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Toxic epidermal necrolysis and coronavirus disease 2019: A rare association

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ABSTRACT

Cutaneous manifestations of Coronavirus disease 2019 (COVID-19) are variable. We report a 57-year-old woman who developed toxic epidermal necrolysis (TEN) in association with COVID-19. The patient had not received any drugs prior to the onset of TEN. She responded to treatment with cylosporine. Previous authors have suggested a better prognosis for TEN associated with COVID-19 in comparison to drug-induced TEN.

Keywords: Cutaneous manifestations, Coronavirus disease 2019, Toxic epidermal necrolysis, Cyclosporine, Drug

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome cornonavirus-2 (SARS-CoV-2) has spared none of the geographic areas. With the increase noted in the number of cases, more and more cutaneous manifestations are seen. We report a 57-year-old woman who developed toxic epidermal necrolysis (TEN) in association with COVID-19.

CASE REPORT

Fifty-seven-year-old woman, with no known comorbidities, tested positive (on real-time reverse transcription-polymerase chain reaction) for COVID-19. As per the treatment guidelines practiced in the state at that time, she was admitted in our COVID-19 ward with frequent monitoring of vitals and oxygen saturation. She did not receive any medicines while in hospital since she remained asymptomatic. She was discharged on the 12th day of admission following a negative COVID-19 rapid antigen test (RAT). On the 2nd day of discharge, the patient returned with high-grade fever, vomiting, sore throat, oral erosions, foreign body sensation in the eyes, and purpuric macules involving the whole body of 1 day duration. At the time of discharge, the patient claimed, that she had some foreign body sensation in the eyes which she did not complain about at that time. She denied any drug intake prior to the onset of the lesions. At the time of re-admission, she had swelling of the lips, conjunctival congestion, erosions of buccal and genital mucosae, targetoid lesions, generalized purpuric rash, and detachment of skin involving >30% of body surface area [Figures 1 and 2]. With these findings, we made a clinical diagnosis of TEN. Her vital parameters were normal. Systemic examination was within normal limits. Complete hemogram, urine microscopy, serum bicarbonate level, random blood sugar, chest radiography, and renal and liver function tests were within normal limits. Based on the investigations and

Figure 1 (a): Showing epidermal necrosis and erosions on the forearm of a patient who manifested toxic epidermal necrolysis following coronavirus disease 2019; (b) showing epidermal necrosis and erosion on the leg of the same patient.

clinical examination, we calculated her score of TEN (SCORTEN) as 2.[1] She had a score of 2 on ABCD-10 (age, bicarbonate, cancer, dialysis, 10% body surface area) risk prediction model.[2] The features that earned one point each on SCORTEN and ABCD-10 risk prediction model were age >40 years and detachment of the skin involving >30% of body surface area. Her blood culture was sterile. After discussion with her relatives, we started cyclosporine 100 mg 3 times a day per orally for 5 days, followed by twice a day for 4 days and once a day for 5 days. Ophthalmology evaluation confirmed the presence of keratitis for which she was prescribed eye lubricants and steroid-antibiotic eye drops with regular monitoring by the ophthalmologist. Her condition gradually improved and she remained asymptomatic during the 1 month follow-up period.

DISCUSSION

COVID-19 caused by SARS-CoV-2 has affected all the regions in the world since its first report from Wuhan, China.[3] Although the major brunt of attack by SARS-CoV-2 is suffered by the respiratory system, the disease can affect all the major organs of the body. Cutaneous manifestations are reported from different parts of the world. Genovese *et al*. described six main patterns of cutaneous

Figure 2: Showing hemorrhagic crusting of lips and epidermal necrosis and skin detachment involving the face and neck of a patient who manifested toxic epidermal necrolysis following coronavirus disease 2019.

manifestations in COVID-19.[4] They are urticarial rash, confluent erythematous/maculopapular/morbilliform rash, papulovesicular exanthem, chilblain-like acral pattern, livedo reticularis/racemosa-like pattern, and purpuric vasculitic pattern. Erythema multiforme-like rash and pityriasis rosea-like rash are also observed occasionally.[4] According to literature, the skin lesions may precede or succeed the diagnosis of COVID-19.[4,5] Cutaneous manifestations are reported after recovery from the COVID-19, especially in multisystem inflammatory syndrome in children.[5]

TEN is a hypersensitivity reaction pattern of the skin characterized by widespread keratinocyte necrosis (manifesting as sheets of epidermal detachment) and mucosal sloughing.[6] Stevens Johnson syndrome - TEN is considered as a spectrum of disease and the differentiation depends on the extent of detached or detachable skin.[6] Although, mostly drug-induced, there are occasional reports of TEN associated with infection.[7-9] Fournier *et al*. reported a 16-year-old girl who developed TEN during mycoplasma pneumonia infection.[7] Her initial symptoms were pharyngitis and non-productive cough and the skin lesions appeared one day later. She manifested severe respiratory distress syndrome, diffuse

bilateral pulmonary infiltrates, and moderate pericardial effusion.

A concomitant mycoplasma infection seemed unlikely in our patient since her chest X-ray was normal and no abnormality was detected on systemic examination. Viral infections including herpes simplex virus infection, rubella, and viral hepatitis, are rarely reported in association with TEN.[7-9] Our patient did not manifest any of the clinical features suggestive of these infections and had tested positive for COVID-19, 13 days before the onset of TEN.

Narang *et al*. reported a case of TEN associated with COVID-19 in a 53-year-old woman with metastatic breast carcinoma.[10] She developed a maculopapular rash, 5 days after receiving a diagnosis of COVID-19, which progressed to TEN after 10 days. The only medication she was receiving at the time of rash was dexamethasone for brain metastasis. Patient continued to receive dexamethasone and the rash responded to conservative management. The authors concluded that TEN associated with COVID-19 could be less severe than drug-induced TEN since the patient improved despite having a score of 4 on SCORTEN.

Rossi *et al*. reported a case of TEN in a 78-year-old COVID-19 patient.[11] Although the patient received multiple drugs, the authors suggested the possibility of hydroxychloroquine-induced TEN after calculating ALDEN (algorithm of drug causality for epidermal necrolysis) causality score.[12] All the suspected drugs were withdrawn and the patient was treated with systemic corticosteroids and intravenous immunoglobulin G.

No clinically evident cause for TEN, other than COVID-19, was noted in our patient. We can not rule out the possibility of coexistence of another subclinical infection in our patient since a detailed virology workup or serology for mycoplasma infection was not carried out. The 13-day interval observed between the diagnosis of coronavirus infection and the onset of TEN was consistent with the documented latent period (4–28 days) in the latter.[13] A drug history was missing in 10 out of the 253 cases of TEN in an epidemiologic study and eight among them did not manifest any clinical or serological evidence of infection.[14] The temporal association of TEN with coronavirus infection in our patient suggested the possibility of infection-induced TEN. The generalized immune stimulation associated with viral infections and subsequent elevation of cytokines in serum and tissues are proposed as the reasons for the increased risk of hypersensitivity reactions in viral infections.[15]

Similar to the previous TEN cases associated with COVID-19, our patient also attained complete recovery. Unlike the previous patients who received systemic corticosteroids (the patient with metastatic breast carcinoma was receiving dexamethasone for her brain metastasis) with or without immunoglobulin G, our patient was treated with cyclosporine.[10,11] Guisado-Vasco *et al*. in a retrospective, single-center, observational study in 607 patients, concluded that among the different treatments adopted for COVID-19 (tocilizumab, glucocorticoids, lopinavir/ritonavir, hydroxychloroquine, and cyclosporine), a significant decrease in mortality was associated with cyclosporine alone.[16] They reported that the hyperinflammatory phase in COVID-19 could be reduced by the inhibition of calcineurin inflammatory pathway. We opted for cyclosporine in our patient since it is considered beneficial in TEN as well.[17,18]

CONCLUSION

The COVID-19 pandemic has not made a retreat even after a year of spread. Varying manifestations of the disease are being reported with the increase in number of cases worldwide. We report this case to highlight the rare association of TEN and COVID 19 and the usefulness of cyclosporine in managing the dermatological emergency of TEN in the setting of COVID-19.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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