# Title Page

Oncology Meets Cardiology: Bevacizumab-Associated Cardiomyopathy in a Patient with Hepatocellular Carcinoma

## Authors List

Mohammad Hamza Bin Abdul Malik1, Muhammad Arham2, Muhammad Salaar Riaz3, Muhammad Awais Bin Abdul Malik4, Javed Iqbal5, Ayesha Ihsan6

1. Nassau University Medical Center, New York, US  
   Email: [m.hamzabinmalik@gmail.com](mailto:m.hamzabinmalik@gmail.com)   
   ORCID: 0000-0002-5557-7961
2. Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.  
   Email: z18.mbbs.429@gmail.com  
   ORCID: 0009-0004-4722-9774
3. Nassau University Medical Center, New York, US  
   Email: [mriaz1@numc.edu](mailto:mriaz1@numc.edu)   
   ORCID: 0009-0002-0536-1836
4. Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.  
   Email: [awaisbinmalik@gmail.com](mailto:awaisbinmalik@gmail.com)  
   ORCID: 0009-0000-3777-5318
5. Nursing Department Hamad Medical Corporation Doha P.O Box 3 no c 050 Doha Qatar.   
   ORCID: 0000-0003-2627-685X   
   Email: [jiqbal3@hamad.qa](mailto:jiqbal3@hamad.qa)
6. University Medical and Dental College, Faisalabad   
   Email: ayshaihsan97@gmail.com  
   ORCID: 0009-0007-9816-2129

## Corresponding Author

**Dr. Mohammad Hamza Bin Abdul Malik**  
Resident, Nassau University Medical Center, New York City, US  
Email: [m.hamzabinmalik@gmail.com](mailto:m.hamzabinmalik@gmail.com)

## Authors Contribution

**Mohammad Hamza bin Abdul Malik:** Conceptualization, Methodology, Supervision, Writing – Original Draft.  
**Muhammad Arham:** Conceptualization, Data Curation, Investigation, Writing – Review & Editing.  
**Muhammad Salar Riaz:** Data Curation, Investigation, Visualization, Writing – Review & Editing.  
**Muhammad Awais bin Abdul Malik:** Investigation, Validation, Writing – Review & Editing.  
**Javed Iqbal:** Funding Acquisition, Project Administration, Supervision.  
**Ayesha Ihsan:** Visualization, Writing – Review & Editing.

# Keywords

Bevacizumab, Congestive Heart Failure (CHF), Cardiomyopathy, Hepatic Carcinoma, TTE (Transthoracic Echocardiogram), GDMT (Guideline-Directed Medical Therapy)

# Introduction

Bevacizumab is a humanized monoclonal antibody of the IgG class that targets vascular endothelial growth factor (VEGF). Overexpression of VEGF is one of several active intrinsic immune-evasion pathways that have been linked to the development and progression of different malignancies, including advanced liver cancer (1) (2). Through its mechanism of action, Bevacizumab reduces VEGF overexpression and is a widely utilized chemotherapeutic agent for malignancies characterized by VEGF overexpression. Notably, it recently received FDA approval for the treatment of advanced liver cancer (3) (4).

However, despite its therapeutic benefits, Bevacizumab has been associated with cardiovascular complications, including hypertension, thromboembolism, and myocardial infarction​ (5). Additionally, it has been linked to reversible cardiomyopathy and left ventricular dysfunction in an exceptionally rare proportion of patients, even those without preexisting cardiac disease (6).

We present a rare case of **bevacizumab-induced cardiomyopathy**, emphasizing the importance of **early recognition** and **prompt intervention.** Discontinuation of bevacizumab, along with **guideline-directed medical therapy**, is crucial for managing this potentially reversible yet life-threatening side effect. This case report adheres to the CARE (CAse REport) guidelines

# Case History/Examination

A 68-year-old male with a history of hepatic carcinoma (receiving chemotherapy every three weeks for 18 months), hypertension, and seizure disorder presented to the emergency department. He was referred by his primary care physician because of bilateral leg swelling that persisted for a month. The patient reported persistent shortness of breath after walking 2–3 blocks without associated syncope, chest pain, headache, or vomiting.

The patient's vital signs, physical examination, and laboratory findings are summarized in Table 1

## **Table 1:** Vital Signs, Physical Examination

|  |  |
| --- | --- |
| Parameter | Findings |
|  |  |
| Vital Signs |  |
| Blood Pressure | 146/106 mmHg |
| Heart Rate | 90 bpm |
| Respiratory Rate | 18 breaths/min |
| SpO₂ | 90% on room air |
| Temperature | Afebrile |
|  |  |
| Cardiac Exam |  |
| Jugular Venous Pressure | Normal |
| Rhythm | Regular |
| Heart Sounds | S1 normal, S2 normal |
|  |  |
| Peripheral Exam |  |
| Lower Extremity Edema | B/L edema, +1 |
|  |  |
| Respiratory Exam |  |
| Respiration | Regular |
| Auscultation | B/L crackles over the lower lobe |

# Investigation and Treatment

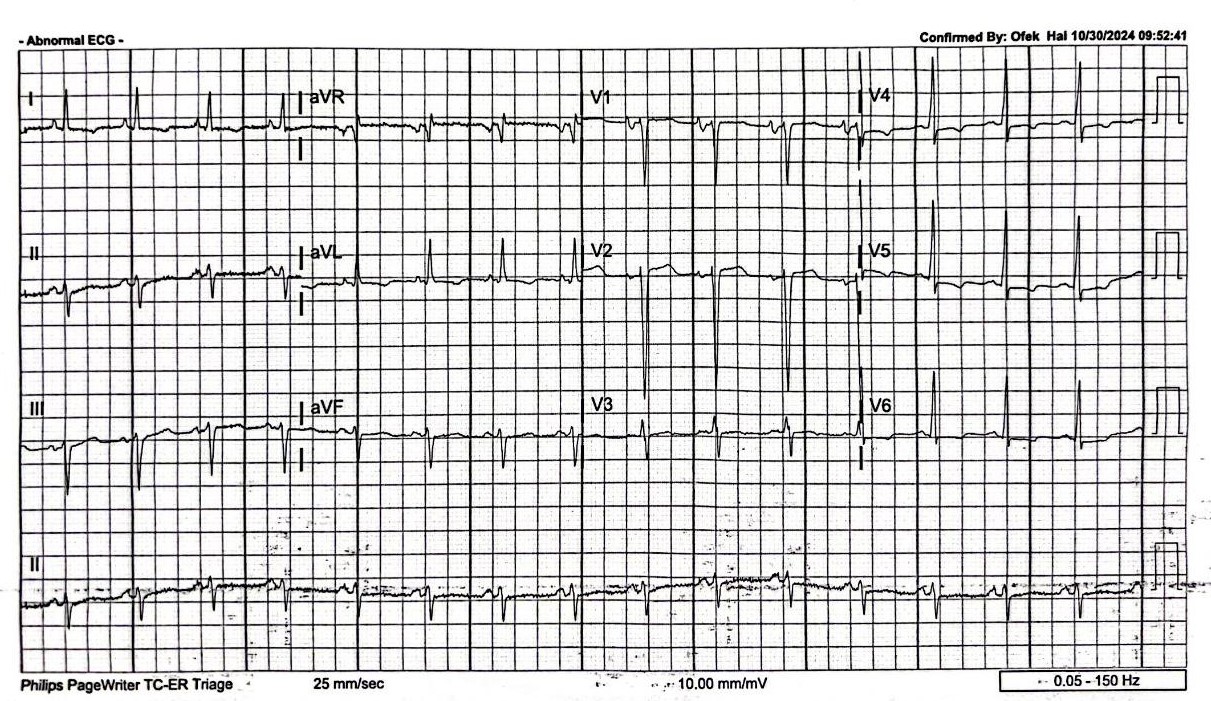
The laboratory findings demonstrated significant abnormalities. Liver function tests revealed elevated ALT, AST, and ALP, indicative of hepatic involvement. **NT-proBNP** and high-sensitivity troponin levels (**hs-cTn)** were elevated, suggesting cardiac stress and myocardial injury. Conversely, lactate levels remained within the normal range, indicating no evidence of significant metabolic acidosis. These findings raise concerns for potential cardiotoxic effects warranting further investigation.

## **Table 2:** Laboratory Findings

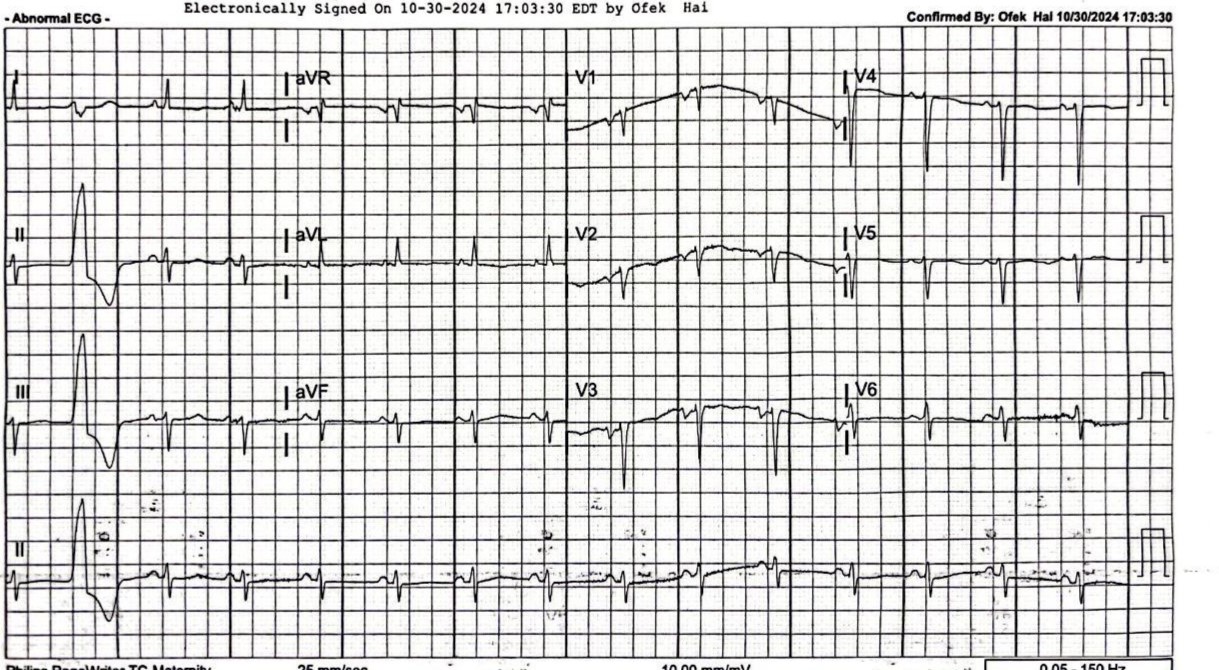
|  |  |
| --- | --- |
|  |  |
| Laboratory Results |  |
| ALT | **87 U/L** |
| AST | **79 U/L** |
| ALP | **297 U/L** |
| **NT-proBNP** | **1941 pg/mL** |
| **hs-cTn** | **63.72 ng/L** |
| Lactate | **1.7 mmol/L** |

The patient's electrocardiogram (ECG) initially demonstrated a sinus rhythm with evidence of a left anterior fascicular block. Subsequently, the ECG also revealed the presence of premature ventricular complexes (PVCs). The findings are illustrated in Figures 1 and 2.

## **Figure 1:** Electrocardiogram (ECG) of the patient demonstrating a left anterior fascicular block (LAFB)

****

## **Figure 2:** Electrocardiogram (ECG) of the patient demonstrating premature ventricular complexes (PVCs)



**Telemetry monitoring** documented multiple PVCs and nine episodes of non-sustained ventricular tachycardia (NSVT). **Chest X-ray** revealed an enlarged cardiac silhouette and blunting of the bilateral costophrenic angles, suggesting the presence of pleural effusion.

The **transthoracic echocardiogram (TTE)** demonstrated a mildly dilated left ventricle with moderate wall thickness, concentric hypertrophy, and severely increased ventricular mass. Systolic function was severely reduced, with an ejection fraction (EF) of less than 15% and severe diffuse hypo kinesis. The mitral and tricuspid valves both showed moderate regurgitation. Pulmonary pressures were moderately elevated, with an estimated peak systolic pressure of 48.1 mmHg. Given low EF and hypo-kinesis, cardiac catheterization was performed to rule out ischemic cause. No significant coronary artery disease or ischemic changes were observed, suggesting a non-ischemic etiology for the cardiomyopathy. Cardiac Catheterization is illustrated in Figure 3.

## **Figure 3:** Normal cardiac catheterization showing no abnormalities in coronary arteries and heart function



Cardiac MRI showed no structural heart disease or infiltrative cardiomyopathy, indicating that the heart failure is likely due to Bevacizumab-induced cardiotoxicity. The summary of the diagnostic findings is presented in **Table 3.**

## **Table 3:** Summary of Diagnostic Findings

|  |  |
| --- | --- |
| Investigation | Findings |
| Electrocardiogram (ECG) | Sinus rhythm, PVCs, Left anterior Fascicular block |
| Telemetry | PVCs,9 runs of NSVT |
| Chest X-Ray | Enlarged cardiac silhouette and blunting of bilateral costophrenic angles |
| Transthoracic Echocardiogram (TTE) | Severe LV dysfunction (EF <15%), concentric hypertrophy, moderate mitral and tricuspid regurgitation |
| Cardiac Catheterization | No significant coronary artery disease or ischemic changes were observed |
| Cardiac MRI | No structural heart disease or infiltrative cardiomyopathy |

In light of the development of CHF, the patient was initiated on guideline-directed medical therapy (GDMT), including beta-blockers, angiotensin-converting enzyme inhibitors (ACEi), aldosterone antagonists, and diuretics. Bevacizumab was promptly discontinued.

# Outcome and Follow-up

The patient showed significant clinical improvement following treatment, as evidenced by a notable increase in ejection fraction from baseline. The patient was followed up four weeks later and remained clinically stable with sustained improvement in ejection fraction.

# Discussion

Bevacizumab is a monoclonal antibody that inhibits Vascular Endothelial Growth Factor A (VEGF-A) and is widely used to treat various malignancies. Despite its high efficacy as a therapeutic agent, bevacizumab is associated with a range of cardiovascular complications, which require careful monitoring during treatment (7) (8). This case adds to the limited literature on Bevacizumab-associated Cardiotoxicity. Also, it underscores the importance of timely diagnosis and managing congestive heart failure (CHF) in patients on this chemotherapy drug.

The patient, in this case, developed congestive heart failure after being started on Bevacizumab for hepatocellular carcinoma (HCC). Bevacizumab’s side effect profile can be explained by its mechanism of action. It is a monoclonal antibody that binds and inhibits Vascular Endothelial Growth Factor A, which plays a significant role in angiogenesis in cancer cells, both physiologically and pathologically. Doing so can cause endothelial dysfunction, increasing the risk of thromboembolic events, bleeding, and wound healing. Inhibiting VEGF also causes an increase in vascular permeability, which can, in turn, cause proteinuria. Additionally, inhibition of VEGF-induced vasodilation leads to an increase in vascular resistance and, ultimately, hypertension. Cardiac dysfunction is primarily caused by increased afterload due to uncontrolled hypertension leading to Left Ventricular Hypertrophy (9). Additionally, the loss of cardiac angiogenesis negatively affects cardiac growth and contractile function due to the inhibition of VEGF, furthers Cardiac dysfunction from hypertrophy to CHF

It is important to note that specific individuals may be at a higher risk of developing cardiovascular toxicity due to certain underlying predisposing factors in addition to receiving Bevacizumab therapy (10). These can include age >65, smoking, hypertension, and prior history of cardiovascular disease. Risk factors associated explicitly with CHF risk include individuals having a specific tumor type and the amount of Bevacizumab they receive during their treatment course. The latency period before severe cardiotoxicity manifests clinically remains undefined in the literature and warrants further investigation (11).

Therefore, it is critical for patients who receive chemotherapeutic drugs with potential cardiotoxicity to have intensive follow-ups with vigilant monitoring for the development of any cardiovascular symptoms. This also highlights the importance of patient education on symptoms of CHF, which can prompt them to see their provider early and prevent future morbidity.

# Conclusion

This case underscores the significant cardiovascular risks of Bevacizumab in patients with hepatocellular carcinoma, including cardiomyopathy and left ventricular dysfunction. Early recognition, timely discontinuation of Bevacizumab, and guideline-directed medical therapy are critical for mitigating these risks. Integrating cardio-oncology approaches with vigilant monitoring and proactive management is essential to minimize cardiotoxicity and improve patient outcomes and quality of life.

# Key Clinical Message

Early recognition and intervention are critical in bevacizumab-induced cardiomyopathy. Given the uncertain latency period, serial TTE and EF monitoring are essential throughout and after therapy. Vigilance is paramount, particularly in high-risk patients—those receiving higher cumulative doses, specific tumor types, age >65, smoking history, hypertension, or prior cardiovascular disease.

# Acknowledgments

None

# Declarations

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Informed Consent

The author confirms that written informed consent was obtained from the patient using the Oxford University Press Patient Consent Form.

## Ethics Approval

This study did not require specific ethics approval as it is a case report.

## Funding

This work was supported by the Qatar National Library for Open Access.

## Data Availability Statement

The datasets of this study are available in the **case report and supplementary materials**. Additional data can be provided upon reasonable request from the corresponding author.

## Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used Grammarly to ensure a formal tone, improve rephrasing, and correct punctuation. After using this tool, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

# Guarantor

Mohammad Hamza bin Abdul Malik

# Figure Legends

## **Figure 1:** Electrocardiogram (ECG) of the patient demonstrating a left anterior fascicular block (LAFB)

## **Figure 2:** Electrocardiogram (ECG) of the patient demonstrating premature ventricular complexes (PVCs)

## **Figure 3:** Normal cardiac catheterization showing no abnormalities in coronary arteries and heart function

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