

COVID-19 and TEN Treated With IVIG and Total Plasma Exchange: Simultaneous Systemic Treatment for Both Diseases

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Toxic epidermal necrolysis (TEN) is a rare but potentially fatal systemic disease that mainly affects the skin. The plethora of known causal factors includes antibiotics, nonsteroidal anti-inflammatory drugs, and antihistamines). Several treatment regimens have been proposed, the most common being corticosteroids and cyclosporine [1-3]. Given that, since 2019, we have all been struggling with the pandemic environment brought about by the SARS-CoV-2 virus infection (COVID-19) [4], these diseases have received little attention in the literature [5,6]. We present a case of concomitant TEN and COVID-19 treated with intravenous immunoglobulin (IVIG) infusion and total plasma exchange (TPE). The treatment protocol consisted of daily TPE followed by an IVIG infusion [7]. A 76-year-old woman was admitted to our unit with a positive COVID 19 result (GeneFinder COVID-19 Plus RealAMP). The RdRp, N, and E genes were present. Her medical history included hypertension and type 2 diabetes mellitus. She had a long history of treatment with indapamide 1.5 mg (Tertensif SR, Servier), ramipril 5 mg (Polpril, Polpharma), and metformin 3 × 850 mg (Siofor, Berlin-Chemie AG). Two days before admission, she had contacted her primary care physician because of flu-like symptoms and abdominal pain. Examination revealed no specific findings, fever, or tachypnea. The patient's symptoms were treated with intramuscular injection of metamizole 1.0 (Pyralgin, Polpharma), and a swab was taken for COVID-19. She was then discharged home to self-isolate until the test results were known. Skin and mucosal lesions began to develop 2 days after her visit to primary care. The patient was admitted to the unit with typical COVID-19 symptoms (fever, respiratory distress) from her home, where she had been staying in isolation, owing to the positive test result. There was no evident cause of TEN (in the absence of a recently taken drug), although the most possible explanation seems to have been metamizole (2 days from administration to onset of TEN). The total body surface area affected by erythematous blistering was 70%, with involvement of the oral and vaginal mucosa (Figure). The



Figure. Lesions on admission.

diagnosis of TEN was confirmed by a consultant dermatologist. Biopsy revealed subepidermal bullae, epidermal necrosis, and moderate dermal infiltration with lymphocytes. The patient was obese (body mass index, 38.06) and was admitted with respiratory distress (non-rebreathing mask oxygen 6 L/min and blood oxygen saturation of 80%). Her SCORTEN score on admission was 4. Laboratory test results on the day of admission were as follows: C-reactive protein, 138 mg/L; procalcitonin, 0.9 ng/mL; D-dimer, 3.65 µg/mL. The patient's wounds were treated mainly with Suprathel (PolyMedics Innovations GmbH). However, owing to failure of adhesion due to body pressure, Aquacel Ag (Convatec) was applied on her back. Systemic treatment was provided with daily TPE followed by an IVIG infusion. She received a total of 5 cycles of TPE with 50 fresh frozen plasma units and 90 g of IVIG. Sepsis caused by *Escherichia coli* during hospitalization was treated with targeted antibiotic therapy (levofloxacin and cefuroxime). Every day, the patient also received enoxaparin 2 × 0.4 mL (Clexane, Sanofi), ramipril 5 mg (Polpril, Polpharma), metformin 3 × 850 mg (Siofor, Berlin-Chemie AG), and furosemide 2 × 20 mg (Furosemidum, Polfarmex). Her skin lesions had stabilized on day 7. External oxygenation was stopped on day 8. Her laboratory parameters normalized, and, on the day of discharge (day 14), C-reactive protein was 21 mg/L and procalcitonin 0.1 ng/mL. Her skin had almost fully healed, with small patches of erythema and superficial epidermal exfoliation. We believe that IVIG and TPE could ameliorate the bradykinin or cytokine storm associated with COVID-19 by immunomodulating cytokine activity (IL-6, TNF-α) and by eliminating exogenous antigens [8-10]. We believe that this systemic treatment had a positive effect on both diseases and stopped the impending deterioration caused by dysregulation of the immune system. Nevertheless, broader implementation of IVIG and TPE in COVID-19 needs to be

evaluated in terms of its potential benefits and cost-benefit ratio in a multicenter, randomized trial.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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