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ISCHEMIC STROKE AS A RARE PRESENTATION OF MULTIPLE MYELOMA IN A 69-YEAR-OLD FEMALE PATIENT

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Abstract: **Multiple myeloma (MM) is characterized by an abnormal rise in monoclonal immunoglobulins, accounting for around 10% of all hematologic malignancies. Individuals with MM face an elevated risk of both arterial and venous thrombosis, which is believed to result from a combination of patient comorbidities, the hypercoagulable state caused by the disease, and the effects of certain treatments. This case describes acute ischemic stroke as a presenting manifestation of MM. A 69-year-old female with a history of MM presented with loss of consciousness and right lateralization, suggesting acute ischemic stroke. We present a case of a 69-year-old female who was admitted with sudden loss of consciousness. Upon examination, she exhibited a GCS of E2V4M5 and neurological signs indicative of right lateralization. Initial laboratory results revealed mild anemia, leukopenia, and electrolyte imbalances, including moderate hypokalemia and hyponatremia. A CT scan of the brain on the day of admission revealed a subacute ischemic infarction in the left external capsule, cerebral atrophy, and mild hydrocephalus. After an extensive evaluation, common stroke etiologies were ruled out, resulting in a final diagnosis of cerebral infarction associated with MM. MM is a known risk factor for stroke due to chemotherapy, patient-related factors like advanced age and immobilization, and tumor-related factors such as increased plasma viscosity and a hypercoagulable state. The patient's clinical presentation and imaging findings emphasize the need for heightened awareness of stroke as a potential first manifestation of MM, particularly in older adults.**

Keywords: **acute ischemic stroke, multiple myeloma, thrombosis, hypercoagulability.**

I. INTRODUCTION

Multiple myeloma is a hematologic malignancy that arises from the proliferation of malignant plasma cells in the bone marrow. It is characterized by the excessive production of monoclonal immunoglobulins (M protein), which can lead to various complications such as anemia, hypercalcemia, osteolytic bone lesions, and renal dysfunction. Multiple myeloma accounts for approximately 10% of all hematologic malignancies and is predominantly found in older adults, with a peak incidence between the ages of 65 and 74.[1] In addition to these classical complications, patients with multiple myeloma are at increased risk of both venous and arterial thrombotic events. The hypercoagulable state in multiple myeloma is multifactorial, involving increased blood viscosity due to paraproteins, activation of coagulation factors, endothelial dysfunction, and secretion of pro-inflammatory cytokines.[2-3] This risk is further exacerbated by older age, immobilization, infection, and certain chemotherapeutic agents such as thalidomide and lenalidomide.[4]

Ischemic stroke is typically associated with traditional vascular risk factors such as hypertension, diabetes, dyslipidemia, and heart disease. However, several reports have shown that stroke can also occur as a complication of multiple myeloma, although this is rare and often under-recognized in clinical practice.[5] The presentation of stroke as an initial manifestation of multiple myeloma is unusual and can obscure the primary diagnosis and delay timely intervention.

Central nervous system involvement in multiple myeloma may occur through various mechanisms, including metabolic complications, drug toxicity, or vascular events such as stroke. Although rare, reports have documented stroke as an early presentation of multiple myeloma, even before a definitive diagnosis is established. A retrospective study by Costa et al. (2019) reported a notable prevalence of arterial thromboembolism, including stroke, in multiple myeloma patients, which is associated with increased short-term mortality.[5]

II. CASE-REPORT

A 69-year-old female presented to the Emergency Room of Wangaya Regional General Hospital, Denpasar, Bali, on April 8, 2025, with a chief complaint of sudden loss of consciousness two hours prior to admission. She also reported a decreased appetite for several days. The patient had been previously diagnosed with multiple myeloma in 2022 and had undergone six cycles of chemotherapy at RSUP Prof. IGNG Ngoerah Hospital in 2022 and another six cycles in 2025, though the treatment was incomplete. She also had a history of ORIF for a right supracondylar femur fracture in August 2022 at the same hospital. Additional comorbidities included coronary artery disease (CAD) and controlled hypertension.

Initial assessment revealed a fluctuating Glasgow Coma Scale (GCS) of E2V4M5. The patient appeared restless and unresponsive to verbal commands. Neurological examination showed right-sided hemiparesis, with no cranial nerve deficits and negative pathological reflexes.

Laboratory findings showed leukopenia (WBC 3.8), mild anemia (Hb 8.8), hematocrit of 26.2%, and severe hypokalemia (K+ 2.8 mmol/L). Non-contrast head CT scan revealed a subacute ischemic infarction in the left external capsule, with cerebral atrophy and mild hydrocephalus. No evidence of intracerebral hemorrhage or mass lesion was seen. Chest X-ray showed bilateral rib deformities, suspected to be due to osteolytic lesions of multiple myeloma, with an elevated left hemidiaphragm.

Based on clinical findings and investigations, the patient was diagnosed with ischemic stroke secondary to suspected septic and metabolic encephalopathy, multiple myeloma, mild anemia, multiple osteolytic lesions, congestive heart failure, CAD with complete right bundle branch block (RBBB), severe hypokalemia, and suspected pneumonia versus pneumonic-type pulmonary metastasis. Treatment included citicoline 2x500 mg IV, aspirin 80 mg peroral, and supportive management. From internal medicine fluids (NaCl 0.9%, D5, and Aminofluid in a 1:1:1 ratio), KCl 50 mEq drip, ceftriaxone 2 gr IV, ondansetron 3x4 mg IV, and lansoprazole 1x30 mg IV. From cardiology candesartan 1x8 mg peroral, spironolactone 1x25 mg peroral, and atorvastatin 1x10 mg peroral. Pulmonary management included oxygen therapy via nasal cannula (SpO2 >94%), acetylcysteine, and combivent nebulizer as needed.

Fig 1. Bilateral rib deformities suspected to be due to osteolytic lesions of multiple myeloma, with an elevated left hemidiaphragm.

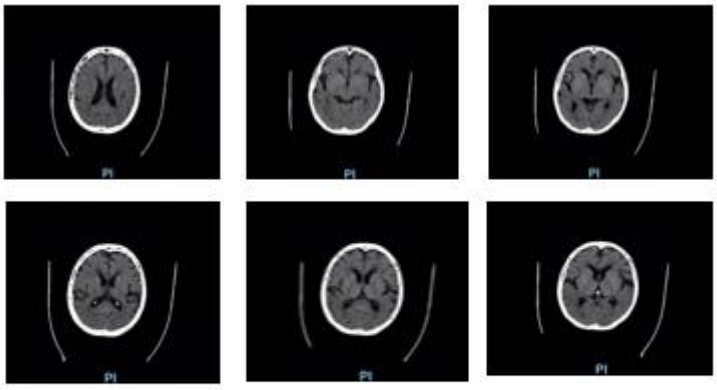

Fig 2. Non-contrast head CT scan showing a subacute ischemic infarction in the left external capsule, accompanied by cerebral atrophy and mild hydrocephalus.

III. DISCUSSION

Multiple myeloma is associated with an increased risk of both arterial and venous thrombosis through several pathophysiological mechanisms. The overproduction of monoclonal immunoglobulins increases blood viscosity, triggers platelet aggregation, and causes endothelial dysfunction, all of which collectively heighten thrombotic tendencies.[2-6]

In this patient, subacute ischemic stroke occurred in the context of active multiple myeloma with mild anemia and multiple osteolytic lesions, in the absence of classical vascular risk factors. This supports the possibility that stroke was a thrombotic

complication of multiple myeloma. A study by Kristinsson et al. (2022) reported that multiple myeloma patients have a 2–3 times higher risk of arterial thromboembolism than the general population, particularly within the first six months of diagnosis.[7] Other comorbidities, such as advanced age, suspected pneumonia, and severe hypokalemia, may have further worsened the patient's neurological status by impairing cerebral perfusion.[8] Although this patient was not receiving immunomodulatory agents, multiple myeloma itself has been shown to induce a procoagulant state through interactions between malignant plasma cells and the bone marrow microenvironment.[6]

Non-focal symptoms such as delirium at initial presentation can obscure stroke diagnosis, but this is commonly observed in lobar or subcortical strokes among elderly patients. Therefore, brain imaging is crucial in multiple myeloma patients presenting with altered mental status.[5,10] Lesions in the left external capsule, as observed in this case, are anatomically related to right-sided hemiparesis due to disruption of the corticospinal motor tract, consistent with the findings of Pasmanasari et al. on the impact of lesion location on motor function in ischemic stroke.[10]

Previous case reports have described stroke as an initial manifestation of multiple myeloma, even preceding the definitive diagnosis. A literature review by Zhou et al. (2021) highlighted the importance of considering multiple myeloma as an underlying cause of cryptogenic ischemic stroke in the elderly, particularly when hematological or radiological abnormalities are present.[9] In clinical practice, evaluating the possibility of multiple myeloma is essential. Basic laboratory tests such as ESR, total serum protein, and serum protein electrophoresis can offer early clues. If indicated, further assessments such as bone marrow aspiration and skeletal imaging may confirm the diagnosis and guide treatment.

IV. CONCLUSION

This case demonstrates that ischemic stroke can be an initial presentation of multiple myeloma, especially in elderly patients without traditional vascular risk factors. The cerebral infarction in this patient was most likely triggered by a hypercoagulable and hyperviscous state due to active multiple myeloma, compounded by risk factors such as advanced age, immobility, and electrolyte imbalance. These findings underscore the importance of considering hematologic malignancies as a potential etiology of stroke, particularly in cases with atypical or cryptogenic presentations. Timely diagnosis and multidisciplinary management are essential to prevent further complications and improve clinical outcomes.

Central nervous system involvement due to thromboembolic mechanisms in multiple myeloma remains rarely reported and may be easily overlooked, especially when neurological symptoms precede or occur outside the active phase of the disease. Thus, in elderly patients presenting with sudden altered consciousness and no clear vascular risk profile, multiple myeloma should be included in the differential diagnosis, particularly in the presence of anemia, bone lesions, or suspicious laboratory findings.

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