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## A Young Patient with Hyperhomocysteinemia Developed Ischemic Stroke, Hypertrophic Cardiomyopathy, and CKD: A Case Report

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### Abstract

Hyperhomocysteinemia, a metabolic disorder with elevated plasma homocysteine levels, contributes to vascular disease, atherosclerosis, and increases the risk of ischemic stroke due to endothelial dysfunction and prothrombotic state. A 34-year-old male with hypertension presented with right hemiparesis and expressive aphasia. Diagnostic imaging revealed claudication of the left middle cerebral artery and internal carotid artery, leading to a malignant left MCA stroke. Despite a dose of tissue plasminogen activator and mechanical thrombectomy, the patient required surgical intervention due to rising intracranial pressure. He was operated through hemicraniectomy and postoperatively in a neuro-intensive care unit. Despite the lesions fading, the patient required long-term rehabilitation. This case highlights the importance of early diagnosis, interprofessional team approach, and proper rehabilitation plans for the best outcome.

### Keywords

Hyperhomocysteinemia; Renal dysfunction; Ischemic stroke; Atherosclerosis; Neurocritical care; Multidisciplinary Approach.

## Introduction

Hyperhomocysteinemia, a pathological state that involves high plasma homocysteine concentration. Homocysteine is a sulfur containing amino acid which is an intermediate product in the metabolism of methionine [1]. It is normally metabolized via two primary pathways: as remethylation process to methionine is dependent on folate and vitamin B12 and transsulfuration to cysteine is accomplished with vitamin B6. Lack of these vitamins or genetic variation in the enzymes cause Hyperhomocysteinemia [2,3].

Hyperhomocysteinemia is a condition that results in vascular diseases and ischemic strokes through endothelial dysfunction, oxidative stress and pro thrombotic state [4, 5]. It favours blood clot formation and atherosclerosis – a process through which fatty deposits accumulate on the vascular walls. Reactive oxygen species (ROS) are also formed and results in increased oxidative stress and inflammation. Inflammation within vascular walls also plays a role to the progression of atherosclerosis and creation of a clot [6].

High homocysteine levels are known to affect the integrity of the blood brain barrier BBB leading to tissue loss. This may lead to several problems for a patient including increased afterload, CAD, oxidative stress, myocardial damage, prothrombotic state, hypertension, and impaired myocardial perfusion [7, 8]. Hypertrophy also induces endothelial dysfunction and blunts blood vessel dilation and this has the probable effect of making vascular resistance worse in hypertrophic cardiomyopathy patients. High homocysteine levels have been positively associated with atherosclerosis which leads to coronary artery disease (CAD) that results in reduced blood supply to the heart muscle and evokes chest pains and irregular heartbeat [9, 10]. Another possible negative effect of hyperhomocysteine is oxidative stress that can be a threat to the myocardial tissue aggravating hypertrophy and fibrosis in HCM [11].

Hyperhomocysteinemia in hypertrophic cardiomyopathy (HCM) increases the risk of stroke or systemic embolism due to its hypercoagulable state [12]. It is associated with hypertension and left ventricular hypertrophy, a characteristic of HCM [13]. Homocysteine-induced endothelial dysfunction can hinder coronary microcirculation, leading to decreased oxygen demand, myocardial ischemia, chest pain, and increased arrhythmia risk in HCM patients [14,15].

Hyperhomocysteinemia, can lead to renal artery atherosclerosis and decreased kidney function, contributing to chronic kidney disease (CKD). This condition can also cause glomerular alterations, increased oxidative stress, inflammation, blood pressure, renal fibrosis, and decreased Hcy clearance. The kidneys are responsible for removing homocysteine from the blood, but when kidney disease progresses, the clearance of homocysteine is impaired, increasing levels and damaging the kidney further.

Homocysteine autooxidation generates reactive oxygen species (ROS), causing lipid and protein oxidation and DNA injury, leading to atherosclerosis, thromboembolic events, ischemic stroke, cardiovascular diseases, and CKD.

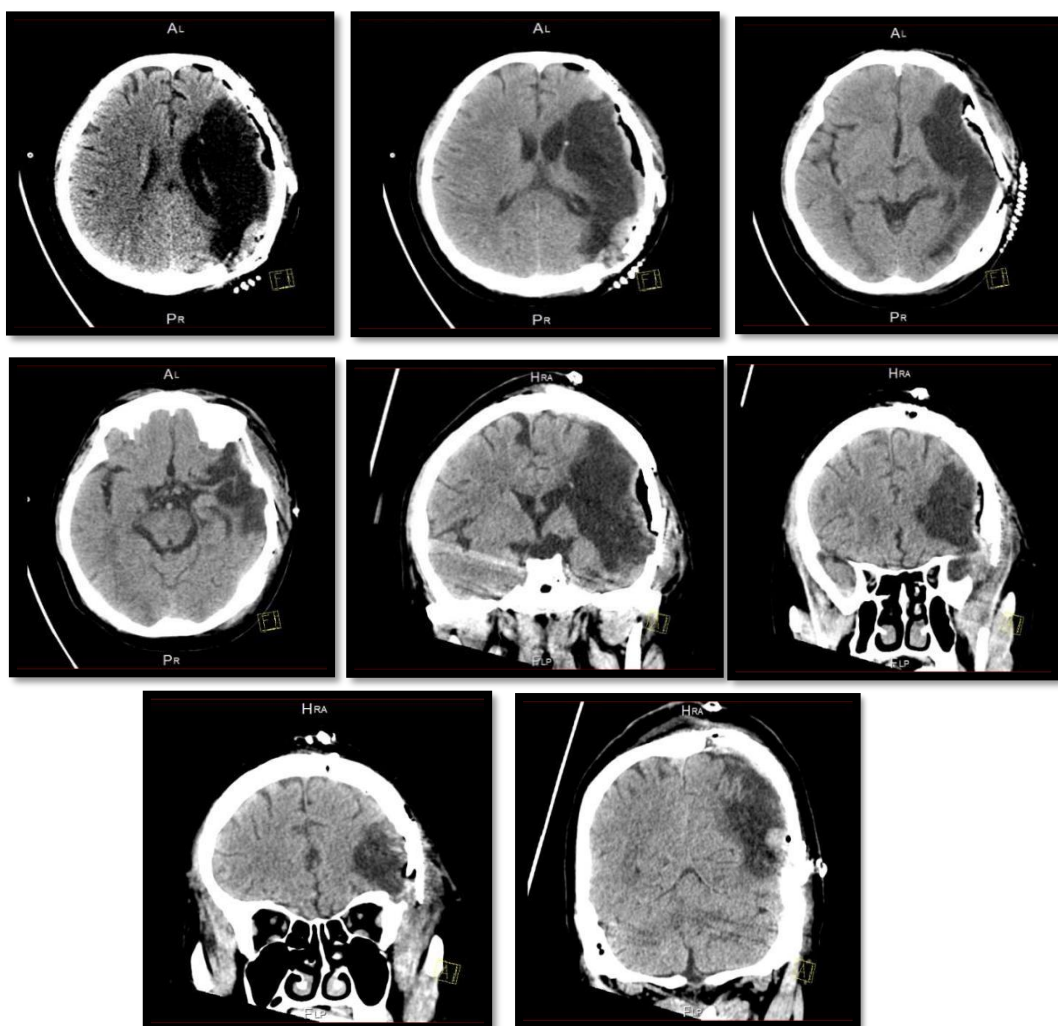
This case report aimed to analyze the association between hyperhomocysteinemia and multi-organ dysfunction, highlighting its role in stroke, cardiovascular complications, and chronic kidney disease. It emphasizes the need for a multidisciplinary approach for optimal patient outcomes.

### Case presentation

A 34-year-old male with a prior history of hypertension presented to the emergency department on May 30, 2024, with an acute onset of right-sided weakness and difficulty speaking. His initial National Institutes of Health Stroke Scale (NIHSS) score was 11.

### Clinical Findings

Upon admission, the patient's diastolic blood pressure was recorded at 110 mmHg. A computed tomography (CT) scan of the head revealed no acute hemorrhage. However, a CT angiogram demonstrated occlusion of the left M1 and M2 segments of the middle cerebral artery (MCA) and the left internal carotid artery (ICA), as depicted in (Figure 1).



**Figure:1** CT angiogram: left M1 and M2 segments of the middle cerebral artery (MCA) and the left internal carotid artery (ICA), confirming significant vascular compromise.

Blood pressure was managed with a total of 60 mg of labetalol followed by a nicardipine infusion. Despite the administration of tissue plasminogen activator (tPA) in the emergency room, attempts at mechanical thrombectomy were unsuccessful due to the inability to catheterize the left ICA.

### **Initial Examination**

The initial neurological examination revealed expressive aphasia, right lower extremity weakness, and right upper extremity weakness.

### **Diagnostic Assessment**

Further investigations indicated multi-organ impairment, including renal dysfunction, cardiomyopathy, and cerebral ischemia. Laboratory findings showed impaired complement levels, elevated erythrocyte sedimentation rate (ESR), increased beta-2 microglobulin, and raised kappa and lambda light chains. Additionally, brain natriuretic peptide (BNP) levels were significantly elevated.

The patient's elevated homocysteine levels pointed to Hyperhomocysteinemia as a potential underlying cause of his multi-organ dysfunction. This biochemical abnormality likely contributed to endothelial damage, promoting atherosclerosis and thromboembolism.

### **Neurocritical Care**

The patient was admitted to the neuro-intensive care unit (ICU). Due to worsening intracranial pressure, he underwent a left hemicraniectomy on May 31, 2024.

The patient was diagnosed with various conditions including right-sided weakness, malignant left MCA stroke, post-surgical decompression, tandem extra cranial left ICA occlusion, unsuccessful mechanical thrombectomy, ischemic stroke, hypertension, acute kidney injury, dysphagia, postcraniectomy, Stage 1 chronic kidney disease, left atrium disorder, pre-diabetes, Hyperhomocysteinemia, other hyperlipidemia, and hypertrophic non-obstructive cardiomyopathy.

### **Treatment with Management**

Following a hemicraniectomy, the patient's condition stabilized in the neuro ICU, but significant neurological deficits remained. On July 9, 2024, the patient was transferred to a rehabilitation center in Al Ain, where a multidisciplinary approach was implemented to restore functional independence. The plan included intensive inpatient rehabilitation, a multidisciplinary team approach, strict monitoring, nutritional support for Hyperhomocysteinemia, prediabetes, and CKD, skin care and wound care protocols, and routine speech-language pathology assessments. The patient's medication regimen included Amlodipine, Aspirin, Atorvastatin, Carvedilol, Empagliflozin, Heparin, Hydralazine, Movicol, Sennosides, and Sertraline.

### **Discussion**

This case highlights the connection between hyperhomocysteinemia and multi-organ dysfunction, with hyperhomocysteinemia contributing to ischemic stroke and cardiovascular disease. High homocysteine levels can cause endothelial dysfunction, oxidative stress, and prothrombotic states, leading to vascular disease. The patient's creatinine levels and GFR indicate CKD, which has a strong relationship with

cardiovascular disease and may worsen hyperhomocysteinemia. This progressive condition often leads to hypertrophic cardiomyopathy, which can lead to heart failure and arrhythmias. Therefore, hyperhomocysteinemia and CKD are closely related. Its treatment involves identifying root causes like vitamin deficiencies and prescribing effective drugs, focusing on extensive rehabilitation for individual treatment plan.

The case of a 34-year-old male demonstrates the complexity of managing acute ischemic stroke, highlighting the challenges posed by significant comorbidities. The patient, initially presenting with right-sided weakness and expressive aphasia, with an NIHSS score of 11, was diagnosed with a moderate to severe stroke. The CT angiogram revealed a critical occlusion of the left M1 and M2 segments of the middle cerebral artery and left internal carotid artery, necessitating urgent intervention [16, 17].

A stroke patient was treated with tissue plasminogen activator, but mechanical thrombectomy was unsuccessful due to catheterization limitations [18]. Increased pressure from cerebral ischemia led to left hemicraniectomy, a life-saving procedure, but left the patient with neurological deficits, highlighting the limitations of Large Vessel Occlusion management [19, 20].

The patient's condition was complicated by multi-organ impairments such as renal dysfunction, cardiomyopathy, and hyperhomocysteinemia. Elevated kappa and lambda light chain levels, increased ESR, and beta-2 microglobulin suggest an inflammatory or hematological disorder [21], potentially impacting stroke severity and patient prognosis [22-24]. Hyperhomocysteinemia, characterized by elevated homocysteine levels, is a significant risk factor for stroke and other cardiovascular events due to its role in endothelial dysfunction and atherosclerosis [25, 26]. It can lead to thromboembolism by exacerbated atherosclerotic changes and endothelial damage, potentially causing large vessel occlusions, as seen in a stroke patient [27].

The patient's cardiovascular profile, including hypertension and (Hypertrophic Non-Obstructive Cardiomyopathy) HNCM, complicates the clinical picture, with hypertension likely playing a central role in the malignant left MCA stroke [28, 29]. However, the use of labetalol and nicardipine for blood pressure management was effective, but persistent high diastolic pressure suggests hypertension control difficulties, possibly linked to HNCM and other cardiovascular abnormalities [30, 31].

While the patient's care transitioned from acute to long-term management of chronic conditions, requiring a multidisciplinary approach in a rehabilitation center to address residual deficits like dysphagia and motor impairments. Speech-language pathology assessments are crucial for patients with expressive aphasia and dysphagia, common complications after a significant stroke [32, 33].

The patient's condition was highly complex, requiring a comprehensive medication regimen including antihypertensives like Amlodipine and Carvedilol for blood pressure control and anticoagulants like Aspirin and Heparin for thromboembolic prevention [34, 35]. The use of Atorvastatin targets hyperlipidemia, while Empagliflozin targets prediabetes and CKD, indicated to reduce ongoing

cardiovascular and renal risks [36, 37]. Movicol and Sennosides were used to manage constipation, a common issue in patients with reduced mobility and those on multiple medications [38], while Sertraline addressed potential post-stroke depression, which is a frequent complication in such cases [39-41].

### Limitations

Current imaging and thrombectomy techniques face limitations in treating Hyperhomocysteinemia and multi-organ dysfunction patients, presenting challenges in treatment and management, and long-term outcomes and patient-specific factors need evaluation.

### Conclusion

Hyperhomocysteinemia significantly affects the brain, heart, and kidneys, and its interplay with comorbidities like hypertension and hypertrophic cardiomyopathy makes acute ischemic stroke management complex. The patient's large vessel occlusions and complications highlight the need for early intervention and comprehensive management strategies. A multidisciplinary approach is crucial, addressing both acute stroke symptoms and underlying metabolic and vascular abnormalities. Rehabilitation and ongoing care in a specialized setting are essential for maximizing recovery and improving quality of life.

### Recommendations

Further research is needed to understand hyperhomocysteinemia's pathophysiological mechanisms and develop effective management strategies for patients, emphasizing the need for holistic patient care involving medical and rehabilitative interventions.

### References

- Zaric BL, Obradovic M, Bajic V, Haidara MA and Jovanovic M et al. (2019) Homocysteine and hyperhomocysteinemia. *Curr Med Chem.* 26(16): p. 2948-2961.
- Rehman T, Shabbir MA, Muhammad I-U-R, Manzoor MF and Ahmed N et al. (2020) Cysteine and homocysteine as biomarker of various diseases. *Food Sci Nutr.* 8(9): p. 4696-4707.
- Kožich V, Morris AA, and Blom HJ. (2022) Disorders of sulfur amino acid metabolism, in *Inborn metabolic diseases: diagnosis and treatment.* Springer. p. 407-422.
- Eldibany MM. and Caprini JA. (2013) Hyperhomocysteinemia: an overview. *Pharm Globa.* 4(5): p.1.
- Faraci FM and Lentz SR. (2004) Hyperhomocysteinemia, oxidative stress, and cerebral vascular dysfunction. *Stroke.* 35(2): 345-47.
- Li S, Li G, Luo X, Huang Y. (2021) Endothelial dysfunction and hyperhomocysteinemia-linked cerebral small vessel disease: underlying mechanisms and treatment timing. *Front Neurol.*12:736309
- Tawfik A, Elsherbiny NM, Zaidi Y and Rajpurohit P. (2021) Homocysteine and age-related central nervous system diseases: role of inflammation. *Inte j Mol Sci.* 22(12):6259.
- Beard Jr, R.S., J.J. Reynolds, and S.E. Bearden, Hyperhomocysteinemia increases permeability of the blood-brain barrier by NMDA receptor-dependent regulation of adherens and tight junctions. *Blood, The Journal of the American Society of Hematology,* 2011. 118(7): p. 2007-2014.
- Tsigkou, V., et al., Molecular mechanisms and therapeutic implications of endothelial dysfunction in patients with heart failure. *International Journal of Molecular Sciences,* 2023. 24(5): p. 4321.

10. Drera, A., et al., Endothelial Dysfunction in Heart Failure: What Is Its Role? *Journal of Clinical Medicine*, 2024. 13(9): p. 2534.
11. Gogiraju, R., M.L. Bochenek, and K. Schäfer, Angiogenic endothelial cell signaling in cardiac hypertrophy and heart failure. *Frontiers in cardiovascular medicine*, 2019. 6: p. 20.
12. Liu, L., et al., Thromboembolism in patients with hypertrophic cardiomyopathy. *International Journal of Medical Sciences*, 2021. 18(3): p. 727.
13. Houston, B.A. and G.R. Stevens, Hypertrophic cardiomyopathy: a review. *Clinical Medicine Insights: Cardiology*, 2014. 8: p. CMC. S15717.
14. Cheng, Z., et al., Hypertrophic cardiomyopathy: from phenotype and pathogenesis to treatment. *Frontiers in cardiovascular medicine*, 2021. 8: p. 722340
15. Allbritton-King, J.D. and G. García-Cardena, Endothelial cell dysfunction in cardiac disease: driver or onsequence? *Frontiers in Cell and Developmental Biology*, 2023. 11: p. 1278166.
16. Herpich, F. and F. Rincon, Management of acute ischemic stroke. *Critical care medicine*, 2020. 48(11): p. 1654-1663.
17. Phipps, M.S. and C.A. Cronin, Management of acute ischemic stroke. *Bmj*, 2020. 368.
18. Zivelonghi, C. and S. Tamburin, Mechanical thrombectomy for acute ischemic stroke: the therapeutic window is larger but still "time is brain". *Functional neurology*, 2018. 33(1): p. 5.
19. Lin, J. and J.A. Frontera, Decompressive hemicraniectomy for large hemispheric strokes. *Stroke*, 2021. 52(4): p. 1500-1510.
20. Fotakopoulos, G., et al., Role of decompressive craniectomy in the management of acute ischemic stroke. *Biomedical Reports*, 2024. 20(2): p. 1-10.
21. Gudowska-Sawczuk, M. and B. Mroczko, Free light chains  $\kappa$  and  $\lambda$  as new biomarkers of selected diseases. *International Journal of Molecular Sciences*, 2023. 24(11): p. 9531.
22. Tsagalis, G., et al., Renal dysfunction in acute stroke: an independent predictor of longterm all combined vascular events and overall mortality. *Nephrology Dialysis Transplantation*, 2009. 24(1): p. 194-200.
23. Miwa, K., et al., Etiology and outcome of ischemic stroke in patients with renal impairment including chronic kidney disease: Japan Stroke Data Bank. *Neurology*, 2022. 98(17): p. e1738-e1747.
24. Sulaiman, M.M., et al., Role of renal dysfunction as a prognostic factor in acute stroke patients at a tertiary hospital in northeastern Nigeria. *Saudi Journal of Kidney Diseases and Transplantation*, 2021. 32(1): p. 199-203.
25. Pinzon, R.T., V.O. Wijaya, and V. Veronica, The role of homocysteine levels as a risk factor of ischemic stroke events: A systematic review and meta-analysis. *Frontiers in Neurology*, 2023. 14: p. 1144584.
26. Niazi, F., et al., Frequency of homocysteinemia in young ischemic stroke patients and its relationship with the early outcome of a stroke. *Cureus*, 2019. 11(9).
27. Rabelo, N.N., et al., Homocysteine is associated with higher risks of ischemic stroke: A systematic review and meta-analysis. *PloS one*, 2022. 17(10): p. e0276087.
28. Treadwell, S.D. and B. Thanvi, Malignant middle cerebral artery (MCA) infarction: pathophysiology, diagnosis and management. *Postgraduate medical journal*, 2010. 86(1014): p. 235-242.
29. Masuda, H., et al., An unusual case of malignant hypertension causing stroke in a young adult. *Annals of Vascular Surgery-Brief Reports and Innovations*, 2022. 2(1): p. 100052.
30. Liu-DeRyke, X., et al., A comparison of nicardipine and labetalol for acute hypertension management following stroke. *Neurocritical care*, 2008. 9: p. 167-176.
31. Abdullah, A. and M.K.M. Yusof, Labetalol: a brief current review. *Pharmacophore*, 2019. 10(6-2019): p. 50-56.
32. Richardson, C.R., et al., Advances in rehabilitation for chronic diseases: improving health outcomes and function. *Bmj*, 2019. 365.

33. Rehabilitation for chronic conditions. 2017
34. Tedesco, M.A., F. Natale, and R. Calabrò, Effects of monotherapy and combination therapy on blood pressure control and target organ damage: a randomized prospective intervention study in a large population of hypertensive patients. *The Journal of Clinical Hypertension*, 2006. 8(9): p. 634-641.
35. Del Mauro, J.S., et al., Effects of carvedilol or amlodipine on target organ damage in LNAME hypertensive rats: their relationship with blood pressure variability. *Journal of the American Society of Hypertension*, 2017. 11(4): p. 227-240.
36. McIver, L.A. and M.S. Siddique, Atorvastatin. 2017.
37. Green, J.B., et al., Design of the COmbination effect of FInerenone anD EmpaglifloziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint study (CONFIDENCE). *Nephrology Dialysis Transplantation*, 2023. 38(4): p. 894-903.
38. Portalatin, M. and N. Winstead, Medical management of constipation. *Clinics in colon and rectal surgery*, 2012. 25(01): p. 012-019.
39. Stuckart, I., et al., Sertraline for Functional Recovery After Acute Ischemic Stroke: A Prospective Observational Study. *Frontiers in neurology*, 2021. 12: p. 734170.
40. Bai, Z.-f. and L.-y. Wang, Efficacy of sertraline for post-stroke depression: A systematic review protocol of randomized controlled trial. *Medicine*, 2019. 98(16): p. e15299.