# COVID-19 in a case of Toxic Epidermal Necrolysis

Mohammad Shahidi-Dadras[1], Shaghayegh Shahri-Gharahkoshan[2], Esmat Yazdi[3], Alireza Fatemi[1], Zahra Mahboubi-Fooladi[1], and Sahar Dadkhahfar[4]

[1]Shahid Beheshti University of Medical Sciences
[2]Université Laval Faculté de médecine
[3]Shohada-e Tajrish Hospital
[4]Affiliation not available

March 30, 2022

**Abstract**

The COVID-19 pandemic is a major health issue and patients with underlying conditions are more susceptible to catastrophic outcomes. Toxic epidermal necrolysis (TEN) is a severe systemic disease caused by immune system hypersensitive reaction. We present a case of TEN that later complicated with COVID-19,Deep Vein Thrombosis(DVT),Pulmonary Emboli(PE),and death.

**Manuscript word** # 794 and **Figure** # 3

**Authors:**

Mohammad Shahidi-Dadras[1*], Shaghayegh Shahrigharahkoshan[2*], Esmat Yazdi[3], Alireza Fatemi[4], Zahra Mahboubi-Fooladi[5], Sahar Dadkhahfar[1]

1. Skin research center, Shahid Beheshti University of medical sciences, Tehran, Iran
2. Faculty of medicine, Université Laval, Quebec, Qc, Canada
3. Department of internal medicine, clinical research development unit of Shohada-e-Tahrish Hospital, Shahid Beheshti University of medical sciences, Tehran, Iran
4. Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Department of Radiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

* Mohammad Shahidi-Dadras and Shaghayegh Shahrigharahkoshan should be considered joint first author.

**Corresponding author** : Sahar Dadkhahfar, Shahid Beheshti University of medical sciences, Shohada-e Tajrish hospital, Tehran, Iran. Tel: +9821-22741507-10, Fax: +9821-22744393, sahar.dadkhahfar@gmail.com

**Abstract**

The COVID-19 pandemic is a major health issue and patients with underlying conditions are more susceptible to catastrophic outcomes. Toxic epidermal necrolysis (TEN) is a severe systemic disease caused by immune system hypersensitive reaction. We present a case of TEN that later complicated with COVID-19,Deep Vein Thrombosis(DVT),Pulmonary Emboli(PE),and death.

**Keywords** : Toxic epidermal necrolysis, Covid-19, cyclosporine, fatal myocardial infarction

**Key clinical message**

This patient was a patient with a catastrophic outcome of Toxic epidermal necrolysis that later complicated by Covid-19. Primary prevention is the best way to manage these two conditions during this crucial era.

**Introduction**

The COVID-19 pandemic is a major health issue and patients with underlying conditions are more susceptible to catastrophic outcomes[1]. Although, this virus mainly involves the pulmonary system, it can also severely affect other organs causing gastrointestinal distress, cardiovascular compromise, acute kidney injury, coagulopathies, cutaneous manifestations and ultimately death from multi-organ failure [2].

Toxic epidermal necrolysis (TEN) is a severe systemic disease caused by immune system hypersensitive reactions characterized by >30% sheet-like epidermal detachment of body surface[3]. Drug hypersensitivity is responsible for 85–90% of cases of TEN [3]. The main manifestations of TEN are mucoucutaneous but multiple organs, such as trachea, bronchi, lungs, etc., are also involved. The mortality rate of TEN ranges from 25% to 30% that makes it the most critical dermatologic emergency[3]. Here we present a case of TEN that later complicated with COVID-19, Deep Vein Thrombosis (DVT), Pulmonary Embolism, and death.

**Case history / examination**

A 52-year-old woman admitted to our hospital with suspected TEN. Her symptoms had begun five days earlier following two weeks of sulfasalazine treatment for rheumatoid arthritis. Initial symptoms included fever and stinging eyes followed by dusky red macular and flat atypical target lesions that had first appeared on her palms and sole with rapid progression to more than 70% of her body surface (Fig. 1). Erythema and erosions of the buccal, ocular, and genital mucosae were present. Both Nikolsky and Asboe-Hansen signs were positive. Tense blisters were observed on her palms and soles (Fig. 2). The clinical diagnosis of TEN necrolysis was made.

**Differential diagnosis, investigations and treatment**

The histopathological investigations approved the diagnosis of TEN (Fig. 3). On day 1, she presented with 38.3$^*$C fever and 98% oxygen saturation in room air. Lab tests revealed elevated lactate dehydrogenase (648 units/liter (U/L), normal: 140–280 U/L), C-reactive protein level (52 milligrams/Liter (mg/L), normal: <10 mg/L), aspartate aminotransferase (59 U/L, normal: 10–40 U/L). Polymerized chain reaction (PCR) for COVID-19 was negative.

After sepsis work up and an infectiologist consultation, we started her on IV meropenem and vancomycin. For the TEN treatment she received supportive care and oral cyclosporine 200 mg daily that led to the amelioration of her skin condition within three days. In the fourth day of cyclosporine administration re-epithelialization of lesions began. Despite marked improvement of skin lesions, her temperature rose to 38.8$^*$C after five days and she developed orthopnea. Spiral non-contrast chest CT scan was then performed which revealed consolidation in right lower lobe and posterior segment of right upper lobe with air bronchogram sign, most likely due to bacterial pneumonia. Bilateral moderate size pleural effusion was also present compatible with volume overload. The antibiotics was then changed to ceftazidime and colistin according to antibiogram of sputum culture. Cyclosporine was discontinued after 10 days.

**Outcome and follow-up**

On her 10th day of admission, her skin showed marked improvement but she developed productive cough and exacerbation of dyspnea. Follow-up CT scan showed bilateral peripheral and peribronchovascular ground glass opacity and interlobular septal thickening (acute crazy paving pattern) predominantly in lower lobes in favor of COVID-19 infection. Further PCR was positive for COVID-19.

She was immediately transferred to COVID-19 special ward where she received dexamethasone 6mg/daily and subcutaneous interferon beta-1a for five days. After 17 days of intensive care in COVID-19 ward, she showed marked improvement and discharged to home quarantine after 27 days of total hospitalization. Unfortunately, she died of DVT and PE one month later.

## Discussion

Toxic epidermal necrolysis is a rare skin condition in which the body loses its barrier function and renders individual susceptible to contract infections. A recent systematic review and meta-analysis has shown that, apart from supportive care, several immunodulators such as cyclosporine could have potential mortality benefits for TEN patients[4]. Recently, protective effect of cyclosporine has been determined in Covid-19 patients due to its potential to downregulate the cytokine storm and toxic T-cells proliferation induced by SARS-CoV-2, to inhibit viral replication and to prevent acute lung injury [5,6].

In addition, the initially negative PCR for Covid-19 in our patient could have been a false negative result. There is a previous report of one symptomatic SJS/TEN case whose PCR turned positive following two negative results [7]. The false negative PCR should be considered in patients with respiratory symptoms specially in high-risk ones.

Finally, both bleeding and thrombotic complications are commonly reported following Covid-19 infection mainly due to the disseminated inflammation leading to hypercoagulability causing DVT or PE, and eventually death [8]. In managing Covid-19 patients, the physicians should screen for these complications and use anticoagulants when necessary. Although our patient was receiving Rivaroxaban, she developed DVT and pneumatic emboli even after being discharged in a favorable condition. Thus, in managing patients with multiple respiratory comorbidities during Covid-19 era a multidisciplinary approach is to be preconized.

## Author contributions

Author 1: contributed in writing, reviewing, editing, and supervision.

Author 2: contributed to investigation, resources, data curation, writing original draft, visualization.

Author 3: contributed in reviewing, editing, and supervision.

Author 4: contributed in reviewing, editing, and supervision.

Author 5: contributed in reviewing, editing, and supervision.

Author 6: contributed to conceptualization, writing original draft, reviewing, editing, supervision, project administration, and data curation.

## Conflict of interest

The authors do not have any conflict of interest to declare.

## References

1. Drugs@FDA: FDA-Approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process Accessed 22 Jul, 2020.

2. Yi Y, Lagniton PN, Ye S, Li E, Xu R-H. COVID-19: what has been learned and to be learned about the novel coronavirus disease.*International journal of biological sciences.* 2020;16(10):1753.

3. Schwartz RA, McDonough PH, Lee BW. Toxic epidermal necrolysis: Part II. Prognosis, sequelae, diagnosis, differential diagnosis, prevention, and treatment. *J Am Acad Dermatol.* 2013;69(2):187 e181-116; quiz 203-184.

4. Ng QX, De Deyn M, Venkatanarayanan N, Ho CYX, Yeo WS. A meta-analysis of cyclosporine treatment for Stevens-Johnson syndrome/toxic epidermal necrolysis. *Journal of inflammation research.* 2018;11:135-142.

5. Cour M, Ovize M, Argaud L. Cyclosporine A: a valid candidate to treat COVID-19 patients with acute respiratory failure? *Crit Care.*2020;24(1):276.

6. Poulsen NN, von Brunn A, Hornum M, Blomberg Jensen M. Cyclosporine and COVID-19: Risk or favorable? *Am J Transplant.* 2020.

7. Lagziel T, Quiroga L, Ramos M, Hultman CS, Asif M. Two False Negative Test Results in a Symptomatic Patient with a Confirmed Case of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) and Suspected Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN). *Cureus.* 2020;12(5):e8198.

8. Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood.* 2020;136(4):489-500.

**Figures Legend**

Figure 1. Cutaneous manifestation of TEN: The tense blisters along with the sheet-like epidermal detachment of the body

Figure 2. Cutaneous manifestation of TEN: The blisters on the palms

Figure 3. Histopathologic features: Blisters along with the suprabasilar acantholysis of the skin.