## Ciclosporin/interferon-beta-1a

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### Various toxicities and off-label use: case report

A 39-year-old woman developed thrombotic thrombocytopenic purpura (TTP) and thrombotic-microangiopathy (TMA) during immunosuppressive treatment with ciclosporin and off-label interferon-beta-1a for COVID-19 infection. Additionally, she developed posterior reversible encephalopathy syndrome (PRES) during treatment with ciclosporin, and antibody-mediated rejection (AMR) during treatment with interferon-beta-1a.

The woman, who had been diagnosed with liver cirrhosis secondary to primary sclerosing cholangitis, underwent liver transplantation from a negative crossmatch, ABO-compatible, deceased donor. She tested negative for COVID-19 before transplantation. Per protocol, she started receiving maintenance immunosuppressive therapy with ciclosporin 75mg twice a day, prednisolone and mycophenolate mofetil. Five days after transplantation, she developed fever and dyspnea. A polymerase chain reaction test and chest CT scan confirmed COVID-19 infection. Her immunosuppression was reduced by discontinuing mycophenolate mofetil, and she received 5 doses of SC injection of off-label interferon-beta-1a 44µg on alternate days. After a few days, her symptoms improved. On day 14 after transplantation, a liver biopsy specimen collected at the closure of abdominal fascia revealed AMR. She had normal liver function tests.

The woman received methylprednisolone pulse therapy to treat AMR. Laboratory tests revealed decreased platelet count, elevated levels of serum LDH and creatinine, stable haemoglobin level at around 8.5 g/dL and normal levels of partial thromboplastin time, prothrombin time and INR. A peripheral blood smear test detected schistocytes. She had normal ADAMTS13 activity and negative ADAMTS13 inhibitor activity. On day 16 after transplantation, she developed a single episode of seizure with transient loss of consciousness, mental status alteration and substantial increase in BP. She started receiving treatment with levetiracetam and nitroglycerin. A brain MRI findings were consistent with PRES. Additionally, she had intraparenchymal haemorrhage at the left occipital lobe. The serum trough level of ciclosporin was found to be elevated. Therefore, the ciclosporin dose was reduced to 50mg twice a day. She was diagnosed with TTP and TMA and was started on therapeutic plasmapheresis and immune-globulin. After 10 sessions of the plasmapheresis, she regained consciousness, and her serum LDH level and platelet count improved. About 2 months after the transplantation, she was discharged home with mycophenolate, sirolimus and prednisolone. At 1 month follow-up visit, her liver function tests and platelet counts were normal.

Dashti-Khavidaki S, et al. Thrombotic Microangiopathy, Antibody-Mediated Rejection, and Posterior Reversible Leukoencephalopathy Syndrome in a Liver Transplant Recipient: Interplay Between COVID-19 and Its Treatment Modalities. Experimental and Clinical Transplantation 19: 990-993, No. 9, Sep 2021. Available from: URL: http://doi.org/10.6002/ect.2021.0020

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