Critical Rounds
Vol 4 | Issue 43 | 2023

Critical Rounds Newsletter
VOL 4 | Issue 43 | 2023

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care.

This issue contains:

1. Evaluation of Prognostic Value of Lymphocyte Subpopulations in Sepsis Patients with ICU-Acquired Infections.

2. Accuracy of bedside sonography for the identification of cerebral hypertension in the emergency department.

3. Study on relationship between Variations in Plasma Metabolism and Clinical Results of Sepsis.

4. A case report of Multiple organ failure due to atypical drug-induced hypersensitivity syndrome treated by combined acute blood purification.

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in
free to contact us at medicalservices@microlabs.in
Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

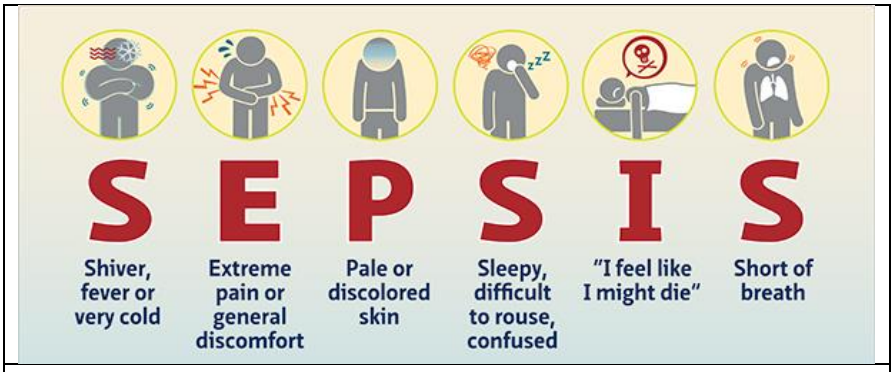
Critical Rounds
Vol 4 | Issue 43 | 2023

1. Evaluation of Prognostic Value of Lymphocyte Subpopulations in Sepsis Patients with ICU-Acquired Infections

Introduction:

Sepsis is a potentially fatal organ failure caused by an unbalanced host response to infection. According to the most recent data on global illness burden, approximately 50 million people globally experienced sepsis in 2017, resulting in 11 million deaths[1].Although advances in sepsis therapy, sepsis-induced immunosuppression can result in infections in early-survivor ICU patients, resulting in longer hospital stays and greater long-term mortality. Reduced lymphocyte counts, including CD4+ T cells, CD8+ T cells, CD19+ B cells, and CD16/56+ NK cells, characterise immunosuppression in sepsis. These cells are key in the dysregulated immune response seen in critical disease, including sepsis. Another method for predicting individuals with a poor prognosis for sepsis is to monitor lymphocyte subpopulations [2]. The purpose of this study was to investigate if lymphocyte subpopulations might predict ICU-acquired infections in patients admitted to the critical care unit for sepsis.

When sepsis patients are admitted to the hospital, lymphocyte subpopulations, especially CD3+ and CD4+ T cells, are examined. These findings may be helpful for identifying patients who are at a high risk of infection while staying in the critical care unit.



Sepsis

Methods:

This retrospective cohort study gathered data on 188 sepsis patients admitted to ICU on peripheral blood lymphocyte subpopulations (CD3+ T cells, CD4+ T cells, CD8+ T cells, CD16+CD56+ NK cells, and CD19+ B cells). Patients' clinical information, which included their medical history, the number of organ failures, ratings of the severity of their illnesses, and the characteristics of infections acquired up in the intensive care unit, was assessed. The incidence of ICU-acquired infections was the primary outcome, whereas in-hospital mortality, death after 28 days, and the length of ICU care were the secondary outcomes.

Results:

According to study findings, the counts of lymphocyte subpopulations were considerably lower in patients who got an infection in the ICU vs those who did not. The disease severity scores (The Sequential Organ Failure Assessment (SOFA) score OR: 1.69, 95% CI: 1.41-2.02; APACHE II OR: 1.26, 95% CI: 0.17-1.36), history of immunosuppressive use (OR: 2.41, 95% CI: 1.01-5.73), and lymphocyte subpopulations (CD3+T cells OR: 0.60, 95% CI: 0.51-0.71; CD4+T cells OR: 0.51, 95% CI: 0.41-0.63; CD8+T cells OR: 0.32, 95% CI: 0.22-0.47; CD16/CD56+NK cells OR: 0.41, 95% CI: 0.28-0.59; CD19+B cells OR: 0.52, 95% CI: 0.37-

0.75) were linked to infections acquired in ICUs showed by univariate analysis. APACHE II, CD3+T cells, and CD4+T cells were shown to be independent risk factors for ICU-acquired infections by multifactor logistic regression analysis, with APACHE II (OR: 1.25, 95% CI: 1.13-1.38), CD3+T cells (OR: 0.66, 95% CI: 0.54-0.81), and CD4+T cells (OR: 0.64, 95% CI: 0.50-0.82) showing significant associations (table 1).

Table I findings of the univariate and multivariate analysis of infections acquired in ICUs

Variable	Univariable		Multivariable	
	OR（95CI%）	P value	OR（95CI%）	P value
Age (1 year increase)	1.02 (0.99, 1.04)	0.1360	-	-
Male Gender	1.25 (0.66,2.36)	0.4866	-	-
Sofa	1.69 (1.41, 2.02)	<0.0001	-	-
APACHE II	1.26 (1.17, 1.36)	<0.0001	1.25 (1.13,1.38)	<0.0001
Sepsis shock	12.91 (5.45, 30.60)	< 0.0001	-	-
The number of organ failures	3.37 (2.25, 5.05)	< 0.0001	-	-
History of immunosuppressant use	2.41 (1.01, 5.73)	.0469	-	-
the presence of invasive medical procedures	9.23 (4.65, 18.33)	< 0.0001	-	-
CD3 +T cells, per 100/ul increase	0.60 (0.51, 0.71)	< 0.0001	0.66 (0.54,0.81)	<0.0001
CD4 +T cells, per 100/ul increase	0.51 (0.41, 0.63)	< 0.0001	0.64 (0.50,0.82)	0.003
CD8 +T cells, per 100/ul increase	0.32 (0.22, 0.47)	< 0.0001	-	-
CD4+/CD8+ratio	1.25 (1.05, 1.48)	0.0128	-	-
CD19 + B cells, per 100/ul increase	0.52 (0.37, 0.75)	0.0003	-	-
CD16/56 + NK cells, per 100/ul increase	0.41 (0.28, 0.59)	< 0.0001	-	-

Discussion:

In this current investigation, CD3+ T cells and CD4+ T cells were found to be distinct risk factors for ICU-acquired infections in patients with sepsis. Additionally, they showed a substantial negative predictive value when the numbers of these lymphocyte subpopulations went below particular thresholds, indicating that they may be utilised to predict the onset of such illnesses [(2)]. Lymphocytes, a key component of the immune system, perform a variety of functions in sepsis pathogenesis. According to previous studies by Polilli E et al and Jensen I et al showed that the quantity and function of lymphocyte subpopulations might be abnormal

in sepsis patients. CD4+ T cells and CD8+ T cells, in particular, are important lymphocyte groups whose numbers and functions are linked to sepsis prognosis [3,4].

Conclusion:

The results of the present research showed that lymphocyte subpopulations, such as CD3+ and CD4+ T cells, measured in sepsis patients upon hospital admission may be useful indicators for identifying those at higher risk of infection during their stay in the critical care unit.

References:

1. Pei F, Yao RQ, Ren C, Bahrami S, Billiar TR, Chaudry IH, Chen DC, Chen XL, Cui N, Fang XM, Kang Y. Expert consensus on the monitoring and treatment of sepsis-induced immunosuppression. Military Medical Research. 2022 Dec;9(1):1-8.
2. gang Zhuang Y. Prognostic Significance of Lymphocyte Subpopulations for ICU-acquired Infections in Sepsis Patients: A Retrospective Study. Journal of Hospital Infection. 2023 Jul 1.
3. Polilli E, Esposito JE, Frattari A, Trave F, Sozio F, Ferrandu G, et al. Circulating lymphocyte subsets as promising biomarkers to identify septic patients at higher risk of unfavorable outcome. BMC Infect Dis 2021;21.
4. Jensen IJ, Sjaastad FV, Griffith TS, Badovinac VP. Sepsis-induced T cell immunoparalysis: the ins and outs of impaired T cell immunity. The Journal of Immunology. 2018 Mar 1;200(5):1543-53.

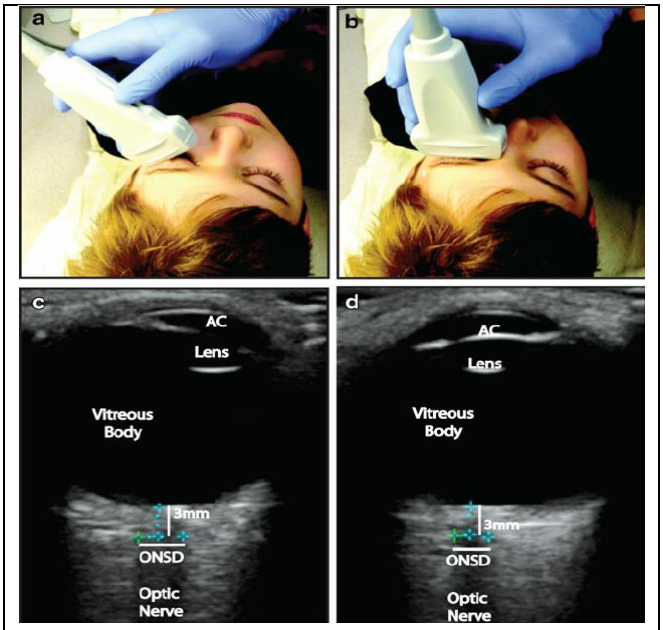
Critical Rounds
Vol 4 | Issue 43 | 2023

2. Accuracy of bedside sonography for the identification of cerebral hypertension in the emergency department.

Introduction:

With a threshold of 5.5 mm, the Ultrasound measurement of the diameter of the optic nerve sheath (US ONSD) might be used safely in the emergency department to rule out EICP in patients with traumatic and non-traumatic brain damage.

Ultrasound measurement of the diameter of the optic nerve sheath (US ONSD) has been proposed as a method of detecting increased intracranial pressure (EICP), however the appropriate threshold is unknown[1]. Increased intracranial pressure (ICP) may be caused by a variety of aetiologies. Idiopathic intracranial hypertension (IIH) is a common reason for this condition assessment at the bedside. Direct measurement using opening pressure during lumbar puncture or with external ventricular drainage is the gold standard for elevated ICP detection, which is both time consuming and risky. One new option is to measure the ONSD using head computed tomography (CT) or ultrasonography. A meta-analysis of the literature on CT and ocular ultrasonography for the detection of ICP found that ultrasound outperforms CT in terms of diagnostic accuracy for increased ICP. Both CT and ultrasound measurements of ONSD have been correlated with measured ICP via ICP monitoring[2]. The aim of the study was to assess the precision of US ONSD to head computed tomography (CT) in differentiating between EICP with traumatic and non-traumatic origins.



Sonographic method for assessing the diameter of the optic nerve sheath

Methods:

This was a prospective, cross-sectional, multicenter research. The US ONSD was used to evaluate patients who presented to the emergency room with suspected traumatic or non-traumatic brain injury and were sent for an urgent head CT. A positive US ONSD of ≥5.5 mm was considered. Sensitivity, specificity, positive and negative predictive values, and positive and negative probability ratios were determined for three ONSD cut-offs: 5.5 (primary outcome), 5.0, and 6.0 mm. The area under the receiver operating characteristic (ROC) curve was computed after producing the ROC curve.

Results:

Ninety-nine individuals were included in the study. The CT was positive in 15(15%) of cases, while the US ONSD was positive in all of them, obtaining 100% sensitivity [95% confidence interval (CI) 78; 100] and 100% negative predictive value (95% CI 79; 100). The US ONSD had a positive result in 68(69%) of cases compared to the CT's 84(85%) negative results, with a specificity of 19% (95% CI 11; 29) and positive predictive value of 18% (95% CI 11; 28) (table 1). In patients with traumatic and non-traumatic brain injury, the US ONSD with a 5.5 mm cut-off may be utilised safely in the ED to rule out EICP.

Table 1. Diagnostic accuracy for ONSD ≥0.55

	CT +	**CT -**	**Total**
US +	15	68	83
US -	0	16	16
Total	15	84	99

US, ultrasound; CT, computed tomography.

Discussion:

Using the head CT as the reference standard, the current investigation found that the US ONSD, with a cut-off of 5.5 mm, has 100% sensitivity and 19% specificity for detecting EICP. In numerous circumstances and populations, strong sensitivity (100%) with poor specificity was demonstrated, and validated in met analyses, although a precise cut-off was not clear [(1)]. In a similar study by Robba et al, presented that US ONSD measurement was compared to ICP using invasive equipment and discovered that US ONSD had high diagnostic accuracy [(3)]. In a similar study by Kim et al discovered that US ONSD >5.0 mm had a sensitivity of 99% and a specificity of 73% in i ncreased ICP detection shown by CT, suggesting that US ONSD may be used to diagnose EICP in adult patients [(4)].

Conclusion:

In patients with traumatic and non-traumatic brain injury, the US ONSD with a 5.5 mm cut-off may be utilised safely in the ED to rule out EICP. A negative US ONSD may help emergency physicians to rule out EICP in low-risk patients in situations when resources are few, delaying the head CT.

References:

1. Busti C, Marcosignori M, Marchetti F, Batori G, Giovenali L, Corea F, Calabrò G, Monti M, Germini F. Accuracy of bedside sonographic measurement of optic nerve sheath diameter for intracranial hypertension diagnosis in the emergency department. Emergency Care Journal. 2023 Jun 23;19(1).
2. Wilson CL, Leaman SM, O'Brien C, Savage D, Hart L, Jehle D. Novice emergency physician ultrasonography of optic nerve sheath diameter compared to ophthalmologist fundoscopic evaluation for papilledema. Journal of the American College of Emergency Physicians Open. 2021 Feb;2(1):e12355.
3. Robba C, Santori G, Czosnyka M, Corradi F, Bragazzi N, Padayachy L, Taccone FS, Citerio G. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive care medicine. 2018 Aug;44:1284-94.

4. Kim SE, Hong EP, Kim HC, Lee SU, Jeon JP. Ultrasonographic optic nerve sheath diameter to detect increased intracranial pressure in adults: a meta-analysis. Acta Radiologica. 2019 Feb;60(2):221-9.

Critical Rounds
Vol 4 | Issue 43 | 2023

3. Study on relationship between Variations in Plasma Metabolism and Clinical Results of Sepsis

Introduction:

Sepsis is a severe healthcare issue that affects millions of individuals worldwide. Patients who develop the disease have a significant death rate (at least one in every four). Early detection and treatment of the condition improves results significantly. Sepsis is a condition in which patients develop an inflammatory response to an infection that damages their own organs and results in organ dysfunction[(1)]. Even though medical breakthroughs, sepsis continues to be a major worldwide health issue, with an estimated 48.9 million cases and 11 million deaths per year. The Acute Physiology and Chronic Health Evaluation (APACHE) II score is now used in ICUs to determine the severity of hospitalised patients . This technique, however, has several limitations and does not predict prognosis in individuals who's disease peak is not observed during the first 24 hours after arrival [(2)]. The purpose of this study was to evaluate dynamic lipid metabolomics and their relationship with septic immunological response and clinical outcomes in sepsis.

The relationship between lipid changes and lymphocyte subsets indicates that lipid metabolism is implicated in the immunological disturbance that occurs during sepsis.

Methods:

This prospective cohort study included patients with sepsis who satisfied the Sepsis 3.0 criteria. Plasma samples were taken on 1st and 7th day of hospitalisation, and patients were subjected to liquid chromatography with tandem mass spectrometry. The research included 40 patients, with 24 (60%) of them being men.

Results:

The patients included had a median age of 81 (68-84) years. A primary infection site of the lung was found in 141 (77.5%) of the patients. Participants were divided into two groups depending on their 28-day survival status: survivors (25 instances) and nonsurvivors (15 cases). Finally, 113 lipids were found in plasma samples on D 1 and D 7, with 42 lipids being the most prevalent in plasma samples. Lysophosphatidylcholine (LysoPC) (16: 0, 17: 0, 18: 0), and 18:1 Sphingomyelin (SM) lipid expression levels were substantially lower in the nonsurvival group on D7–D1 than in the survival group (p= 0.05). According to the correlation analysis, the percentage of CD3+ T cells in the D7-D1 was favourably correlated with the D7-D1 LysoPC levels of 16:0 (r = 0.367, p=0.036), 17:0 (r = 0.389, p=0.025), and 18:0 (r = 0.472, p=0.006). Study analysed the lymphocyte subsets on D1 and D7 in survivor and nonsurvivor groups to reveal the correlation between changes in

lipid metabolism and lymphocyte disturbance in sepsis, and found that there were significant differences in CD3+ T lymphocytes in the blood on D1 and D7 in both survivor and nonsurvivor groups (table 1).

Table 1: D1 and D7 immune cell subgroups in sepsis patients.

Variable (%)	Survivors ($n = 25$)	Nonsurvivors ($n = 15$)	p-value
D1			
$CD3^+T$	66.68 (60.73–72.89)	46.75 (41.92–62.88)	0.007*
$CD4^+T$	57.48 (45.25–66.51)	66.77 (56.28–71.22)	0.093
$CD8^+T$	38.58 (27.22–48.92)	27.64 (23.87–34.99)	0.081
NKT	6.77 (3.48–9.65)	3.28 (2.14–6.28)	0.028*
NK	18.52 (11.79–32.85)	24.99 (15.55–36.18)	0.426
B	9.16 (5.09–18.69)	13.72 (8.04–32.46)	0.166
Neu	83.89 (68.46–87.61)	85.94 (74.54–93.37)	0.361
Monocyte	3.92 (2.83–6.26)	3.94 (1.82–6.79)	0.952
MDSCs	0.51 (0.17–3.65)	0.95 (0.34–4.17)	0.469
D7	*Survivors ($n = 25$)*	*Non-survivors ($n = 8$)*	*p-value*
$CD3^+T$	72.23 (61.91–77.52)	47.40 (35.90–58.93)	0.000*
$CD4^+T$	57.74 (50.80–62.87)	48.23 (31.83–72.79)	0.298
$CD8^+T$	37.63 (23.85–42.07)	37.20 (20.43–48.17)	0.853
NKT	7.38 (3.84–10.27)	5.53 (2.92–7.26)	0.334
NK	15.87 (8.99–22.31)	20.47 (13.16–35.76)	0.176
B	8.14 (5.00–16.44)	13.73 (5.07–35.23)	0.352
Neu	79.38 (66.92–84.84)	89.58 (76.13–92.94)	0.074
Monocyte	3.68 (2.10–5.95)	4.03 (1.86–5.48)	1.000
MDSCs	0.72 (0.21–3.16)	0.17 (0.11–4.22)	0.344

Values are expressed as n (%) or median (25%–75%) unless otherwise stated.

Discussion:

Study explored differences in lipid metabolism between surviving and nonsurviving sepsis patients depending on their 28-day survival. Plasma contains 42 lipids, including. Lysophosphatidylcholine (LysoPC), Phosphatidylcholines (PC), Phosphatidylethanolamine (PE), lysophosphatidylethanolamine (LysoPE), lysophosphatidylinositol LysoPI, Sphingomyelin (SM), and ceramide. In current investigation, the nonsurvivor group's LysoPC concentrations decreased significantly by D7. In current investigation, lower LysoPC levels in the nonsurvivor group were linked to sepsis-induced immunological overreaction, which might contribute to LysoPC consumption [(2)]. A study by S. H. Law et al showed that the consistently low LysoPC levels in sepsis patients are caused mostly by abnormalities in metabolic balance [(3)].

Conclusion:

Study findings suggest that regular monitoring of lipids in plasma LysoPC and SM, (sphingomyelin) may assist to predict the outcome of sepsis patients. Furthermore, the relationship between lipid changes and lymphocyte subsets indicates that lipid metabolism has a role in the immunological disturbance that occurs during sepsis.

References:

1. Mecatti GC, Messias MC, de Oliveira Carvalho P. Lipidomic profile and candidate biomarkers in septic patients. Lipids in Health and Disease. 2020 Dec;19(1):1-9.

2. Li X, Yin Z, Yan W, Wang M, Chang C, Guo C, Xue L, Zhou Q, Sun Y. Association between Changes in Plasma Metabolism and Clinical Outcomes of Sepsis. Emergency Medicine International. 2023 Jun 13;2023.

3. Law SH, Chan ML, Marathe GK, Parveen F, Chen CH, Ke LY. An updated review of lysophosphatidylcholine metabolism in human diseases. International journal of molecular sciences. 2019 Mar 6;20(5):1149.

Critical Rounds
Vol 4 | Issue 43 | 2023

4.A case report of Multiple organ failure due to atypical drug-induced hypersensitivity syndrome treated by combined acute blood purification.

Introduction:

Drug-induced hypersensitivity syndrome (DIHS) is an extreme drug reaction that can reactivate herpesviruses like human herpesvirus 6 and cause organ damage as well as symptom flare-ups[1]. Drugs that might cause it include carbamazepine, phenytoin, phenobarbital, zonisamide, allopurinol, salazosulfapyridine, diaphenyl sulfone, mexiletine, and minocycline. It has a significant mortality rate (10-20%). The symptoms of DIHS can be managed by stopping the suspected medicines, using systemic steroids, using steroid pulse therapy in extreme instances, and receiving supportive care, such blood purification for organ damage[2]. In this case study, blood purification treatment was used to successfully treat a patient who had suffered multiple organ failure as a result of DIHS.

Multiorgan failure resulting from atypical Drug-induced hypersensitivity syndrome (DIHS) that is challenging to identify may be successfully treated with n hemodiafltration + plasma exchange; (HDF+PE).

Case Presentation:

A 60 years male patient was admitted to hospital with autoimmune encephalitis. Steroid pulse treatment, acyclovir, levetiracetam, and phenytoin were used to treat the patient. He began exhibiting fever (≥38 °C) on the 25th day, along with miliary-sized erythema on the limbs and trunk, followed by erosions. Linezolid was substituted for the suspected substance vancomycin (VCM) on day 3. However, as his skin rash began to expand on day 5 (Fig. 1A, right panels), steroid pulse therapy (1000 mg/day for 3 days) was initiated. In addition, his respiratory state rapidly deteriorated, and NPPV (noninvasive positive pressure ventilation) was instituted for him. Levetiracetam and phenytoin were subjected to drug-induced lymphocyte stimulation tests (DLST) on day 5. On day six, the NPPV was no longer able to maintain the patient's oxygenation. His Glasgow Coma Scale score was 14 upon admission to the intensive care unit (ICU) (eye, verbal, and motor scores of 4, 4, and 6 respectively). Upon physical

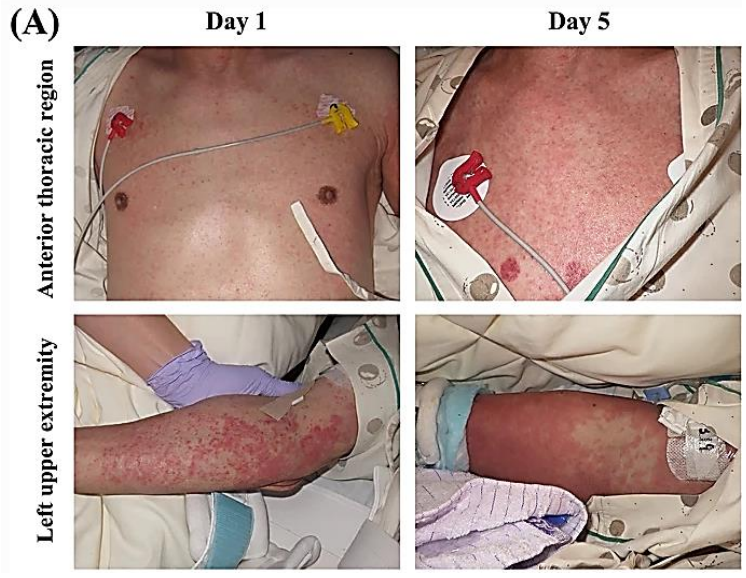


Fig. 1 Skin examinations on days 1 and 5, as well as a chest radiograph and CT scan. The anterior thoracic region and upper left extremities have lesions. On day 1, erythema of miliary size was noted on the limbs and trunk (A). On day 5, the skin rash had become larger.

examination, the patient's body temperature was measured at 38.5 °C, and other findings included tachypnea (respiratory rate: 20 breaths/min), a heart rate of 103 bpm, and a blood pressure reading of 129/57 mmHg. He was brought to the critical care unit for ventilatory treatment on the 30th day as his health continued to worsen. Following admission to the intensive care unit, the patient had a three-day course of therapy for a severe drug eruption, severe pneumonia, or acute respiratory distress syndrome using intravenous immunoglobulin 5.0 g/day, meropenem, and sivelestat.He start receiving hemodiafiltration (HDF) the next day for his acute renal damage after experiencing multi-organ failure the day before. He did not match the diagnostic requirements for DIHS or SJS/toxic epidermal necrolysis, despite having hepatic impairment and the presence of atypical lymphocytes. He thus received a diagnosis of severe drug eruption-induced multi-organ failure and had a 3-day plasma exchange (PE) therapy in addition to HDF. The patient was subsequently identified as having atypical DIHS. The skin rash started to go away once blood purification therapy was started; also, the organ damage improved, with a steady rise in urine production. On the 101st day, the patient was eventually withdrawn from the ventilator and sent to the hospital.

Discussion:

DIHS and Stevens-Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) are examples of severe cutaneous adverse responses to medicines. There are seven and five diagnostic criteria for DIHS and SJS/TEN, respectively [(2)]. Even though seven diagnostic criteria for DIHS and five diagnostic criteria for SJS/TEN but still Perello MI et al described both DIHS and SJS/TEN cause severe systemic symptoms; also, there may be overlapping cases, which makes identification difficult in certain situations [(3)].

Conclusion:

Hemodiafltration combined with plasma exchange (HDF+PE) may successfully treat multi-organ failure caused by difficult-to-diagnose atypical DIHS.

References:

1. Korekawa A, Nakajima K, Fukushi K, Nakano H, Sawamura D. Three cases of drug-induced hypersensitivity syndrome associated with mRNA-based coronavirus disease 2019 vaccines. The Journal of dermatology. 2022 Jun;49(6):652-5.
2. Oiwa H, Yoshida S, Okada H, Yasunishi M, Kamidani R, Suzuki K, Miyake T, Doi T, Shimohata T, Ogura S. Atypical drug-induced hypersensitivity syndrome with multiple organ failure rescued by combined acute blood purification therapy: a case report. International Journal of Emergency Medicine. 2023 May 9;16(1):33.
3. Perelló MI, de Maria Castro A, Nogueira Arraes AC, Conte S, Lacerda Pedrazzi D, Andrade Coelho Dias G. Severe cutaneous adverse drug reactions: diagnostic approach and genetic study in a Brazilian case series. Eur Ann Allergy Clin Immunol. 2022 Sep;54(5):207-17.