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CASE REPORT

Burns

Enzymatic Debridement in Severe Burn COVID-19 Patients: A Case Series

Francesco Coletta, MD*
Crescenzo Sala, MD*
Giovanna Paola De Marco, MD†
Ilaria Mataro, MD‡
Carlo Petroccione, MD‡
Pietro Bonagura, MD†
Rossella Pirolli, MD§
Giuseppe Foreste, MD*
Antonio Tomasello, MD*
Romolo Villani, MD*

Summary: The presence of a high number of positive SARS-CoV-2 patients is found daily in the emergency room database, finding evidence of infection also in trauma and burns. Surgical debridement remains the gold standard for eschar removal, but it does not come without complications such as bleeding and high heat loss. In recent years, there has been an increase in the use of enzymatic debridement techniques, replacing surgical escharotomy. Early eschar removal is proven to be important; it has been proved that an early and effective burn treatment in COVID-19 patients can reduce other infection. Five clinical cases of patients arrived at our COVID-19 Major Burns Intensive Care Unit. On admission, burns extension and depth were assessed by an expert burn surgeon. We evaluated eschar removal modality, adverse events, and potential side effects. Enzymatic debridement was efficient in all patients treated with complete eschar removal, and no serious adverse events. All patients were treated within 24 hours of arrival at our facility with Nexobrid by specialized personnel in deep sedation and with O_2 support using a face mask or nasal goggles. The use of enzymatic debridement in COVID-19–positive burn patients within dedicated pathways through nonsurgical treatment optimizes the treatment time. We believe that the use of enzymatic debridement could be a valid therapeutic option in burn patients, even with SARS-CoV-2 infection, and its use, when indicated, is safe and effective for the patient and optimizes the use of instrumental and human resources in a pandemic emergency.
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Patients with SARS-CoV-2 infection can present clinical manifestations ranging from no symptoms to severe disease.[1] A predictor of its clinical evolution may be the presence of SARS-CoV-2 in the urine.[2] The efficacy and safety of COVID-19 vaccines are widely demonstrated.[3–5] However, a high number of positive SARS-CoV-2 burn and trauma patients is found daily in the emergency room. In a recent epidemiological study, a significant increase in the rate of burned children and an increase in the severity of injuries is noted.[6] Severe burns are accompanied by an immune and inflammatory response and distributive shock that is hard to manage and can lead to multi-organ failure[7]; early eschar removal (<48 hours)[8] is associated with shorter hospital stays, reduced infection rates, reduced complications from sepsis, and better wound closure. The high ICU admission rate and high mortality in SARS-CoV-2 patients, combined with the critical clinical condition of burn patients, has an inpatient management protocol designed to minimize viral spread among patients and healthcare workers.[9]

Surgical debridement remains the gold standard for eschar removal, but comes with complications such as bleeding and high heat loss. Furthermore, a slowed healing of skin lesions is described in COVID-19–positive patients, probably due to the established inflammatory pathway.[8] In recent years, there has been an increase in the use of enzymatic debridement, which has proved to be less traumatic and invasive and reduce intercompartmental pressure, replacing surgical escharotomy.[9] Nexobrid is a debriding bromelain-based compound. Its main benefit is eschar removal without altering any healthy tissue, allowing for closure of the wound.[10]

In this case series, we have described five clinical cases of burn patients, managed at the Multidisciplinary Operative Unit Pavilion M and COVID-19 Major Burns Intensive Care

*From the *Emergency and Acceptance Department, Anesthesia, Emergency and Burn Intensive Care Unit, "A.O.R.N. A. Cardarelli", Naples, Italy; †Covid 19 Intensive Care Unit, "A.O.R.N. A. Cardarelli", Naples, Italy; ‡Department of Burn Unit and Plastic Surgery, "A.O.R.N. A. Cardarelli", Naples, Italy; and §Anesthesia, Emergency and Intensive Care Unit, ASL Caserta, PO San Giuseppe Moscati – Aversa, Italy.*

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Unit of AORN "A. Cardarelli" in Naples, where enzymatic debridement was performed using Nexobrid.

MATERIALS AND METHODS

The Study complies with the criteria of the Declaration of Helsinki.

General Information

Five clinical cases of patients arrived at the COVID BICU (Burn Intensive Care Unit) at AORN (National Relief Hospital) "A. Cardarelli" of Naples, from June 2021 to March 2022. On admission, a surgeon assessed burns extension (total body surface area) and depth. All patients tested positive for SARS-CoV-2 on a real-time polymerase chain reaction (PCR) swab. All patients were assisted on a dedicated COVID-19 assistance path by specialized personnel. All received Parkland infusion treatment, continuous complete monitoring of vital signs, and microbiological surveillance and antithrombotic prophylaxis with low molecular weight heparin.

Debridement Procedure

Enzymatic debridement was performed within the first 72 hours after the accident, and the application was limited to 15% total body surface area in a single application (Fig. 1A). Superficial burns were treated conservatively with standard dressings, whereas very deep burns were treated surgically. All patients signed informed consensus for enzymatic debridement procedure and for the collection of personal data for scientific purposes.

Intervention

The treatment was performed under deep sedation, in spontaneous breathing with O_2 support through a Venturi mask 60% FiO_2 and target controlled infusion remifentanil infusion. The powdered proteolytic preparation in 20 g of gel was placed on the burned area with a gel layer thickness of 1.5–3 mm on no more than 15% of total body surface area (Fig. 1B). All lesions were covered with an occlusive film dressing. The preparation was applied to the lesions for 4 hours, and then removed in a sterile manner. At the end of the procedure, a gauze soaked in an antibacterial solution was applied for 2 hours, and then temporary or permanent bandages were applied. Each patient performed a real-time PCR SARS-CoV-2 swab every 5 days; after the SARS-CoV-2 swab came out negative and infectious disease specialist consultation was performed, the patients were transferred to the non-COVID BICU.

End Points Measurement

The end point of this study is to assess the correct timing and effectiveness of the procedure in COVID-19 patients. The secondary end point was time to treatment and adverse effects.

Statistical Analysis

The demographic and anamnestic information regarding age, sex, and surgical times were summarized with descriptive methods—in particular, categorical variables by estimating relative frequencies, continuous variables with mean and standard deviation, or median and interquartile range.

RESULTS

Enzymatic debridement was efficient in all patients treated (four men, one woman; mean age 60.2 years) with complete eschar removal (Fig. 1B). All patients were treated within 24 hours of arrival at our facility with Nexobrid by specialised personnel. All patients had partial

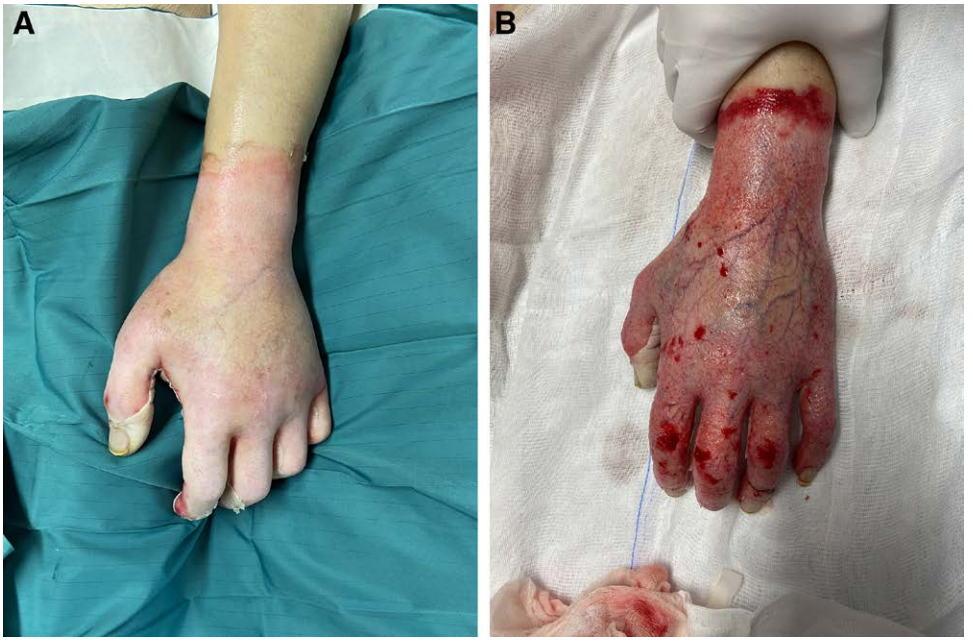

Fig 1. Effects of enzimatic escharectomy. A, Deep dermal hand burn. B, Complete eschar removal after enzymatic debridement.

Table 1. Burn Characteristics

Patient	Total Body Surface Area %	Anatomic Areas	Partial Thickness %	Full Thickness
P1	40	Head, neck, trunk, upper extremity, lower extremity	15	25
P2	30	Head, neck, trunk, upper extremity	20	10
P3	45	Trunk, upper extremity, lower extremity	10	35
P4	50	Trunk, upper extremity, lower extremity	10	40
P5	35	Head, neck, trunk upper extremity	20	15

Table 2. Patient Characteristics

Patient	Total Body Surface Area %	Hours Post Injury ED Applied	Dose Vaccine	Inalation Injury	Ventilated
Patient 1	40	<72 h	3	No	No
Patient 2	30	<72 h	3	No	No
Patient 3	45	<72 h	3	No	No
Patient 4	50	<72 h	2	Yes	Yes
Patient 5	35	<72 h	2	No	No
Patient	T0	T (at 3 h)	T (6 h)	Tmax 24 h	Tmax 48 h
Patient 1	37.5	38.5	37.5	37	37
Patient 2	36	37.3	37.5	36.8	37
Patient 3	36.8	38	36.8	37.1	36.8
Patient 4	37.2	37.5	36.8	37.2	36.2
Patient 5	37.4	37.2	37.4	36.7	36.7

and deep thermal burns affecting 30% to 50% of the total body surface area (total body surface area %) (Table 1). None of the treated patients presented injuries to the oral cavity, nose, or airways (Table 2). None of the patients had a respiratory failure or interstitial ground glass lung lesions on computer tomography scan. Only one patient underwent invasive ventilation by tracheal intubation for fumes inhalation injury. The anatomic areas treated were upper extremities, 64%; trunk, 23%; lower extremities, 11.5%; and head, 2.5%, with an average of 13% of burn surface area. No hemodynamic alterations were observed requiring the support of inotropic drugs; diuresis was maintained in the range of 0.5–1 mL/kg/h. Three patients underwent skin grafting as the final treatment. Two patients did not receive skin graft: they were treated conservatively with allograft or fatty gauze, and healed spontaneously within 3 weeks. No serious adverse events or allergic reactions were reported. No patient developed pathogenic microbial flora requiring treatment on the treated skin. The results are comparable to those described in the Nexobrid technical data sheet evaluated on non-COVID–positive patients (Table 3). All patients were transferred to the non-COVID ward within 1 month after negative PCR swab. None of the patients was affected by thrombotic phenomena. For one patient, a cross-linked blood bag was administered.

DISCUSSIONS

The management of critically-ill burn patients, SARS-CoV-2 positive, is a real challenge for national health systems. The need for dedicated and specifically trained personnel must deal with the modular management of the dual care pathway: one for positive and negative COVID-19 patients, and the other dedicated to management for fire injuries.[11] The data on the use of enzymatic debridement on COVID-19–positive patients are poorly

Table 3. The InflammationIndex

Patient	PCT (ng/mL)	Colonna3	Colonna4	PCR (mg/mL)	Colonna6	Colonna7	Fibrinogen (mg/dL)	Colonna1	Colonna2
	T0	T1 (48 h)	T2 (72 h)	T0	T1 (48 h)	T2 (72 h)	T0	T1 (48 h)	T2 (72 h)
P1	0.1	0.5	0.3	102	130	122	630	600	594
P2	0.3	0.8	0.5	143	165.58	118.41	462	527	629
P3	0.8	0.5	0.5	180.07	110.02	107	662	680	600
P4	0.6	1.2	1.3	186	294.19	180	760	709	699
P5	0.1	0.4	0.2	166.51	200.59	154.7	375	642	527
Mean	0.38	0.68	0.56	143.6	130	136.42	577.8	631.6	609.8
Median	0.3	0.5	0.5	143	130	122	630	642	600
Q1	0.1	0.5	0.3	122.5	130	118.41	462	600	594
Q3	0.6	0.8	0.5	164.5	130	154.7	662	680	629
IQR	0.5	0.3	0.2	42	0	36.29	200	80	35
Q1	First quartile								
Q3	Third quartile								
IQR	Interquartile range								

PCR indicates polymerase chain reaction; PCT, procalcitonin.

documented in the literature, although suggested as a therapeutic approach.[12] Its practical use and the possibility of not resorting to surgical procedures have allowed an objective optimization of resources. In addition to the lack of human resources, the pandemic emergency has raised a further problem: the shortage of blood, blood products, and their rationalization.[13]

The use of enzymatic debridement in COVID-19–positive burn patients optimizes the treatment time; in fact, all patients were treated within 24 hours of admission to the BICU. The temporal factor is particularly important in reducing the risk of clinical complications in older and comorbid patients.[14] All patients came out negative for pathogenic bacterial colonies. In this case, there is evidence in the literature that using enzymatic debridement reduces blood loss with less use of blood bags and blood-derived products.[15] The study of SARS-CoV-2 infection has numerous lines of research, and various therapeutic approaches have been followed,[16–18] even for burned patients.[19] The study described by us is limited to a few cases; therefore, it is desirable to extend the research to a greater number of patients. We believe that the use of enzymatic debridement could be a valid therapeutic option in burn patients even with SARS-CoV-2 infection, and its use, when indicated, is safe and effective for the patient and optimizes the use of instrumental and human resources.

CONCLUSIONS

The side effects associated with the use of Nexobrid in SARS-CoV-2-positive burn patients were in line with those described in the product data sheet. The use of Nexobrid allowed early treatment of burn wounds.

Crescenzo Sala, MD
Via Amato n 27
Zip code 80053
Castellammare di Stabia (Na)
Napoli, Italy
E-mail: crescenzosala@hotmail.it

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