µmol/L	150-450	Hyperuricemia
Sodium	132 mmol/L	136-145	Mild hyponatremia
Potassium	3.7 mmol/L	3.8-5.5	Slightly decreased
Calcium-phosphate metabolism			
Total calcium	3.9 mmol/L	2.1-2.6	Severe hypercalcemia
Corrected calcium	4.2 mmol/L (16.9 mg/dL)	—	Hypercalcaemic crisis
Parathyroid hormone	92.6 pg/mL	12-88	Inappropriately normal/slightly elevated (secondary to renal dysfunction)
Vitamin D (25-OH)	<20 nmol/L	50-125	Deficiency
Alkaline phosphatase	67 U/L	36-126	Normal (osteolytic pattern)
Protein profile and immunology			
Total protein	127 g/L	63-83	Marked hyperproteinemia
Albumin	23 g/L	35-50	Hypoalbuminemia
Globulins	104 g/L	28-33	Markedly elevated
IgG	96.6 g/L	7.8-16.2	Monoclonal IgG excess
Free light chains (λ)	11.8 g/L	0.9-2.1	Markedly increased
Free light chains (κ)	0.08 g/L	1.7-3.7	Suppressed
κ/λ ratio	0.007	1.35-2.65	Lambda-restricted clonality
Serum protein electrophoresis			
Gamma globulin fraction	81.1 g/L (68.2%)	4.8-11.9 g/L (6.2-15.4%)	Dominant monoclonal component
Albumin fraction	23.1 g/L (19.4%)	46-56 g/L (60.3-72.8%)	Reduced
M-component	M1: 76.7 g/L (64.5%)	—	Paraproteinemia
A/G ratio	0.24	—	Markedly reduced
Urine analysis			
Bence-Jones protein	Negative	Negative	Absent
Coagulation marker			
D-dimer	2100 ng/mL	<500	Elevated (stress/inflammation related)

eGFR: Estimated glomerular filtration rate, IgG: Immunoglobulin G, CRAB: HyperCalcaemia, renal impairment, anaemia, and bone lesions, A/G: Albumin-to-globulin ratio

excretion. Empirical cephalosporin therapy was initiated due to mildly elevated inflammatory markers. Following a haematology consultation, multiple myeloma was strongly suspected, and a bone marrow biopsy was planned. Corticosteroid therapy was commenced; however, bisphosphonate treatment with zoledronic acid was contraindicated due to a severely reduced eGFR (18 mL/min).

Despite supportive measures, the patient's neurological and cardiovascular status deteriorated rapidly. Thirty-one hours after admission, she progressed to a deep coma and developed

refractory bradycardia, followed by asystole. Cardiopulmonary resuscitation was unsuccessful. Post-mortem evaluation, including review of skeletal imaging and skull radiographs, revealed multiple lytic bone lesions and a monoclonal spike on serum protein electrophoresis, confirming previously unrecognized multiple myeloma as the underlying cause of the hypercalcaemic crisis and acute kidney injury.

The patient described in this report is deceased, and written informed consent could not be obtained; however, all identifying information has been removed to ensure complete anonymity.

Discussion

Multiple myeloma may remain clinically silent for prolonged periods, with diagnosis frequently established only after the development of end-organ damage. Although hypercalcaemia is a recognized feature of symptomatic disease, presentation as a hypercalcaemic crisis is uncommon and is associated with substantial mortality (3,7-9,12). In the present case, the severity of metabolic derangement and neurological impairment at admission suggests that the underlying plasma cell disorder had progressed significantly before clinical recognition.

The pathogenesis of hypercalcaemia in multiple myeloma is predominantly related to excessive osteoclastic bone resorption driven by tumour-derived cytokines, including receptor activator of nuclear factor-κB ligand and interleukin-6, with concomitant suppression of osteoblast activity (3,7,14). This mechanism accounts for the presence of extensive osteolytic lesions and explains the normal alkaline phosphatase levels observed in this patient, a finding that helps distinguish osteolytic malignancy from primary hyperparathyroidism or osteoblastic metastatic disease (3,7,14).

Neurological deterioration, progressing from confusion to stupor and coma, represents a hallmark of severe hypercalcaemia and reflects direct neurotoxicity, cerebral dehydration, and impaired neuronal excitability (10,11). In this case, electrocardiographic abnormalities, including QT interval shortening, left bundle branch block, and Osborn (J) waves, indicated profound electrolyte imbalance. Although Osborne waves are classically associated with hypothermia, they have been rarely described in severe hypercalcaemia and may signal advanced metabolic instability with increased risk of fatal arrhythmias (15). Their presence may therefore serve as an important, albeit under-recognized, diagnostic clue in hypercalcaemic emergencies.

Renal dysfunction in this patient was likely multifactorial, resulting from hypercalcaemia-induced renal vasoconstriction, intravascular volume depletion, and light-chain-mediated nephrotoxicity (4,12). The combination of acute kidney injury and markedly reduced eGFR significantly limited therapeutic options, precluding early administration of bisphosphonates and delaying consideration of renal replacement therapy. This narrow therapeutic window highlights the critical importance of early detection and intervention before irreversible organ damage occurs. In patients with malignancy-associated acute kidney injury, severe renal impairment substantially restricts therapeutic options, and the use of potentially nephrotoxic agents such as intravenous bisphosphonates should be avoided or postponed because of the risk of further deterioration in kidney function (4).

The absence of detectable Bence-Jones protein in the urine does not exclude multiple myeloma, as urinary testing may be negative in cases with predominant intact immunoglobulin secretion or low free light-chain excretion. Serum protein electrophoresis and free light-chain assays were more sensitive in detecting monoclonal gammopathies and were diagnostic in this patient.

In this case, the acute kidney injury was considered predominantly prerenal, resulting from severe dehydration and hypercalcaemia-induced renal vasoconstriction, with a possible contributory role of light-chain-related nephrotoxicity.

Although intravenous bisphosphonates represent standard therapy for malignancy-associated hypercalcaemia, their use was deferred in this patient due to severely reduced renal function (eGFR 18 mL/min/1.73 m^2) and the associated risk of worsening acute kidney injury, particularly given the limited time window for therapeutic benefit.

Given the extremely rapid progression to cardiopulmonary arrest within 31 hours, the window for initiating renal replacement therapy was critically limited. Despite initially stable hemodynamics, the progression to deep coma and refractory bradyarrhythmia occurred before dialysis could be safely initiated, reflecting the fulminant nature of the hypercalcaemic crisis in this elderly patient.

The rapid and fatal course observed in this case underscores the diagnostic challenge posed by non-specific symptoms in elderly patients, in whom early manifestations of hypercalcaemia may be misattributed to ageing or comorbid disease. Clinicians should maintain a high index of suspicion for multiple myeloma in older individuals presenting with unexplained hypercalcaemia, renal impairment, anaemia, or neurological changes. Prompt biochemical evaluation and timely initiation of disease-directed therapy remain essential to preventing catastrophic outcomes in this high-risk population.

Conclusion

This case highlights hypercalcaemic crisis as a rare but severe initial presentation of multiple myeloma, particularly in elderly patients with non-specific symptoms. The combination of marked hypercalcaemia, acute kidney injury, and delayed diagnosis resulted in a rapid and fatal course. Early recognition of the clinical triad of hypercalcaemia, renal dysfunction, and

anaemia is essential, as prompt treatment and timely myeloma-directed therapy may significantly improve outcomes.

Ethics

Informed Consent: Written informed consent could not be obtained due to the patient's death; publication was approved in accordance with institutional policy and ethical standards.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.S., S.P.K., B.G., Concept: H.S., S.P.K., A.C.T., B.G., Design: H.S., S.P.K., Data Collection or Processing: H.S., S.P.K., A.C.T., Z.P., B.G.; Analysis or Interpretation: H.S., S.P.K.; Literature Search: H.S., S.P.K., A.C.T., Z.P., B.G.; Writing: H.S., S.P.K., B.G.

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