# COVID-19 and TEN treated with IVIG and Total plasma exchange. Simultaneous systemic treatment for both diseases

Krajewski A[1], Mlynska-Krajewska E[1], Kaczynska K[1], Strużyna J[2], Mazurek MJ[1]

[1]West Pomeranian Center for Severe Burns and Plastic Surgery, Gryfice, Poland

[2]Eastern Burns and Reconstructive Surgery Center, Łęczna, Poland

Corresponding:

Maciej Mazurek

ul. Niechorska 27 72-300 Gryfice, Poland

E-mail: maciek.j.mazurek@gmail.com



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**Palabras clave:** COVID 19. Infusión inmunoglobulina. Intercambio total de plasma. Sars Cov-2. Sistémico.

Toxic epidermal necrolysis (TEN) is a rare, but potentially fatal systemic disease, with most prominent dermal presentation. There is a plethora of known causing factors (among others antibiotics, non-steroidal inflammatory drugs, anti-histamines), and proposed treatment regimens, with most commonly used glucocorticoids and cyclosporine.[1-3] Since 2019, we all have been struggling with new, pandemic environment due to SARS-CoV-2 Virus. [4] There is a scarce literature regarding the simultaneous incidence of these diseases.[5, 6] We would like to present you a concomitant TEN and SARS-CoV-2 infection (COVID-19) treated with intravenous immunoglobulin infusion (IVIG) and total plasma exchange (TPE). The treatment protocol consist of daily TPE with following IVIG infusion.[7] 76-year old woman was admitted to our unit with positive COVID 19 test (GeneFInder COVID-19 Plus RealAMP) with present RdRp, N, and E genes. Her medical history consists of blood hypertension and diabetes mellitus type 2. She had long history of treatment with Indapamide 1.5 mg (Tertensif SR, Servier, France), Ramipril 5mg (Polpril, Polpharma, Poland) and Metformin 3x 850 mg (Siofor, Berlin-Chemie AG, Germany). Two days before admission she had contacted with primary care doctor due to flu-like symptoms and abdominal pain. After examination, without any specific findings, and without either fever or tachypnoea, she received Metamizole 1,0 im injection (Pyralgin, Polpharma, Poland) for symptomatic treatment and was swabbed for COVID-19.

 
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Afterwards she was released home for quarantine until the test results were concluded. Skin and mucosal lesions began to develop 2 days after primary care visit. Patient was admitted to the unit with typical COVID-19 symptoms (fever, respiratory distress) from her home, where she had been staying in isolation, due to the positive test result. There is no evident causing factor of TEN (lack of any newly taken drug) but the most possible cause seems to be Metamizole (2 days since administration to TEN development). Total body surface area affected with erythematosus blistering was 70%, with mucosal involvement of oral cavity and vagina. (Fig 1.) TEN diagnosis was confirmed by consultant dermatologist. Biopsy showed subepidermal bullae, epidermal necrosis, and moderate dermal infiltration with lymphocytes. Patient was obese with BMI 38,06. She was admitted with respiratory distress with 6L/min reservoir mask oxygen and blood oxygen saturation of 80%. SCORTEN score on admission 4. Her laboratory test on the admission day were CRP 138 mg/l, procalcitonin 0,9 ng/ml, D-Dimers 3,65 ug/ml. Her wounds were mainly treated with Suprathel (Polymedics Innovation Ghmb, Germany), and due to failure of adhesion due to body pressure with Aquacel Ag (Convatec, UK) on her back. Systemic treatment was provided with daily TPE with following IVIG infusion. She had total 5 TPE with total 50 fresh frozen plasma (FFP) units and received 90 g of IVIG overall. We have observed E. coli sepsis during hospitalization, treated with aimed antibiotic therapy (Levofloxacin and Cefuroxime). Additionally, she received daily: Enoxaparine 2x0,4 mL (Clexane, Sanofi, France), Ramipril 5mg (Polpril, Polpharma, Poland) Metformin 3x 850 mg (Siofor, Berlin-Chemie AG, Germany) and Furosemide 2x20 mg (Furosemidum, Polfarmex, Poland). Skin lesion stabilization was observed on 7$^{th}$ day of hospitalization. Patient had stopped to be provided with external oxygenation on 8$^{th}$ day since the admission. Her laboratory parameters normalized and on the day of release CRP was 21



 
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mg/l, procalcitonin 0,1ng/ml. Her skin was almost fully healed with small fields of erythema and superficial, epidermal exfoliation. She was discharge on the 14$^{th}$ day of hospital stay. We believe that IVIG and TPE could ameliorate either bradykinin or cytokinin storm associated with COVID-19 by immunomodulating cytokine activity (IL-6, TNF-alfa), and by elimination of exogenous antigens.[8-10] We reckon that this systemic treatment has a positive effect on both diseases and stopped the impeding deterioration cause by deregulation of immune system. Nevertheless, broader implementation of IVIG and TPE in COVID-19 alone needs to be evaluated regarding the potential benefits, and benefits/costs ratio in multicenter, randomized scenario.

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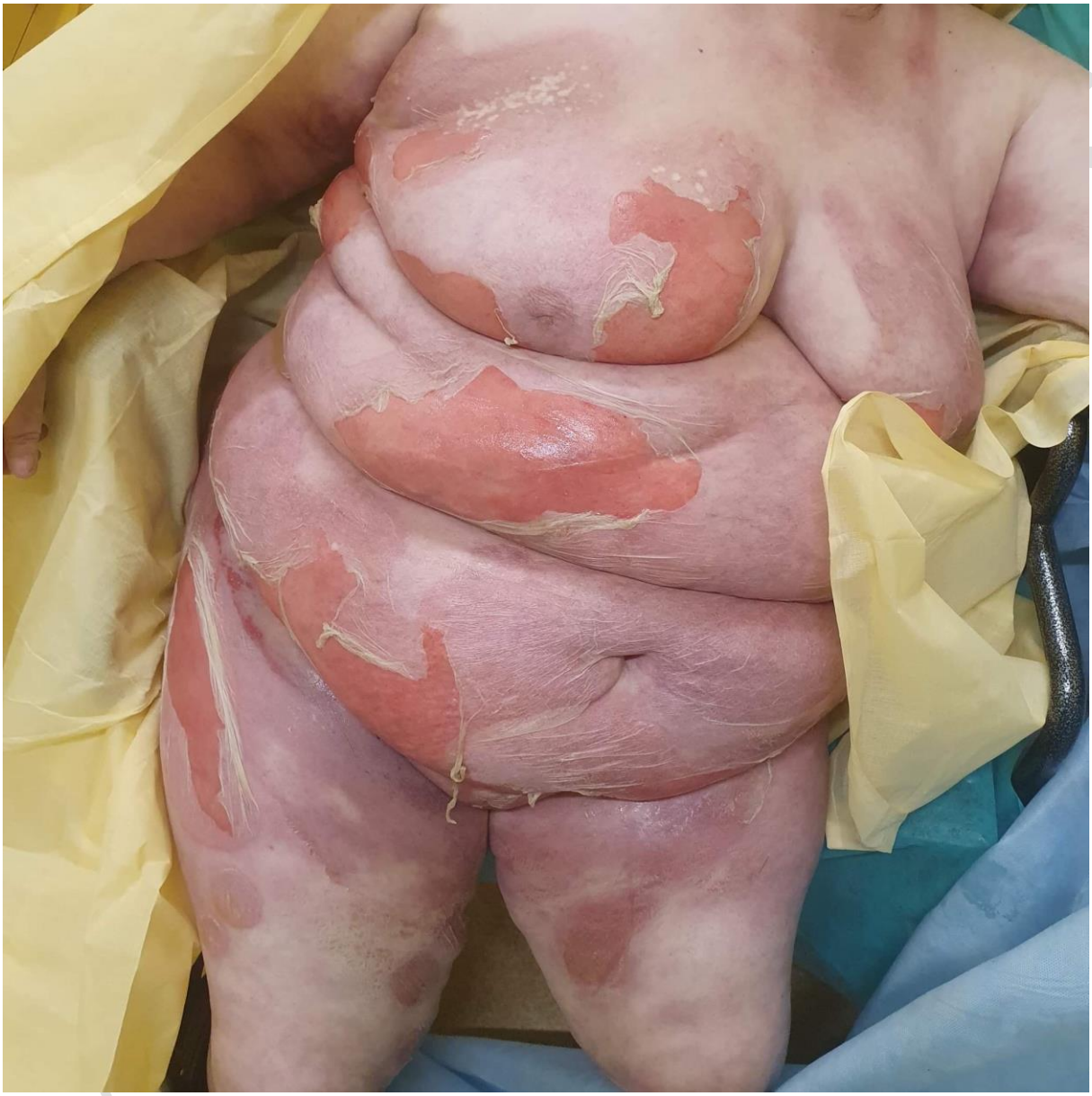
**Figure legends:**

Figure 1. Lesions on admission





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