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Case Report

Biochemistry Section

Elevated NT-proBNP in a Patient with Grade 1 Renal Cell Carcinoma undergoing Axitinib Therapy: A Case Report

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ABSTRACT

The N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) elevation in oncology patients underscores the importance of considering paraneoplastic syndromes, specific drug toxicities, and tumour-related vascular complications alongside primary cardiac. A 58-year-old male with Grade 1 clear cell Renal Cell Carcinoma (RCC) on Axitinib therapy presented with a three-week history of progressive fatigue, significant weight loss (5 kg), and anaemia. Despite normal renal function and preserved cardiac ejection fraction (60%), his NT-proBNP level was persistently elevated above 35,000 pg/mL. Comprehensive cardiac workup, including troponin, Electrocardiogram (ECG), and echocardiography, revealed no evidence of heart failure. Diagnosis was confirmed via Positron Emission Tomography (PET)-Computed Tomography (CT), which identified a right renal mass with an Inferior Vena Cava (IVC) thrombus and bilateral lung lesions, and biopsy with immunohistochemistry. This case highlights an extreme elevation of NT-proBNP in low-grade RCC, potentially mediated by paraneoplastic activity, Axitinib-related cardiotoxicity, anaemia, or tumour thrombus effects, suggesting its role as a biomarker beyond cardiac dysfunction. Monitoring NT-proBNP in such patients may offer insights into tumour behaviour and treatment-related stress.

Keywords: Anaemia, Brain, N-terminal pro-B-type natriuretic peptide, Paraneoplastic syndromes

CASE REPORT

A 58-year-old male was admitted to a tertiary care hospital in November 2024 with a three-week history of progressive fatigue, significant weight loss (approximately 5 kg), and worsening anaemia. He was a known case of RCC and had been on Axitinib therapy (5 mg twice daily) for one year.

Vitals on admission were as follows: Blood Pressure (BP) 80/60 mmHg, Heart Rate (HR) 80 bpm, Respiratory Rate (RR) 18/min, temperature 98.6°F, and SpO_2 97% on room air. He had no prior history of cardiovascular disease, diabetes, or chronic kidney disease.

Relevant laboratory findings included:

- Haemoglobin: 8.2 g/dL
- White Blood Cell (WBC): 13,100/µL, Platelets: 121,000/µL
- Serum Glutamate Oxaloacetate Transaminase (SGOT): 83 U/L, Serum Glutamate Pyruvate Transaminase (SGPT): 90 U/L, Alkaline Phosphatase (ALP): 371 U/L
- Creatinine: 0.32 mg/dL (ref: 0.70-1.30 mg/dL), Urea: 28 mg/dL
- Sodium: 124 mmol/L, Potassium: 3.42 mmol/L, Chloride: 93 mmol/L
- Creatine Kinase (CK)-MB: 0.53 ng/mL, Troponin I: <10 pg/mL
- NT-proBNP: >35,000 pg/mL (ref: <125 pg/mL), persistently elevated
- Cardiac evaluation showed normal Electrocardiography (ECG) findings. ECG revealed preserved ejection fraction (60%), mild left ventricular hypertrophy, mild mitral regurgitation, no regional wall motion abnormalities, and no pericardial effusion.

Imaging and histopathological evaluation:

- Positron Emission Tomography (PET)-Computed Tomography (CT) demonstrated a right renal mass (3.8×2.7 cm) with tumour thrombus extending into the IVC, and bilateral lung lesions (metastatic versus infective).
- Biopsy confirmed clear cell RCC, the World Health Organisation (WHO)/International Society of Urological Pathology (ISUP) grade 1. Histological examination showed characteristic features, including clear cytoplasm and round nuclei (400× magnification).
- Immunohistochemical staining was positive for Vimentin and CD10, and negative for Pax8.
- The histopathological and immunohistochemical features were consistent with a diagnosis of clear cell RCC, WHO/ISUP grade 1 [1].

The patient's management involved a multi-faceted approach focussing on continuing oncologic control while addressing acute treatment-related complications. Axitinib therapy (5 mg twice daily) was maintained following a careful risk-benefit assessment, considering its importance in controlling metastatic RCC despite the biomarker elevation and the absence of clinical heart failure. Supportive care included transfusion of two units of packed red blood cells for symptomatic anemia (Hb 8.2 g/dL) to improve functional capacity and reduce cardiac workload, along with aggressive electrolyte repletion for his significant hypokalaemia (3.42 mmol/L) and hyponatraemia (124 mmol/L) through intravenous and oral supplementation. A strict monitoring protocol was implemented, including regular clinical assessments for heart failure signs and serial measurements of NT-proBNP and troponin-I to detect early cardiotoxicity. With this regimen, the patient's condition stabilised with improved fatigue, normalised electrolytes, and no signs of cardiac decompensation, leading to discharge with close outpatient follow-up with both Oncology and Cardiology services for continued vigilant surveillance during Axitinib therapy.

DISCUSSION

This case presents a remarkable clinical scenario of extreme NT-proBNP elevation (>35,000 pg/mL) in a patient with low-grade (grade 1) clear cell RCC, occurring in the absence of significant

cardiac or renal dysfunction. This finding is particularly unusual given the relatively low-grade tumour characteristics and warrants thorough exploration of potential underlying mechanisms beyond conventional heart failure explanations.

Several pathophysiological mechanisms may account for this profound biomarker elevation. First, a paraneoplastic phenomenon must be considered, as RCC is known to produce various cytokines and hormones [2]. Tumour-secreted factors, potentially related to Vascular Endothelial Growth Factor (VEGF) pathway activation, may directly stimulate NT-proBNP release [3]. Second, the patient's Axitinib therapy, a VEGF tyrosine kinase inhibitor, represents another plausible mechanism. VEGF inhibitors are well-documented to cause subclinical cardiotoxicity, including hypertension and left ventricular dysfunction, which can manifest as elevated cardiac biomarkers even before overt clinical heart failure develops [4,5]. Third, the patient's significant anaemia (Hb 8.2 g/dL) could have contributed to a high-output state, increasing cardiac wall stress and subsequently elevating NT-proBNP levels [6]. Finally, the tumour thrombus extending into the IVC may cause circulatory compromise through impaired venous return, indirectly increasing cardiac strain and NT-proBNP production [7].

When contextualised within existing literature, the magnitude of NT-proBNP elevation in this case is exceptional. Previous studies have established correlations between elevated NT-proBNP levels and advanced tumour burden in RCC, typically demonstrating increases approximately 3-fold above normal ranges [3,8]. However, levels exceeding 35,000 pg/mL are rarely reported, particularly in WHO/ISUP grade 1 disease. This discrepancy suggests that in this specific clinical context, NT-proBNP may serve less as a marker of tumour volume and more as an indicator of specific tumour biology (paraneoplastic secretion), therapy-related stress, or vascular complications such as IVC thrombus. This perspective aligns with emerging concepts that biomarkers like NT-proBNP can function as early indicators of subclinical cancer therapy-related cardiotoxicity [9], a monitoring strategy that has proven beneficial in managing cardiotoxicity associated with other chemotherapeutic agents [10].

Alternative cardiac aetiologies were rigorously considered and excluded. Subclinical diastolic dysfunction was not evident on comprehensive echocardiography, and chemotherapy-induced cardiomyopathy was considered unlikely given the preserved ejection fraction. There was no echocardiographic evidence supporting pulmonary hypertension.

CONCLUSION(S)

This case expands the differential diagnosis for extreme NT-proBNP elevation in oncology patients and underscores the importance of considering paraneoplastic syndromes, specific drug toxicities, and tumour-related vascular complications alongside primary cardiac aetiology. Serial monitoring of NT-proBNP in RCC patients receiving VEGF Tyrosine Kinase Inhibitors (TKIs) like Axitinib may provide valuable insights into treatment-related cardiac stress and potentially signal disease activity. Future follow-up, including post-resection measurements, could help clarify the kinetic profile of NT-proBNP and its utility as a dynamic biomarker in this setting.

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