Co-occurrence of toxic epidermal necrolysis in a human immune deficiency virus infected person due to elthrombopag or ofloxacin – a rare occurrence

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Abstract

Toxic epidermal necrolysis (TEN), a severe drug reaction which is more commonly seen in human immune deficiency virus (HIV) infected persons. It occurs commonly with anti-retroviral treatment and sulfonamides. TEN is reported previously with ofloxacin. But there are no reported cases of elthrombopag induced TEN. Early identification and withdrawal of the culprit will enhance rapid recovery and less mortality. Reporting the noted medications vulnerable for TEN will help medical personal in identifying the drug reaction and causative.

We are reporting a 45 years old male with HIV infection developed TEN with elthrombopag and ofloxacin. We identified skin tenderness of erythematous maculopapular lesions as an early identification feature for TEN before appearing typical mucosal lesions, dusky red necrotic skin patches or nikolsky sign.

Introduction

Retroviral infection give rise to multiple dermatological manifestations. It can give rise to disease related, coinfection related or drug related cutaneous lesions. Cutaneous manifestations may be the initial presenting feature in HIV disease. Drug reactions are more common with retro viral infection and high chance of getting a severe cutaneous adverse skin reaction. Elthrombopag is a thrombopoietin receptor agonist used as a platelet increasing drug. Ofloxacin is used in mycobacterial infections as second line agent.

Drug reactions reported in HIV are morbilliform eruption, urticaria, erythema multiforme and Steven-Johnson syndrome / toxic epidermal necrolysis. They are mostly with sulfonamide and anti-retroviral medications. Toxic epidermal necrolysis (TEN) has been noted with fluconazole, clindamycin, phenobarbital and chlormezanone.

Case report

We report a 45 years old patient presented with a pruritic pigmented papules and plaques over lower extremities and flank suggestive of pruritic papular eruption. Retro-viral infection has been confirmed. He had a thrombocytopenia since the beginning with a platelet count of 82 $*10^3$, White Blood Cells (WBC)-5.2$*10^3$, Neutrophils-62%, Lymphocytes-15%, Eosinophils-6% and Hemoglobin-10.1g / dl. His Mantoux reading was 8mm and there was a right upper lobe haziness in chest Xray. He was started on anti-tuberculous medication with clinical suspicion of active pulmonary tuberculosis. He was on cotrimoxazole prophylaxis for Pneumocystis jirovecii infection. Platelet count has been dropped below 10 $*10^3$, even after withdrawal of rifampicin and cotrimoxazole dropped up to 2.7$*10^3$ with neutrophil count-69% and Hemoglobin dropped to 5.5 g / dl.

Thrombocytopenia was resistant to treatment with repeated platelet transfusion and intra venous immunoglobulin therapy. Blood picture and bone marrow examination revealed a marrow suppression due to HIV infection and drugs. There were no evidence for malignancy, myelodysplastic syndrome or hemophagocytosis. Elthrombopag, a thrombopoietin receptor agonist was started to control the dropping platelet count.

Patient developed a macular papular skin eruption over trunk in five days after starting elthrombopag. And he was on ofloxacin for fifteen days. Other medication were as below:

Isoniazid, pyridoxine, pyrazinamide – day 20.

Rifampicin – started 20 days back, stopped 15 days back due to thrombocytopenia.

Cotrimoxazol – started 37 days back stopped 15 days back due to thrombocytopenia.

Anti-retroviral treatment – Not started.

There were no mucosal lesions, targetoid lesions or necrotic skin patches. He doesn't complain facial or peripheral oedema. Nikolsky sign was negative. He complained a burning sensation of skin with marked

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skin tenderness. Clinical suspicion of toxic epidermal necrolysis was made. Elthrombopag and ofloxacin was discontinued due to clinical suspicion as the culprit drugs for the toxic epidermal necrolysis. All the drugs including anti tuberculous medications were stopped. Intra venous immunoglobulin was commenced.

Nikolsky sign was positive in the third day of the skin eruption. Necrotic skin lesions developed after fourth day and full thickness epidermal detachment continued there onwards. More than 30% of body surface area detachment was evident in sixth day of the skin lesions. He developed erosions over hard palate and glans penis by sixth day.

Empirical antibiotics were continued with negative swab and blood cultures. Anti-retroviral treatment was started after completing intra venous immunoglobulin. SCORTEN was one in first day with no further deterioration thereafter. We adhered to reverse barrier nursing and strict maintenance of input and output[2]. Specialized skin care was delivered with antishear handling[2]. Optimal eye and other mucosal care were given with monitoring for infection according to septic protocol[2]. Gastroprotective medications were given. Protective measures were taken for deep vein thrombosis even the prophylaxis was not given due to cytopenia. Currently we are continuing anti-retroviral treatment and introducing anti-tuberculous medication with an alternative for ofloxacin. Adding the drugs minimally with a three-week interval.

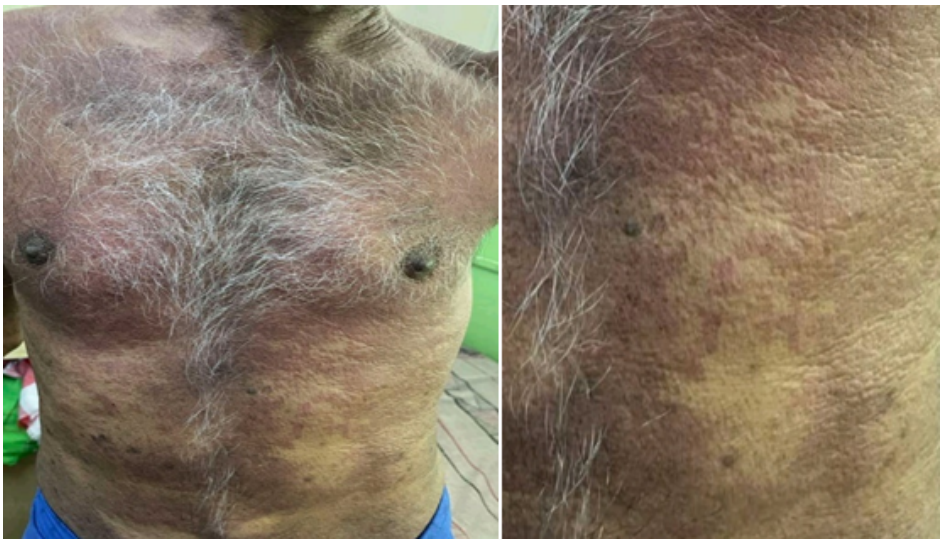

Figure 1. *In day 1.*

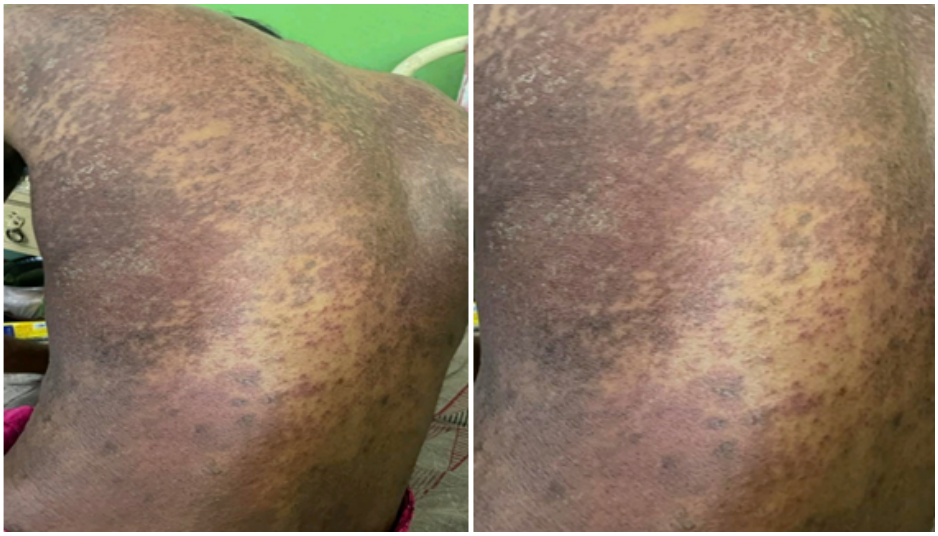

Figure 2. *In day 2.*

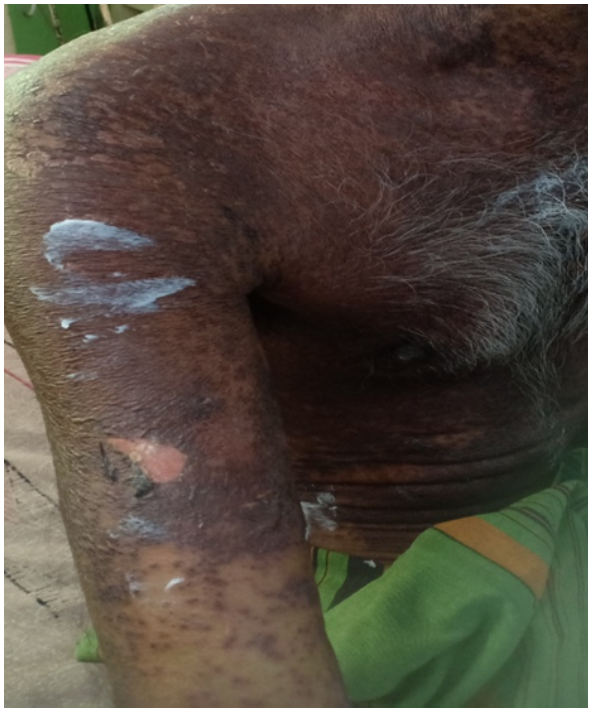

Figure 3. *Positive nikolsky sign in day 3.*

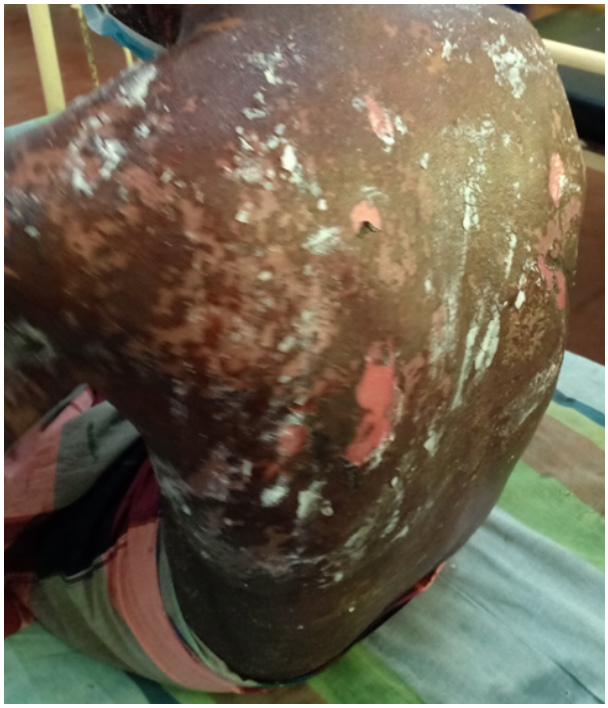

Figure 4. *BSA>30% in day 6.*

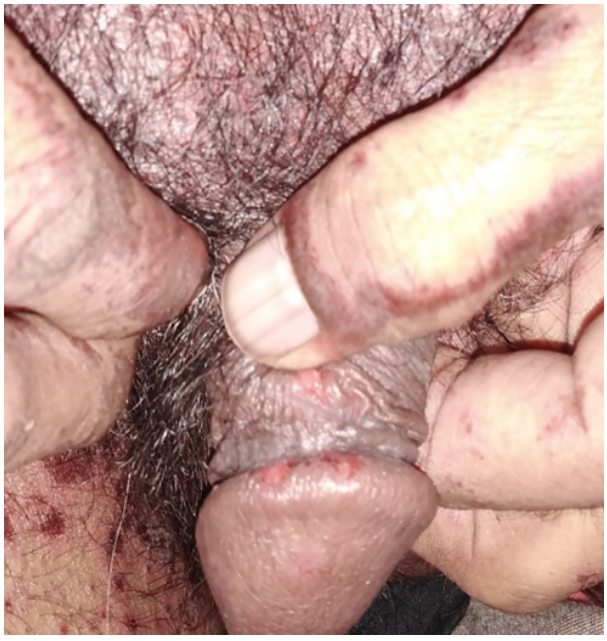

Figure 5. *Mucosal lesions in glans penis in day 6.*

Discussion

We are reporting the first case of toxic epidermal necrolysis with elthrombopag in a retroviral infected person. There are reported cases of ofloxacin giving rise to TEN[1]. Initial evaluation of the skin of the patient revealed a marked tenderness which helped to identify the TEN even without necrotic skin lesions, mucosal lesions or positive nikolskysign. There were no clinical or serological evidence for staphylococcal infection. Therefore, we introduce the skin tenderness as an initial clinical sign in TEN which will enhance early identification and withdrawal of the culprit drug with great benefit in morbidity and mortality.

Why we suspect elthrombopag and ofloxacin as the culprit drugs? Lag period of five days for elthrombopag and lag period of 15 days for ofloxacin. All other drugs were started nearly three weeks before the onset of skin lesions. Most vulnerable drugs fall in between the lag period for TEN documented as 7 days to 21 days are ofloxacin and elthrombopag.

Decision to start the anti-retroviral treatment?

Disease progression will adversely affect the morbidity and mortality due to drug reaction, with further of worsening CD4 count[3]. Further deterioration of cytopenia will give a poor outcome.

References

1. Gupta G. Ofloxacin-induced toxic epidermal necrolysis. I*ndian J Crit Care Med*. 2014 ;**18**(8): 545-6.
2. Creamer D, Walsh S A, Dziewulski P *et al*. U.K. guidelines for the management of Stevens-Johnson syndrome / toxic epidermal necrolysis in adults 2016. *British Journal of Dermatology.* 2016*;* **174**(6): p.1194-227.
3 Yang C *et al*. HIV infection predisposes skin to toxic epidermal necrolysis via a depletion of skin -directed CD4+ T cells. *JAM Acad Dermatol*. 2014; **70**(6): 1096-102.
4. Robert A schwartz *et al*. Cutaneous Manifestations of HIV. Medscape Mar 26 2021.