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Atypical hemolytic uremic syndrome with complement factor I variant triggered by malignant hypertension in a patient with breast cancer: case report and review of the literature

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Introduction: Malignant hypertension (MHT) is a severe form of untreated hypertension, characterised by systolic blood pressure over 200 mmHg and diastolic pressure over 120 mmHg. The MHT is associated with a poorer prognosis and more severe consequences than common arterial hypertension. It is harmful for the endothelium, causing microcirculation damage, which leads to multi-organ ischemic dysfunction, affecting many organs, i.e., the kidneys, the heart, the brain, and the retina. This condition may trigger or accompany atypical hemolytic uremic syndrome (aHUS). We present diagnostic difficulties and therapeutic approach in a patient with MHT unmasking aHUS due to a complement factor I variant.

Case description: A 44-year-old woman with no previous medical history was admitted to a local emergency room with general malaise, dyspnea and one-week lasting hematuria. Physical examination revealed blood pressure 280/150 mmHg, pale skin, and oedema affecting the lower limbs. Laboratory tests showed severe normocytic anaemia, thrombocytopenia, schistocytosis, reticulocytosis, and elevated lactate dehydrogenase activity. Kidney function was poor – serum creatinine concentration (sCr) was 5.9 mg/dl, urinalysis was abnormal, active sediment with massive erythrocyturia and subnephrotic range of proteinuria were present. The Coombs' test was negative. Daily urine output was up to 3.5 l. Ultrasound ruled out urine obstruction, edematous renal parenchyma and renal artery stenosis. Brain computed tomography scan excluded intracranial bleeding. Echocardiography showed left ventricular hypertrophy. Hypertensive crisis was diagnosed, and antihypertensive treatment was administered with improvement.

Due to suspicion of aHUS patient was referred to our hospital for consideration of anti-complement therapy (anti-C5). Kidney biopsy revealed acute ischemic glomerulopathy without thrombotic microangiopathy (TMA) but with fibroelastosis. In the meantime, sCr decreased, so anti-C5 therapy was omitted and the patient was discharged home. Within a few months, kidney function improved. Genetic testing confirmed a pathogenic variant in CFI, indicating aHUS as the cause of kidney injury. Three years later, the patient was diagnosed with left breast invasive ductal carcinoma of no specific type, which did not trigger aHUS recurrence.

Conclusions: The MHT is a well-known trigger of aHUS. This case highlights the importance of early hypertension diagnosis and management to prevent complications such as MHT that might lead to aHUS in genetically predisposed patients.