

IMMUNOTHERAPY AND TARGET THERAPY RELATED VTE

IMMUNE THROMBOTIC THROMBOCYTOPENIC PURPURA RELATED TO DELAYED IMMUNE CHECKPOINT INHIBITORS TOXICITY: A CASE REPORT

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Introduction. Immunotherapy with immune checkpoint inhibitors (ICIs) is widely used in both solid and hematologic tumors, although it is associated with several immune and nonimmune adverse events (AEs). Among them, cases of immune thrombotic thrombocytopenic purpura (iTTP) related to ICIs are emerging (Yikilmaz AS et al, *J. Immunother Precis Oncol.* 2025).

Aim. Our aim is to describe the case of a patient presenting with a delayed ICI-related iTTP.

Case report. A 68-year-old male, affected by non-small cell lung carcinoma, had been treated with a combination of ICIs (ipilimumab and nivolumab) for 7 months, with optimal disease control. The therapy was then discontinued due to ICI-related colitis, treated with high dose steroids. Three months later, during steroid tapering, the patient was hospitalized for a colitis relapse and *C. difficile* infection. A few days later, a significant drop in hemoglobin and platelet counts was observed, with no detectable hemolysis signs. The day after, the patient was aphasic: urgent brain CT ruled out hemorrhage or stroke, while the blood smear demonstrated schistocytes. The PLASMIC score was 6 (1 point each for low platelet count, hemolysis, no history of trans-

plant, MCV <90 fL, INR<1.5, creatinine < 2 mg/dL; 0 point for active cancer), therefore, given the high risk of iTTP diagnosis, he was started on iv high dose methylprednisolone, caplacizumab and therapeutic plasma exchange (TPE). The diagnose of iTTP was confirmed a few hours later by ADAMTS-13 activity of 0% and the presence of anti-ADAMTS-13 antibodies (84 U/mL). Hematological remission was achieved after 6 TPE, thus the patient was shifted to oral steroids and discharged 10 days after the iTTP onset. Caplacizumab was discontinued 30 days after the last TPE for ADAMTS13 remission. He is now TTP free at the 3-month follow-up, while ICI therapy is on hold and intermediate doses of prednisone are maintained due to a further relapse of the ICI-related colitis.

Conclusions. iTTP is a rare ICI-related AE, but due to their wide use, it should be considered when a patient presents with thrombocytopenia and hemolysis. Our case demonstrates that the timing of presentation of iTTP from ICI start/discontinuation may be very variable, as it can occur even after several months. In light of this evidence, the PLASMIC score should be revised in order not to miss iTTP diagnosis among patients with an active cancer, who have received, recently or not recently, an ICIs treatment.