A woman in her late 30s [exact age not stated] developed haemophagocytic lymphohistiocytosis (HLH) during treatment with lamotrigine for major depressive disorder.

The woman presented with fever, dark urine and debilitating myalgias for the last 2–3 days. Her febrile episodes were relapsing despite unspecified conservative treatment. Due to worsening of dark urine discoloration, she was admitted. Her medical history was significant for rheumatoid arthritis, which was in remission for >1 year and major depressive disorder which worsened recently requiring treatment modification to lamotrigine 2 weeks prior to the admission [dosage and route not stated]. RT-PCT of nasopharyngeal swab tested negative for COVID-19 on admission. Physical examination revealed inguinal and cervical lymphadenopathy. During hospital course, laboratory tests showed leucopenia, lymphopenia, thrombocytopenia and haemolytic anaemia. Hepatic function tests showed direct hyperbilirubinaemia and elevated liver enzymes. Renal function tests were within normal limits. Urinalysis showed large urine bilirubin with elevated urobilinogen. It was considered that dark urine could be secondary to urobilinogen overload due to haemolytic anaemia or hyperbilirubinaemia due to acute hepatitis. The initial differential diagnoses included cytokine storm in COVID-19, viral hepatitis or sepsis.

The woman immediately started receiving unspecified broad-spectrum antibacterials [antibiotics] and intravenous hydration. During the hospital course, she developed a patchy, non-itchy, erythematous, blanching maculopapular rash on the lower extremities and abdomen. Infectious workups were negative. A CT scan showed splenomegaly, hilar and subpectoral lymphadenopathy and sparse ground-glass opacities in the lung. At the time, macrophage activation syndrome and HLH were considered in differentials. The HLH workup was performed, including the bone marrow biopsy. She had elevated LDH, ferritin, triglycerides and soluble IL2 receptor level and low fibrinogen levels. The bone marrow biopsy showed trilineage haematopoiesis, haemophagocytosis and megakaryocytic hyperplasia. She was immediately treated with unspecified steroids given the history of rheumatoid arthritis. She fulfilled more than 5/8 criteria, the diagnosis of HLH was confirmed. The lamotrigine treatment was considered as inciting factor given the timing of symptoms onset and inactive rheumatoid arthritis for more than one year. The lamotrigine was already discontinued immediately after admission. She was treated with etoposide [VP-16] for up to 8 weeks as initial therapy and dexamethasone with tapering off within 8 weeks resulting in disease remission prior to the completion of 8 weeks of initial therapy. However, she developed ischaemic optic neuropathy due to anaemia requiring blood transfusion. Eventually, she had a good outcome. At 1-year follow-up visit, she remained in remission, but vision continued to have residual difficulties.

Velu D, et al. Lamotrigine-associated haemophagocytic lymphohistiocytosis (HLH) confounded with underlying rheumatoid arthritis. BMJ Case Reports 15: No. 3, Mar 2022. Available from. URL: http://doi.org/10.1136/bcr-2021-245835