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Case Report

Young woman with high fever and a massive rise in N-terminal pro-B-type natriuretic peptide (NT-pro-BNP)

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ABSTRACT

A 33-year-old lady presented with acute symptoms suggestive of pneumonia. She rapidly deteriorated and needed intensive care unit care. She was found to have an enormous rise in N-terminal pro-B-type natriuretic peptide (NT-Pro-BNP), nearly in six digits without any previous co-morbidity. NT-Pro-BNP high levels could be reflective of cardiac injury, heart failure (HF), or chronic kidney disease (CKD), and a few other medical conditions. The final diagnosis was for acute on chronic kidney disease.

Keywords: Heart Failure, CKD, NT-pro BNP, Chronic Kidney Disease

INTRODUCTION

This case report outlines the clinical presentation, diagnostic challenges, and management of a 33-year-old woman who presented with acute symptoms suggestive of pneumonia. She rapidly deteriorated and needed intensive care unit admission at a multi-specialty hospital. She was found to have an unprecedented elevation in N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) level, raised Troponin I, and markedly increased serum creatinine. High NT-pro-BNP levels can reflect cardiac injury, heart failure, chronic kidney disease (CKD), and other medical conditions. This case underscores the complexity of interpreting NT-pro-BNP levels in the context of comorbidities, particularly renal impairment, which challenges traditional markers of heart failure severity. The final diagnosis was acute on chronic kidney disease. Before this presentation, the patient did not have a prior diagnosis of CKD or any other comorbidity. Further research is warranted to elucidate the clinical implications of extreme NT-pro-BNP elevations and their management in diverse patient populations.

CASE REPORT

A 33-year-old young lady presented with a two-week history of mild, clear, productive cough, chest discomfort, generalised body ache, and a decrease in oral intake. She had a low-grade fever for the last five days. She developed sudden-onset severe breathlessness overnight and a feeling of air hunger. She was urgently brought to a small peripheral clinic-nursing home on the outskirts of Delhi by her family in the night.

On initial clinical assessment, she was found to be alert with a Glasgow Coma Scale of 15/15. Her heart rate was 126/min, respiratory rate was 34/min, temperature 100.5 degrees F and

oxygen saturation was 86%, which improved to only 89% on 6 litres of oxygen. Her blood pressure was low at 90/60 mmHg. Lung auscultation revealed good air entry on both sides, bilateral basal crackles at lung bases, but no wheeze. She was tachycardic with no cardiac murmur, plural or pericardial rub, or any adventitious lung sound. There was no history of COVID-19 infection or other comorbidity. She was not on any medication and had no history of allergy to any medication, food, or inhaled items. There was no leg or calf swelling, and her jugular venous pressure was normal. She was married and had two children. There was no history of any complications during pregnancy or thereafter. Her periods were normal, and a pregnancy test was negative. She denied any severe chest or abdominal pain. She had a skinny build, and her weight was 38 kilograms. After initial emergency care, she was transferred to a higher centre with a blue-light ambulance for intensive care.

In the hospital, she was admitted to the intensive care unit for a few days and was then shifted to the ward. The significant findings during hospital admission were as follows: On arrival, she was restless and very unwell with a low blood pressure of 92/55 mmHg, oxygen saturation of 92% on 10 litres of oxygen, and a Glasgow Coma Scale of 14/15. Her electrocardiogram showed sinus tachycardia and bilateral widespread crackles in the lungs.

Her significant investigation results during hospitalisation: blood sugar 94 mg/dL, serum sodium 131.9 mEq/L, serum potassium 5.63 mEq/L, very high serum creatinine of 9.2 mg/dL, low haemoglobin 8.2 g/dL, low calcium 7.6 mg/dL, Serum parathyroid hormone level 384.2, and a high serum uric acid of 9.8 mg/dL. Her glycosylated haemoglobin was 5.2. The d-dimer level was high at 4413 ng/mL, and a high Troponin I of 25.8 ng/mL. Arterial Blood Gases findings were suggestive of metabolic acidosis. The serum procalcitonin was normal at 0.13 ng/mL and C-reactive protein of 9.3 mg/L. 2D-Echogardiogram was reported as her ejection fraction was 20-25%, with global hypokinesia, no intracardiac clot, vegetations, and no leaking valves. The initial N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) was extremely high at 97,600 pg/mL, which dropped to 25,000 pg/mL on day two. Her Computed Tomography Pulmonary Angiography result was normal. Her polymerase chain reaction for COVID-19 and H1N1 were negative. On routine urine examination, there was evidence of heavy proteinuria (protein+++), RBC++, and WBC++ with no glucose or ketone in it. Ultrasonography of the abdomen and kidney-ureter-bladder revealed findings suggestive of bilateral medical renal disease (right kidney small 7 cm x 2.6 cm, left kidney normal in size), bilateral moderate pleural effusion, and pericholecystic gallbladder wall oedema with mild ascites.

Her blood pressure and oxygen saturation improved to 106/70 and 94% on high-flow oxygen, respectively. She was treated along the lines of chronic kidney disease (CKD) with acute flare and heart failure (HF). Her blood pressure remained within normal limits. She was followed up a week after discharge, and her test results were as follows: haemoglobin 10.1 g/dL, serum creatinine 6.29 mg/dL, calcium 9.07 mg/dL, and urine culture and sensitivity were sterile after 48 hours. Her serological tests for HIV, HBs Ag & HCV were negative.

After two weeks, she visited our clinic with a hospital discharge letter. Her family had been with the clinic for many years for their medical needs. Her family wanted to know how she became so serious and the possible future outcome for her. She was fit and well before this event. On clinical assessment, heart rate was 94/min, respiratory rate of 18/min, afebrile, oxygen saturation was 97% on air. Her blood pressure was 112/70 mmHg. Lung auscultation was satisfactory, and there was no audible cardiac murmur. We repeated her blood tests and NT-pro-BNP level. Her significant blood test results were as follows: haemoglobin 10.7 g/dL, serum creatinine 6.97 mg/dL, serum potassium 3.49 mEq/L, C-reactive protein 3.6 mg/L, erythrocyte sedimentation rate 64 mm/hour, serum uric acid 9.8 mg/dL. Routine urine examination showed protein +++ and no nitrite, RBC, or WBC. Her NT-pro-BNP level remained significantly high at 15,191 pg/mL. Her electrocardiogram showed sinus rhythm left-axis deviation, and there was no evidence of ischemia or q waves. Her Chest X-ray was normal. She was stable on medication and was under specialist follow-up at the hospital.

DISCUSSION

The reason to reflect on this case is the huge rise in NT-Pro-BNP. This case presents a significant increase in NT-Pro-BNP levels, prompting further exploration. We did a Medline search to explore the evidence, but we could not find such a high level in reported cases. We could find a few cases with levels up to 20,000 pg/mL in CKD.

Cardiomyocytes release cardioprotective hormones in response to pressure or volume overload known as Natriuretic peptides. (NPs).[1] Further, these peptides split into equimolar amounts of physiologically active and inactive components. A 32 amino acid fragment is active BNP, while an inactive 76 amino acid fragment is known as NT-pro-BNP. Neutral endopeptidase and natriuretic peptide receptors are the main mechanisms responsible for the clearance of these peptides, but renal filtration also plays a role. The removal of NT pro-BNP depends on renal filtration and has a half-life of one to two hours.[2]

Numerous conditions are correlated with heightened levels of B-type natriuretic peptide (BNP) and N-terminal pro-

BNP (NT pro-BNP). Among cardiovascular ailments are hypertension, myocardial infarction, atrial fibrillation, acute coronary syndrome, cardioversion, valvular heart disease, and myocarditis. Renal factors encompass acute and chronic renal failure. Respiratory triggers include pulmonary hypertension, chronic obstructive pulmonary disease, pneumonia, pulmonary embolism, and acute respiratory distress syndrome. Additionally, older age, female gender, liver cirrhosis, hyperthyroidism, sepsis, and post-chemotherapy situations may lead to elevated BNP levels.[3] Natriuretic peptides, including BNP and NT-pro-BNP, are secreted in response to cardiac stress and are associated with increased mortality in end-stage renal disease patients.[4] In cardiopulmonary conditions, they function as potential biomarkers for diagnosing and predicting cardiopulmonary-related illnesses.[5] Furthermore, BNP and NT-pro-BNP have been linked to ventricular dysfunction in patients with septic cardiomyopathy.[6]

In this case, despite initial suspicions of sepsis, negative COVID-19 tests, and relatively normal inflammatory markers, the extremely high NT-pro-BNP levels, high Troponin I, and abnormal d-dimer level suggested underlying cardiac or pulmonary pathology. However her electrocardiogram did not support myocardial injury, and she denied any chest pain at all. She did have a low ejection fraction initially, which recovered without any evidence to suggest myocardial injury. Computed tomography pulmonary angiography was reported as normal, ruling out a possibility of pulmonary embolism, which could explain most of her initial presenting symptoms. However, in the presence of renal failure, interpreting BNP and NT-pro-BNP levels becomes challenging due to their elevation in chronic kidney disease, irrespective of heart failure presence. This makes both BNP and NT–pro-BNP less reliable for heart failure diagnosis as the cause of the patient's symptoms in patients with CKD.[3] The abysmal rise of NT-pro-BNP levels observed in this case may be attributed to acute-on-chronic kidney disease, anaemia, high-output cardiac failure, and potential uremic myocarditis.

BNP levels rise in heart failure, reflecting its severity, yet the reasons for extremely high levels in some patients remain unclear. Maya Guglin and colleagues retrospectively analysed data from 179 consecutive patients categorised into groups based on predetermined BNP ranges: mild rise (500–1000 pg/mL), moderate elevation (2000–3000 pg/mL), and high elevation (4000–20,000 pg/mL). Interestingly, features of the group with high BNP levels did not significantly differ from those with moderate elevation. In our case, her NT-pro-BNP level was extremely high at 97,600 pg/mL and serum creatinine of 9.2 mg/dL. The study found a correlation between serum creatinine levels and BNP levels, leading researchers to conclude that high BNP levels (4000–20,000 pg/mL) are more indicative of renal dysfunction than heart failure severity.[7] In subsequent tests and follow-ups, her NT-pro-BNP and serum creatinine levels showed a similar trend.

BNP loses reliability at high levels, surpassing 3000 pg/mL, and cannot be consistently used to gauge heart failure severity beyond this threshold. Considering this fact a NT-pro-BNP level approaches six digits in this case cannot be attributed solely due to severe heart failure. A significant proportion of patients with markedly elevated BNP levels show no signs of decompensated heart failure. While extreme BNP elevation typically results from a combination of reduced ventricular function, acute fluid overload, and renal insufficiency, a study by Catherine Law and colleagues revealed that BNP levels can be similarly elevated in the absence of these conditions or with only one.[8]

Our patient did show features of heart failure, global myocardial wall hypokinesia, a low ejection fraction of 20–25%, low blood pressure, tachycardia, and bilateral basal crackles at lung bases, but, this extremely high level of NT pro-BNP at 97,600 pg/mL was unbelievable. Advanced CKD with an acute flare was more responsible for this enormous rise in natriuretic peptide and possible high Troponin I and d-dimmer levels in this young lady. Surprisingly, she never reported any symptoms suggestive of chronic renal dysfunction before. Possibly she might have ignored common non-specific symptoms of renal disease.

CONCLUSION

Overall, while NT-pro-BNP levels can indicate heart failure severity, their interpretation becomes complex at extremely high levels, necessitating consideration of comorbidities such as renal dysfunction. Further research is warranted to better understand the implications of such elevated NT-pro-BNP levels and their clinical significance in diverse patient populations.

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Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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