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The Importance of Blood Pressure Control in End-Stage Renal Disease: A Case Report of Intracranial Hemorrhage

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ABSTRACT

Introduction: End-Stage Renal Disease (ESRD) is a growing global health concern. ESRD often presents with high blood pressure that is unresponsive to medication. Long-standing high blood pressure is the primary cause of intracranial hemorrhage. It is more likely to occur in ESRD patients. Case Illustration: A 69-year-old woman was brought to the emergency room because of unconsciousness four hours earlier. She had a sudden severe headache before that. No history of trauma. Her consciousness was poor (GCS E1M2V1) and her blood pressure was high (213/78 mmHg) in the emergency unit. Head CT revealed intracerebral, intraventricular, and subarachnoid hemorrhages with a total volume of 81 cc and midline shift. The patient had been on dialysis twice a week for six years. She had uncontrolled hypertension said to routinely take antihypertensive drugs independently. Last year's dialysis visits showed high blood pressure, with a mean of 187/72 mmHg (224/112-166/51 mmHg). Given her complex condition, she underwent conservative therapy and died on the third day of treatment. Conclusion: ESRD patients are at high risk of intracranial hemorrhage. It is crucial to closely monitor blood pressure during dialysis visits. ESRD with intracranial hemorrhage has a poor prognosis, emphasizing the importance of preventive care.

Keywords: Blood pressure control, long-standing hypertension, end-stage renal disease, intracranial hemorrhage

Introduction

Stroke represents the second leading cause of mortality on a global scale. Approximately 20% of all strokes are hemorrhagic. It is related to a high mortality rate and serious morbidity (Feigin et al., 2021; Feigin et al., 2009). Hemorrhagic stroke is bleeding in the brain caused by a ruptured blood vessel. The rupture of the vessels results in compression and hypoxic conditions in the distal area, which leads to brain cell death due to low oxygenation (Mudjihartini, 2017). Several risk factors can contribute to the hemorrhagic stroke. Modifiable risk factors include hypertension, abnormal lipid profiles, cigarette smoking, and medications including anticoagulants, antiplatelets, and sympathomimetic drugs. Other risk factors considered non-modifiable include advanced age, male gender, and end-stage renal disease (ESRD) (An et al., 2017).

ESRD patients on renal replacement therapy (dialysis) have an elevated risk of hemorrhagic stroke that is up to tenfold higher than the general population. ESRD has been demonstrated to alter endothelial function, accelerate atherosclerosis, impair platelet function, and disturb cerebral autoregulation. Furthermore, the use of heparin during dialysis has been shown to increase the risk of

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hemorrhagic stroke. Patients with chronic kidney disease (CKD) have also been observed to have higher mortality and poor functional outcomes following a stroke (Ghoshal & Freedman, 2019).

Case Illustration

A 69-year-old female was brought to the emergency unit after a four-hour period of unresponsiveness. A sudden onset of severe headache preceded the loss of consciousness. The patient denied a history of traumatic injury. The Glasgow Coma Scale score was recorded as E1V2M1. On presentation to the emergency unit, the blood pressure was recorded at 213/78 mmHg, her heart rate at 83 beats per minute, and her respiratory rate at 28 breaths per minute with a regular rhythm. The physical examination yielded the findings of anisocoria, positive pupillary reflexes, and positive Babinski signs. Laboratory results demonstrated elevated ureum (73 mg/dL), high creatinine (5.22 mg/dL), high glucose levels (331 mg/dL), and favorable lipid profiles. A non-contrast head computed tomography (CT) scan revealed the presence of an intracerebral hemorrhage in the right temporooccipital lobe, accompanied by intraventricular hemorrhage (total volume 81 mL), subarachnoid hemorrhage, and a midline shift of 0.9 cm (Figure 1).

The patient was diagnosed with ESRD and had been undergoing dialysis for six years. The patient's dialysis regimen entailed two dialysis sessions of 4–4.5 hours each, conducted on Wednesdays and Saturdays. These sessions utilized an AV shunt as vascular access and a continuous infusion of unfractionated heparin (UFH) at a dosage of 1.000 IU per hour per session. The patient had been anuric for five years. Additionally, she had a history of uncontrolled hypertension and diabetes mellitus for seven years. A summary of the patient's blood pressure during dialysis visits over the past year is presented in Table 1. The data showed that her blood pressure remained persistently elevated. The patient had not previously expressed any concerns or symptoms during her dialysis sessions over the past year. The patient's antihypertensive regimen consisted of amlodipine 10 mg/day and irbesartan 300 mg/day, obtained without a prescription. No medication for diabetes mellitus was administered.

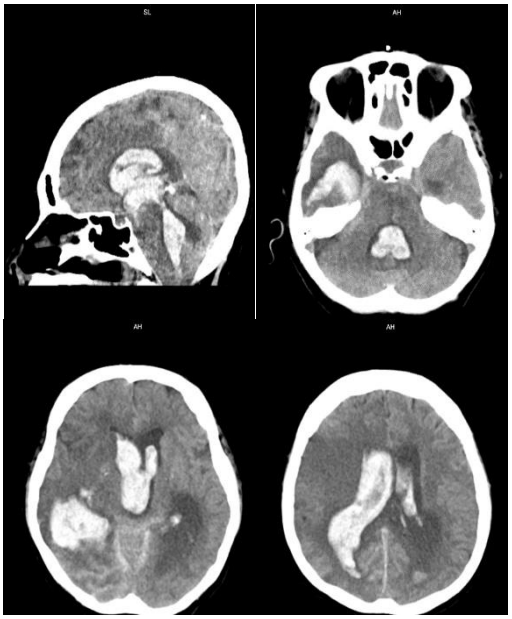

Figure 1. Non-contrast head CT scan

The patient was transferred to the intensive care unit and intubated to maintain an open airway. Given the patient's complex condition, a conservative management approach was ultimately selected. The patient was administered nicardipine via a continuous infusion at titrated doses, tranexamic acid 1gram tid, citicolin 1 gram bid, cefoperazone-sulbactam 1 gram bid, omeprazole 40 mg bid, and

phenytoin 200 mg every 24 hours. On the third day of admission, the patient experienced brainstem death and subsequently expired before dialysis could be performed.

Table 1. Blood pressure records within the last 1 year during dialysis visits

Range	Systolic BP	Diastolic BP
The highest	224	112
The lowest	166	51
Average	187	72

BP: blood pressure

Discussion

A comprehensive evaluation of patients with CKD who present to the emergency department with altered consciousness is essential to determine the underlying cause and establish a definitive diagnosis. In patients with CKD, altered consciousness is frequently attributable to metabolic disorders, including uremic state, electrolyte imbalance, or impaired glucose levels. Nevertheless, it is also conceivable that the loss of consciousness is attributable to an intracranial hemorrhage (Arnold et al., 2016). Therefore, a neurological examination must be performed.

CKD is an independent risk factor for the development of stroke. Patients with ESRD on renal replacement therapy (dialysis) have a four- to tenfold increased risk of stroke compared to the population. In addition, the risk of stroke increases sevenfold during the first year of dialysis (Arnold et al., 2016; Dad & Weiner, 2015; Murray et al., Toyoda & Ninomiya, 2014).

CKD patients are more likely to experience hemorrhagic stroke due to endothelial dysfunction, thrombocyte dysfunction, and the heparin used during dialysis. Thrombocyte and endothelial dysfunction has been identified in the uremic state, including changes in membrane fluidity and inhibition of nitric oxide synthase by NG-monomethyl-L-arginine (L-NMMA), which then inhibits thrombocyte aggregation. Additionally, there is monocyte adhesion to the endothelial cell, hyporesponsiveness of uremic platelets, and abnormal platelet adhesion (Jha et al., 2018; Roumeliotis et al., 2020). Anticoagulation is important for dialysis, with UFH being the most commonly utilized anticoagulant. UFH is a sulfate polysaccharide with an antithrombin binding and activation component. This inhibits thrombin and factor Xa, thereby stopping the coagulation pathway and promoting anticoagulation. The potential risks associated with the utilization of UFH encompass bleeding, heparin-associated thrombocytopenia, hyperkalemia, and anaphylaxis. Heparin is administered by continuous infusion at a rate of 1000 IU/hour (Shen et al., 2012).

It should be noted that although the patient in this case had received heparin at the correct dose during dialysis, long-term heparin use could not be ruled out as a potential risk factor for bleeding. Intracranial hemorrhage is typically the result of ruptured vessels that have been subjected to prolonged hypertension. The affected arteries exhibit a notable deterioration of the media and smooth muscle. Fibrinoid subendothelial necrosis with microaneurysms and focal dilatation may occur in some patients (An et al., 2017). Meanwhile, CKD and hypertension are tightly linked conditions, with persistent hypertension can result in decreased renal function, and a gradual reduction in renal function can lead to increased blood pressure (Ku et al., 2019). In CKD patients, blood pressure should be lowered to a level of ≥140/90 mmHg and treated to maintain a goal of <130/80 mmHg (or <140/80 mmHg in elderly patients). The risk of hemorrhagic stroke increases 2.3-fold in those with a systolic blood pressure of 160-179 mmHg exhibited a 2.12-fold increased risk, while those with SBP ≥180 mmHg demonstrated a 2.3-fold elevated risk (Du et al., 2019). The patient had a history of having blood pressure consistently above 160 mmHg during dialysis visits for the past year. This long-standing hypertension is regarded as the major contributor to the hemorrhagic stroke.

Diabetes is the leading cause of CKD requiring dialysis or kidney transplantation (Levin et al., 2017). The prevalence of CKD in diabetes is high, exceeding 25%. Diabetes is related with an elevated

risk of hemorrhagic stroke, with a relative risk of 1.38 (Muñoz-Rivas et al., 2016). Diabetes has been linked to the progression of pathological angiogenesis and endothelial dysfunction. In hyperglycemia state, the angiogenic response is increased, resulting in a reduction in the maturity of the vessel wall. This condition increases vascular leakage and is prone to bleeding (Ergul et al., 2014). Therefore, to reduce microvascular complications and improve survival, it is recommended that HbA1c be maintained at 6.5-8%. In the context of an acute condition, it is imperative to maintain plasma glucose levels below 180. The patient had a seven-year history of diabetes and was experiencing uncontrolled symptoms, as evidenced by a blood sugar level of 331 mg/dL on arrival to the emergency unit. Plasma glucose levels above the normal range are correlated with an elevated risk of poor prognosis and early mortality. Plasma glucose levels above normal are 1.87 times more likely associated with early mortality and worse prognosis (Chen et al., 2016; Lau et al., 2019).

The management of the hemorrhagic stroke in CKD patients presents a significant challenge. Patients with extensive bleeding greater than 30 mL are considered for surgical intervention. In this case, the patient exhibited low consciousness (GCS E1V2M1), significant bleeding (total volume 81 mL), and elevated intracranial pressure with a midline shift of 0.9 cm, which constituted a contraindication for surgical intervention (Bhaskar et al., 2017; Luzzi et al., 2019). The patient was treated with a conservative approach. Tranexamic acid, an antifibrinolytic lysine analog, was administered to reduce the bleeding time (Jha et al., 2018). In patients with intracranial hemorrhage, mannitol administration is beneficial in lowering intracranial pressure; however, in ESRD with anuria, it is contraindicated (Kim et al., 2023; Davenport, 2007; Davenport, 2008; Hirsch et al., 2012). Unfortunately, the patient did not respond favorably to treatment, resulting in brainstem death and demise before the initiation of dialysis on the third day of hospitalization.

Conclusion

In conclusion, ESRD patients are at high risk of intracranial hemorrhage. Monitoring of risk factors is essential to prevent hemorrhagic stroke. It is crucial to closely monitor blood pressure during dialysis visits. ESRD with intracranial hemorrhage has a poor prognosis, emphasizing the importance of the preventive care

Declaration of Interests

In conclusion, ESRD patients are at high risk of intracranial hemorrhage. Monitoring of risk factors is essential to prevent hemorrhagic stroke. It is crucial to closely monitor blood pressure during dialysis visits. ESRD with intracranial hemorrhage has a poor prognosis, emphasizing the importance of the preventive care

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