

Case Report

Piperacillin/tazobactam induced toxic epidermal necrolysis and drug induced liver injury

Hardeep S. Deep*, Mohit Kumar, Barjinder Pal Singh, Nisha Kajla

Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

Received: 25 December 2017

Accepted: 27 February 2018

***Correspondence:**

Dr. Hardeep S. Deep,

E-mail: deepak_tsr@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

The liver and skin are the organs most commonly involved in serious adverse drug reactions. Rarely a drug reaction can affect both organs concurrently. The association of drug induced liver injury (DILI) and toxic epidermal necrolysis (TEN) is even rarer and may be rarely reported. This is a case report on development of both TEN and DILI following use of piperacillin / tazobactam. We describe our experience of DILI occurring in association with TEN including the etiological agent responsible, its clinical/ biochemical characteristics and ultimate outcome.

Keywords: DILI, Piperacillin, SJS, Steven Johnson syndrome, Tazobactam, TEN, Toxic epidermal necrolysis

INTRODUCTION

Toxic Epidermal Necrolysis (TEN) is a rare life threatening idiosyncratic mucocutaneous reaction affecting only 1-2 cases / million individuals each year. It is characterised by widespread epidermal necrosis followed by epidermal detachment.^{1,2}

It is a part of spectrum of disorders classified on the basis of body surface area (BSA) involved from mild to severe forms. Involvement of less than 10% BSA is Steven Johnson Syndrome (SJS), 10-30 % involvement is SJS-TEN overlap and more than 30% is classified as TEN.³

Drugs are an important cause of liver injury. More than 900 drugs have been reported to account for 20-30 % cases of liver injury.

Drug Induced Liver Injury (DILI) is the most common reason for withdrawal of approved therapeutic drugs. Manifestations can vary greatly from asymptomatic elevation of liver enzymes to fulminant hepatic failure.

CASE REPORT

The patient was 25-year-old female who presented to a private clinic with h/o fever, loose stools and vomiting for last 15 days. She had no known allergies. There was no history of intake of alcohol or other substances of abuse. Patient took treatment from a local practitioner for above symptoms and was given piperacillin/tazobactam as per urine culture and sensitivity report. Other drugs used were inj. calcium gluconate, Paracetamol, inj. hydrocortisone, inj. Sodium bicarbonate.

On 6th day she began to develop rash all over the body and yellowish discoloration of skin and sclera. Her condition deteriorated, and patient was referred to our hospital. Yellowish discoloration of skin and sclera, hepatomegaly and splenomegaly were also present. She was conscious and afebrile. Her heart rate was 90/minute and BP was 130/80mmHg. Cutaneous examination showed involvement of about 80% of TBSA (total body surface area) with skin necrosis, tenderness and positive Nikolsky's sign (dislodgement of intact superficial epidermis by a shearing force), indicating plane of

cleavage in the skin (Figure 1-5). On presentation patient had necrotic lesions and epidermal detachment at multiple areas all over the body on skin. Ulceration and unhealthy lesions in mucous membrane of mouth, nose, eyes and genitalia. There were ulcerations and crusting on oral and genital mucosa. Ocular examination revealed serous discharge along with erosions and crusting of eyelids and yellowish discoloration of sclera.



Figure 1: Detachment of large epidermal sheets in ten.



Figure 2: Ulceration and crusting of mucus membrane of mouth.

On investigating total leucocyte count (TLC) was 18000/cumm and liver function tests (LFT) were deranged [Bilirubin (Total 10.8 mg/ dl) and (direct 8.3 mg/dl), Alkaline phosphatase (ALP) 672 U/L, SGOT (144 U/L), SGPT (119 U/L)]. Viral markers for HIV/HBV/HCV were non-reactive. Ultrasound abdomen showed hepatomegaly (16.6 cm) and splenomegaly (13cm) with normal echo pattern.

All the offending drugs which patient was taking were immediately withdrawn. She was given much needed

treatment in the form of antibiotic (linezolid and tigecycline), steroids, and antihistamines mostly intravenously (I/V).



Figure 3: Areas of patchy desquamated dermis with large area of re-epithelization.



Figure 4: Large areas of desquamation revealing dry bloody dermis



Figure 5: Large areas of re-epithelization with a few areas showing erythematous dermis.

Dermatology and ophthalmology opinions were sought, and appropriate treatment given. Dermatological and mucous lesions improved clinically and symptomatically in few days (10 days' time) but liver function tests showed persistent elevation, ALP (1367 U/L), TB (14 mg/dl), DB (12 mg/dl), SGOT (116), SGPT (107) on 10th day. Liver biopsy (Figure 6-7) was done which showed mixed cholestatic-hepatic pathology indicative of drug induced liver injury. Symptomatic and supportive treatment was continued. Her dermatological lesions resolved completely but liver function tests (LFT's) still remained high even on day 29th ALP (1501), TB (19.2), DB (15.06), SGOT (91) and SGPT (112).

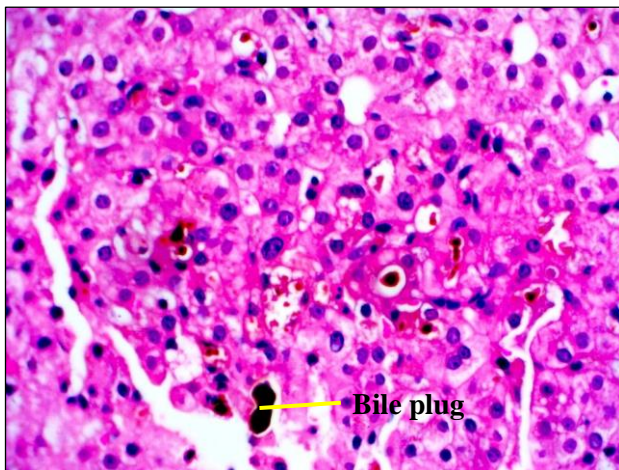


Figure 6: Liver biopsy showing mild distortion of lobular architecture with prominent perivenular cholestasis. There are cholestatic bile plugs with foci of lobular inflammation.

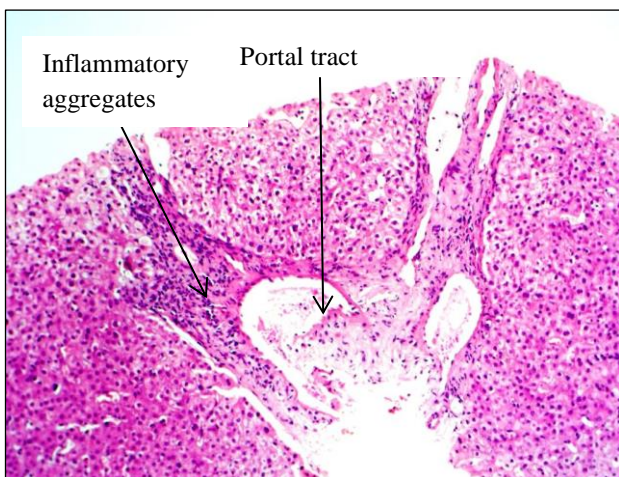


Figure 7: Liver biopsy-portal tract showing moderately increased mixed inflammation, comprising of lymphocytes, plasma cells and eosinophils.

Patient was then discharged on request and was followed up in medicine outpatient Department. LFT (Liver function tests) improved by 4th month (Figure 8-10) after

discharge and her LFT'S was, ALP (110), TB (0.9), DB (0.5), SGOT (30) and SGPT (50).



Figure 8: Complete re-epithelization and healed lesions of TEN after treatment.



Figure 9: Complete re-epithelization and healed lesions of TEN on the mouth and face after treatment.



Figure 10: Complete re-epithelization and healed lesions of TEN on the back after treatment.

DISCUSSION

Toxic Epidermal Necrolysis (TEN) is a rare life threatening idiosyncratic mucocutaneous reaction affecting only 1-2 cases / million individuals each year involving more than 30% of BSA causing epidermal necrosis followed by epidermal detachment.³ Drug induced TEN is the most common amongst other causes like infections, immunization and malignancies. Anti-epileptics, Antibiotics, NSAIDS, and Allopurinol are the agents most commonly implicated. Drug induced liver injury (DILI) occurs roughly between 1-2 weeks from start of drug therapy and presents with acute liver failure and hepatic encephalopathy.⁴

Drug induced TEN and Drug induced liver injury (DILI) occurring in association is rarely reported. There are very few case reports of association between piperacillin-tazobactam and TEN.⁵ Some case reports have been published on post-operative SJS-TEN secondary to piperacillin and tazobactam.⁶

Histopathology of liver biopsy showed mixed cholestatic-hepatic pattern usually seen in DILI due to penicillin group of drugs thus corroborating piperacillin/tazobactam as a cause of DILI now.

There have been case reports and publications citing the role of paracetamol in TEN and DILI. The incidence of injury to liver related to the use of paracetamol in therapeutic dosages was 0.4 / million in patients older than 15 years. Thus, estimated incidence of liver injury related to paracetamol also appears to be very low.⁷ But our patient has been taking paracetamol tablets quite frequently for trivial illnesses for quite a long time as self-medication without any drug reaction. No studies have been published so far stating the role of injection calcium gluconate, sodium bicarbonate or inj. hydrocortisone as a cause of drug induced TEN or DILI.

CONCLUSION

Due to the coincidence in time and exclusion of other possible etiological factors such as alcohol, viral

hepatitis, infections and malignancies, this reported case of TEN and DILI was most likely drug induced due to Piperacillin / Tazobactam. Although uncommon but rare cases had been reported on drug induced TEN and drug induced DILI previously. But drug causing both TEN and DILI together had been very rarely reported. This drug Piperacillin/Tazobactam must be the first to be suspected as its withdrawal lead to improvement of both TEN and DILI signs and symptoms though DILI took longer time (4 months) to recover completely.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Surjit R, Sharanjeet K. Toxic epidermal necrolysis induced by rarely implicating drugs. Indian J. Pharmacol. 2012;44(2):272-3.
2. Milir SM, Kelsy L, Neilendu K. Post-operative SJS secondary to piperacillin-tazobactam. IJLRI. 2013;4(6):36-20.
3. Neki NS, Singh SG, Amritpal S, Amanpreet K. Paracetamol induced Steven Johnson syndrome: toxic epidermal necrolysis overlap: the unusual suspect. Int J Med Health Res. 2016;12(2):59-61.
4. Bjornsson E. Drug induced liver injury in clinical practice. Aliment Pharmacol Ther. 2010;321:3-13.
5. Chopra M, Garcia R, Sultan S. A case of oral sparing TEN. Am J Respiratory Critical Care Med. 2017;195:A592.
6. Milir SM, Kelsy L, Neilendu K. Post-operative SJS secondary to piperacillin-tazobactam. IJLRI. 2013;4(6):36-20.
7. Eulalin P, Luisa I, Monica S. Paracetamol in therapeutic dosages and acute liver injury: Causality assessment in a prospective case series. BMC Gastroenterol. 2011;11(1):80.

Cite this article as: Deep HS, Kumar M, Singh BP, Kajla N. Piperacillin/tazobactam induced toxic epidermal necrolysis and drug induced liver injury. Int J Adv Med 2018;5:460-3.