Methylprednisolone/prednisone/tozinameran

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Haemophagocytic lymphohistiocytosis, treatment failure: 2 case reports

In a report, a 60-year-old man and a 32-year-old woman were described, who developed haemophagocytic lymphohistiocytosis following administration of COVID-19 vaccine tozinameran. Additionally, the man exhibited treatment failure to prednisone for haemophagocytic lymphohistiocytosis and the woman exhibited treatment failure to prednisone and methylprednisolone for haemophagocytic lymphohistiocytosis [*routed not stated; not all dosages stated*].

Patient 1: A 60-year-old man, who had a history of Barrett's esophagus, presented with slurred speech and altered mental status. He had received first dose of tozinameran [BNT162b2 Pfizer-BioNTech vaccine], and after 6 days he reported the symptoms. Initially, he experienced transient ischaemic attack, and eventually his symptoms progressively deteriorated over the next month with development of loss of appetite, delirium, fevers, drenching night sweats, unintentional weight loss and he became non-ambulatory. After presentation, RT-PCR tests were performed, which was negative for COVID-19 infection. Further infectious workup, rheumatologic workup and oncological workup were negative, and ruled out other causes of fever. He met 6/9 HLH criteria including a bone marrow biopsy that showed haemophagocytosis, and a diagnosis of haemophagocytic lymphohistiocytosis (HLH) secondary to tozinameran vaccine was made. The man was treated with prednisone 1 mg/kg for 5 days; however, his symptoms failed to improve (treatment failure), and his condition continued to deteriorate. Then, he started on HLH-directed therapy with dexamethasone and etoposide. After initiation of treatment, his speech, pancytopenia and ambulation significantly improved within 48 hours. Subsequently, he was discharged home, and he continued to improve in outpatient follow up. However, his HLH biomarkers worsen (worsening thrombocytopaenia, rising triglycerides, elevated ferritin) and symptoms (night sweats, malaise) relapse when he tapered off steroids. Then, he started treatment on cyclosporine without meaningful improvement. Therefore, he again re-initiated on steroids. For his neurological manifestations of HLH intrathecal methotrexate was considered. It was noted that his neurological symptoms rapidly improved after treatment with etoposide and steroids.

Patient 2: A 32-year-old woman with no prior history, received second dose of tozinameran [BNT162b2 Pfizer-BioNTech vaccine], and after 4 weeks presented with high fevers. It was noted that 52 days after first dose of vaccine she developed symptoms. She was briefly hospitalised at an outside hospital with hyperferritinaemia (35000 ng/mL), elevated transaminases and anaemia (haemoglobin 80 g/L). Rheumatological, oncological and infectious workups were negative. She received prednisone 50mg daily; however, her condition worsened with progression of fever (treatment failure). Subsequently, her fevers reached 40°C and she became debilitating. Then, she was re-admitted to the hospital for further management. At presentation, elevated levels of ferritin and neopterin was noted. After presentation, RT-PCR tests were performed, which was negative for COVID-19 infection. Further infectious workup, rheumatologic workup and oncological workup were negative, and ruled out other causes of fever. She met 7/9 HLH criteria including a bone marrow biopsy that showed haemophagocytosis. Then, a diagnosis of haemophagocytic lymphohistiocytosis (HLH) secondary to vaccine tozinameran was made. It was noted that initially she was treated with methylprednisolone [Solu-Medrol] 1000mg, 2 doses, and failed to improve (treatment failure). The woman was then treated with dexamethasone and etoposide with improvement in her symptoms and pancytopenia. She developed eutropenic fevers and haemodynamic instability without identifiable infectious source after fourth dose of etoposide. Due to concern for disease refractoriness, she started on emapalumab [emapalumab-lzsg]. After initiation of the treatment, her symptoms rapidly improved, and she was discharged home and continues to improve on outpatient follow-up visits. She received eight treatments of emapalumab, after discontinuation she experienced laboratory markers worsened; therefore, she suggested for a longer course of emapalumab. She was recommended for an allogeneic haematopoietic stem cell transplant for her initial worsening laboratory HLH markers. However, after long course of emapalumab her HLH marker levels improved, and transplant was postponed.

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