International Journal of Research in Dermatology
Ambarita W et al. Int J Res Dermatol. 2024 Mar;10(2):106-109
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20240398

Case Report

Toxic epidermal necrolysis in a 37-year-old man with pneumonia: a case report

Wiryanti Ambarita[1]*, Sri Lestari[2], Anwar Fuadi[3], Ali Raza[4]

[1]Firdaus Hospital, North Jakarta, Indonesia
[2]Department of Dermatology, Firdaus Hospital, North Jakarta, Indonesia
[3]Puri Cinere Hospital, Depok, Indonesia
[4]Glaxo Smith Kline (GSK), Worldwide

Received: 15 January 2024
Accepted: 09 February 2024

***Correspondence:**
Dr. Wiryanti Ambarita,
E-mail: wiryantiambarita@gmail.com

ABSTRACT

Apart from allergy, TEN can be caused by infection, such as *M. pneumoniae* infection. Aim of this case report is to present clinical manifestations of TEN with pneumonia. A 37-year-old man, came to the emergency room with cough and fever since 5 days before hospitalized. The patient received intravenous ceftriaxone (with negative skin test), paracetamol, and n-acetylcysteine. Three days earlier, the patient had gone to primary health center and got paracetamol and n-acetylcysteine. On the first day of treatment, erythematous macules were seen on the anterior and posterior thoracic region, also the patient had sore throat and dysphagia, treated with intravenous dipenhydramine, mefenamic acid, and cetirizine. On the following day, the lesions expanded with multiple bullae on the anterior and posterior thoracic region, and erosion on the labia (BSA 28%). Intravenous methylprednisolone was administered, also Kloderma® and Ikagen® cream, and Kenalog®. Mefenamic acid and paracetamol were discontinued. On the third day of treatment, the lesions expanded (BSA 38%) and the next day, BSA reached 91.5%. The SCORTEN was 1. The patient was referred for treatment at the burn center and IVIg therapy. After the eleventh day of treatment at the referral hospital, the patient was fully recovered. The managements of TEN are stop suspected drugs, wound care, fluid therapy, systemic corticosteroids, and IVIg therapy. Appropriate management of TEN gives complete recovery to patient.

Keywords: TEN, Pneumonia, SCORTEN

INTRODUCTION

In 1956, Lyell introduced term toxic epidermal necrolysis (TEN). TEN is an acute, life-threatening mucocutaneous reaction characterized by extensive necrosis and detachment of epidermis and mucosal epithelium.[1] A global population-based study reported that incidence of TEN is estimated to be 0.4-1.2 per 1 million population with mortality rate of 34%. Frey et al estimated that Asian patients have 2 times risk of TEN when compared to Caucasian patients. Yokohama city university hospital reported that mortality rate of TEN was 14.3%.[2,3]

There are 4 categories of drugs that can potentially cause TEN, namely anti-epileptics/ anti-psychotics, antibiotics/ anti-viral drugs, non-steroidal anti-inflammatory drugs (NSAID), and allupurinol and others. Some drugs that have high potential to trigger TEN are antibiotics such as sulfonamide and cephalosporin groups, NSAID, acetaminophen (paracetamol).[1,4]

Pneumonia can be defined as a pulmonary infection that characteristically involves the alveolar space and is accompanied by an inflammatory response. Pneumonia is classified according to the patient's location at the time of

infection. Infections arising in a hospital setting are called hospital acquired pneumonia (HAP), while community accquired pneumonia (CAP) is acquired from an out-of-hospital environment or in the community. The definitive diagnosis of pneumonia is based on symptoms and signs of respiratory tract infection, radiologic changes, identification of the suspected pathogen, and treatment response, or clinical course.[5]

The management of pneumonia is by administering antibiotics based on the germ pattern in a neighborhood or region. Ceftriaxone is recommended as a first-line antibiotic treatment (with the addition of macrolides) for adults hospitalized with CAP. But on the other hand, ceftriaxone also has the potential to cause TEN.[6,7]

This case report describes 37-year-old male with diagnosis of pneumonia who developed TEN after being hospitalized and receiving treatment. It is hoped that this case report can provide clinical manifestations of TEN patients with pneumonia.

CASE REPORT

A 37-year-old man was admitted to the hospital with complaints of cough with phlegm for 5 days before admission. Cough with phlegm was continuously and increasingly aggravated. Cough with phlegm was also accompanied by fever. Three days before entering the hospital, the patient sought treatment at the primary health center and was given paracetamol 500 mg/8 hours and n-acetylcysteine 200 mg/8 hours. Patient felt that his complaints had not improved, so he decided to go to the hospital 3 days later. History taking, physical examination, and supporting examination were performed to help make the diagnosis. Patient was consulted to pulmonary division, then diagnosed with pneumonia and hospitalized. In the emergency department (ED), patient received NaCl 0.9% infusion therapy 20 drops per minute, intravenous ceftriaxone 2 grams/24 hours (with negative skin test), paracetamol 500 mg/8 hours, and n-acetylcysteine 200 mg/8 hours.

On the first day of treatment, patient complained of itching and erythematous macules in the anterior and posterior thoracic regions. In addition, the patient also complained sore throat and dysphagia. The patient was given additional therapy of intravenous diphenhydramine 10 mg/8 hours, cetirizine 10 mg/24 hours, and mefenamic acid 500 mg/8 hours, but the complaints were not getting better, aggravated by fever and skin blisters. Patient was given intravenous dexamethasone 5 mg/24 hours to relieve his complaints.

On the second day of treatment, the complaints worsened. on the physical examination, there were ulcers on the anterior and posterior thoracic regions, as well as erosions on the labia (BSA 28%). The patient was then consulted dermatovenereology division and diagnosed with SJS/TEN caused by suspected mefenamic acid or paracetamol. The patient received NaCl 0.9% compress therapy 20 minutes/12 hours, methylprednisolone 62.5 mg/12 hours (intravenous), Kloderma® cream/12 hours, Ikagen® cream/12 hours, and Kenalog® (oral base)/12 hours. At the same time, mefenamic acid and paracetamol were discontinued.

On the third day of treatment, the lesion extended to the colli region. In the anterior and posterior thoracic region, multiple erythematous and hyperpigmented macules were seen, accompanied by multiple bullae. On the labia, there were erosions (BSA 37%). On the fourth day of treatment, the lesions extended to almost the entire body (BSA 91.5%) and epidermolysis was seen on the posterior thoracic region. The dermatovenereology division suggested referral for further treatment at the burn center and IVIg therapy. On January 30th, 2023, the patient was referred to Suliyanti Saroso National Infection Center Hospital. During 11 days of treatment there, the patient was diagnosed with TEN, pneumonia, and blepharoconjunctivitis. The patient received 1000 cc NaCl 0.9% and Bfluid 500 cc/24 hours, NaCl 0.9% compression therapy 20 minutes/12 hours, intravenous ceftriaxone 2 grams/24 hours, intravenous methylprednisolone 62,5 mg/8 hours, gentamicin ointment/12 hours, gentamicin ointment/12 hours (for eyelids) and Cendo Lyteers 6 drops/24 hours on the right and left eyes. The patient was discharged after the eleventh day of treatment completely healed lesions (BSA 0%) and generalized hyperpigmentation.

Figure 1 (A-C): Lesions to the facial, anterior thoracic, superior and inferior extremity regions. Epidermolysis to the posterior thoracic region.

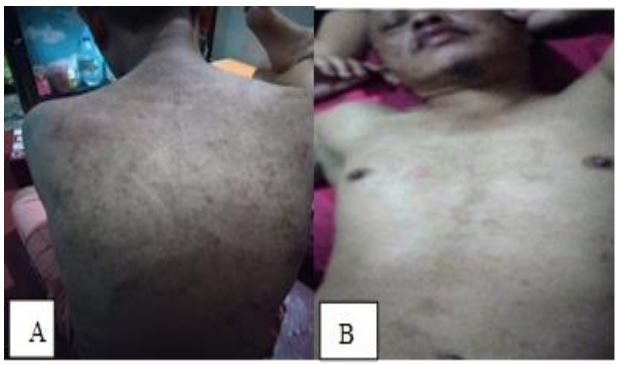

Figure 2 (A and B): Hyperpigmented lesions on the posterior thoracic, anterior thoracic, and facialis regions after 11 days of treatment at referral hospital.

DISCUSSION

Initial symptoms of TEN are usually nonspecific and may precede skin manifestations by several days (1-3 days), including mucosal pain, headache, rhinitis, malaise, cough, sore throat, and myalgia. TEN signs and symptoms generally occur 4 to 28 days after drug administration and may last up to 1 week. After this period, erythematous maculo-papular lesions with irregular shape or similar to morbilliform rash, urticaria, purpura or targetoid on the skin appear suddenly and symmetrically. The lesions usually start on the body and extend to the face, neck and extremities, as well as palms and soles. Maculo-papular lesions become purplish or blackish in color and tend to develop into flaccid blisters and coalesce as atypic and easily ruptured targetoid lesions, resulting in epidermal detachment that is easily infected. Body surface area involvement in TEN is more than 30%.[8] In this case, the patient had a cough and fever for 5 days before hospitalization. Then on the first day of treatment, the patient complained of sore throat and dysphagia. Skin lesions began to appear from the first day of treatment, on the form of erythematous macules in the anterior and posterior thoracic regions. On the next day of treatment, the lesions became more progressive. Bullae began to appear on the same region accompanied by erosion and crustation of the labia with 37% BSA affected. On the third treatment day, the lesion expanded to 37%, and on the fourth treatment day, the affected BSA reached 91.5% and epidermolysis began to appear on the posterior thoracic region.

The most common etiology leading to the onset of TEN is allergic reactions to drugs. Determining the inducing drug is complicated. Identification of the inducing drug can be done by looking at the chronology of drug administration and the ability of the drug to cause TEN. Some drugs that have a high potential to trigger TEN are antibiotic drugs such as sulfonamide and cephalosporin groups, NSAID, and acetaminophen (paracetamol).[4,9,10] The patient received paracetamol for 3 days before admission to the hospital when the patient sought treatment at the primary health center. Then at the hospital, the patient received mefenamic acid on the first day of treatment. Both drugs (mefenamic acid and paracetamol) are suspected to be the trigger for TEN in this patient.

In addition to allergic reactions, TEN can also be caused by infections such as *Herpes Simplex Virus* (HSV) infection, and *M. pneumoniae*, food, and vaccinations. Based on the research to pediatric patients affected by SSJ and TEN for the period 2000-2007 at the Hospital for Children Boston, USA, it was found that the cause of SSJ and TEN in 17 pediatric patients (31%) out of a total of 55 pediatric patients was due to infection. The infections were acute infections caused by *M. pneumoniae* (22%) and HSV infection (9%).[11,12] In this case, pneumonia is also a possible precipitant of TEN, although the incidence is lower than TEN caused by drug allergy.

The managements of TEN are basically to stop the administration of precipitating drugs, wound care, fluid therapy, systemic corticosteroids, and IVIg therapy. Several previous studies have shown that systemic corticosteroids can reduce the risk of mortality in patients when be given in the early stages of the disease.[13,14] In this patient, suspected inducing medicines TEN (mefenamic acid and paracetamol) were stopped on second day of treatment, when the skin lesions started to appear. The patient was treated with steroid ointment (Kloderma® cream) and topical antibiotics (Ikagen® cream) to minimize the infection. The patient was also given fluid therapy, NaCl 0,9% 20 drops per minute and intravenous methylprednisolone 62,5 mg/12 hours, where the recommended dose of methylprednisolone for TEN management is 1-2 mg/kgBB/day. In this case, the patient was referred to Sulianti Saroso National Infection Center Hospital for IVIg therapy, but IVIg was not given because the patient had experienced clinical improvement during follow-up care at Sulianti Saroso National Infection Center Hospital.

Determining the prognosis of SSJ and TEN patients is important. Prognosis assessment with SCORTEN should be done within 24 hours of hospital admission. The higher the SCORTEN, the higher the risk of mortality. SCORTEN is assessed by age, blood pressure, malignancy, affected body surface area, serum urea level, serum bicarbonate level and serum glucose level.[15] SCORTEN in this patient is 1.

CONCLUSION

It is important to recognize the signs and symptoms of TEN as early as possible so that patients receive appropriate management and health care professionals can provide a complete cure for patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Allanoure LJJ. Epidermal necrolysis In: Fritzpatrick's Dermatology General Medicine. 8 ed. Goldsmith LA KS, Gilcherst BA, , Paller AS LD, Wolf K, editors. New York: Mc Graw Hill. 2013.
2. Watanabe TGH, Saigusa Y, Takamura N, Naoko T, Yuko W, Yumiko Y et al. Mortality and risk factors on admission in toxic epidermal necrolysis: A cohort study of 59 patients. Allergol Int. 2021;70(2):229-34.
3. Frey NJJ, Bodmer M, Michael B, Andreas B, Susan SJ, Christoph RM et al. The Epidemiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in the UK. J Invest Dermatol. 2017;137(6):1240-7.
4. Wang Y, Chen CB, Tassaneeyakul W, Yoshiro S,

Michiko A, Siew EC et al. The Medication Risk of Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis in Asians: The Major Drug Causality and Comparison With the US FDA Label. Clin Pharmacol Ther. 2019;105(1):112-20.
5. Lim WS. Pneumonia-Overview. Encyclopedia Respiratory Med. 2022:185-97.
6. Guz DBM, Steinberg Y, Kozlovsky D, Gafter-Gvili A, Avni T. Ceftriaxone versus ampicillin for the treatment of community-acquired pneumonia: A propensity matched cohort study. Clin Microbiol Infect. 2023;29(1):70-6.
7. Rajan AK. Ceftriaxone induced Steven Johnson syndrome: A case report. Int J Pharmaceutical Sci Rev Res. 2020;65:124-7.
8. Dodiuk-Gad RP, Chung WH, Valeyrie-Allanore L, Neil HS. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: An Update. Am J Clin Dermatol. 2015;16(6):475-93.
9. Fitriana A EA, Hidayati AN. Gambaran Klinis Steven Johnson Syndrome dan Toxic Epidermal Necrolysis pada Pasien Anak. Berkala Ilmu Kesehatan Kulit dan Kelamin Periodical Dermatol Venereol. 2018;30(2):102-10.
10. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. Orphanet J Rare Dis 2010;5(39):1-11.
11. Finkelstein YGS, Acuna P, George M, Pope E, Ito S. Recurrence and outcomes of Stevens-Johnson syndrome and toxic epidermal necrolysis in children. Pediatrics. 2011;128(4):723-28.
12. Sharma VKSG, Minz A. Stevens Johnson syndrome, toxic epidermal necrolysis and SJS-TEN overlap: A retrospective study of causative drugs and clinical outcome. Indian J Dermatol Venereol Leprol. 2008;78:238-40.
13. Morita K, Matsui, H., Michihata N, Kiyohide F, Hideo Y. Association of Early Systemic Corticosteroid Therapy with Mortality in Patients with Stevens–Johnson Syndrome or Toxic Epidermal Necrolysis: A Retrospective Cohort Study Using a Nationwide Claims Database. Am J Clin Dermatol. 2019;29:579-92.
14. Stella M, Cassano P, Bollero D, Clemente A, Giorio G. Toxic Epidermal Necrolysis Treated with Intravenous High-Dose Immunoglobulins: Our Experience. Dermatology. 2001;203(1):45-9.
15. Khalili B, Bahna SL. Pathogenesis and recent therapeutic trends in Stevens-Johnson syndrome and toxic epidermal necrolysis. Ann Allergy Asthma Immunolo. 2006;97(3):272-81.

Cite this article as: Ambarita W, Lestari S, Fuadi A, Raza A. Toxic epidermal necrolysis in a 37-year-old man with pneumonia: a case report. Int J Res Dermatol 2024;10:106-9.