Case Report

Docetaxel-Induced Stevens-Johnson Syndrome in a Patient with Metastatic Prostate Adenocarcinoma

Osama Diab,¹ Dan McEntire,² Thamer Kassim,¹ Ali Nayfeh,¹ Abdel Rahman Dajani,³ Mitchell Kerfeld,⁴ Jonathon Campbell,¹ Abdulllah Alsuwaidan,⁵ Mahmoud Abu Hazeem,¹ and Maryam Gbadamosi-Akindele¹

¹Department of Medicine, Creighton University, Omaha, NE, USA
²Department of Medicine, University of Utah, Salt Lake City, UT, USA
³Department of Medicine, Norwalk Hospital, Norwalk, CT, USA
⁴Department of Pathology, Creighton University, Omaha, NE, USA
⁵Department of Anesthesia, Mayo Clinic, Rochester, MN, USA

Correspondence should be addressed to Maryam Gbadamosi-Akindele; maryamgbadamosi@creighton.edu

Received 26 June 2018; Accepted 9 December 2018; Published 8 January 2019

1. Introduction

Stevens-Johnson syndrome (SJS) is a severe and potentially life-threatening skin condition that is associated with a number of medications and a few infectious agents. This condition, characterized by the separation of the epidermis from the underlying dermis, typically presents with a severe and painful rash that includes the conjunctiva and oral mucosa and is considered a dermatological emergency. Here, we present a case of apparent docetaxel-induced Stevens-Johnson syndrome (SJS) in a patient recently treated for metastatic prostate cancer. This medication is not classically associated with the development of SJS but in our case, along with a number of other case reports, and a single phase II clinical trial, an association was recognized. We encourage clinicians who employ the use of this medication to be aware of this relationship.

2. Case Report

A 63-year-old male with a past medical history of hypertension, hyperlipidemia, and metastatic prostate adenocarcinoma to retroperitoneal lymph nodes, lung, and bone presented to the emergency room with a one-week history of a rash. The rash affected the hands, feet, back, and chest. It developed into blisters that later ruptured. The rash was especially painful in the hands and feet. He also reported red eyes and difficulty eating for the past week.

Vital signs upon presentation were as follows: temperature 36.4°C, pulse 83/min, respiratory rate 12/min, and blood pressure 121/60 mmHg. Physical examination of the patient revealed a severe rash covering less than thirty percent of the body, oral ulcers, and conjunctival redness (Figure 1).

Laboratory data at the time of admission is notable for leukocytosis, electrolyte imbalances, and hepatic dysfunction (Table 1).

The patient’s current cancer treatment regimen included active hormonal therapy with leuprolide and active chemotherapy with docetaxel. He had received two cycles of docetaxel therapy (generic form: 75 mg/m²), with the last dose of docetaxel received two weeks prior to presentation. He was not on other medications at the time of admission.

Treatment of the patient included intravenous fluid replacement, prednisone, piperacillin/tazobactam, ondansetron, and morphine. Wound and eye care were provided. Dermatology was consulted.
Because our searches for an established association between SJS and docetaxel were in vain, we elected to obtain a punch biopsy of the lesions to establish pathological evidence of our diagnosis. The punch biopsies were obtained from the edges of lesions on the left forearm and left medial foot. Light microscopy of the hematoxylin and eosin-stained specimens were confirmatory for SJS (Figure 2).

The patient clinically improved with supportive therapy and was discharged home. He was scheduled a follow-up with his oncologist to discuss other treatment options.

3. Discussion

Docetaxel is an antitubulin agent that inhibits mitosis by stabilizing microtubule assembly. It is a widely used chemotherapeutic agent in the treatment of breast, lung, prostate, and other cancers [1]. The classically known side effects of docetaxel therapy include alopecia, pancytopenia, drug-induced liver injury, nausea, vomiting, and diarrhea. There have been an increasing number of generic docetaxel toxicities in comparison to the original drug formulation. Impurities, excipients, and the amount of active agent itself can all have an impact on the efficacy of the drug and impact its narrow therapeutic index resulting in increased side effects [2].
A number of popular clinical pharmacology resources do not include Stevens-Johnson syndrome (SJS) as a known complication of docetaxel chemotherapy. However, the current case and the cases written by a handful of other clinicians may provide clinical evidence that docetaxel therapy is associated with the development of this potentially life-threatening dermatologic condition.

Stevens-Johnson syndrome is one of the life-threatening dermatologic diseases, which is characterized by skin and mucosal involvement and systemic symptoms. Most often, SJS is secondary to medication use but it also could be related to an infection [3]. The treatment of this condition remains controversial but all reach agreement that supportive management is first line and the use of steroids, IVIG, tumor necrosis factor, or even cyclosporine lacks powered data. The mortality rate of SJS in severe cases could exceed 90 percent [4].

The existing reported cases of SJS-like skin reactions in association with docetaxel are few (Table 2). Dourakis et al. [5] described a case of a 60-year-old woman that received docetaxel as salvage chemotherapy for non-Hodgkin’s lymphoma who developed toxic epidermal necrolysis. Similarly, Arshad et al. [6] shared a case of a 40-year-old woman receiving docetaxel for invasive ductal breast carcinoma who developed toxic epidermal necrosis. Despite aggressive supportive measures, the patient died. Sawada et al. [7] reported the development of SJS in a patient with metastatic breast cancer after a single dose. This case also provided pathological evidence of SJS and ruled out conditions such as pemphigus vulgaris. Following the seventh dose of docetaxel in another patient with metastatic breast cancer, Moisidis and Möbus [1] encountered skin lesions consistent with erythema multiforme and SJS. Ohlmann et al. [8] reported the course of a patient receiving docetaxel who developed SJS and acute hepatic failure and died 6 weeks later. Kattan et al. [9] carried out a phase II trial to establish the safety of the combination of docetaxel, zoledronic acid, and estramustine in patients with metastatic prostate carcinoma. Of the 27 patients included in the trial, one patient died of SJS with liver failure.

An interesting point of discussion relative to this case is, first, the finding of elevated liver function tests. Our patient did not have a history of hepatic disease. However, docetaxel is known to be associated with hepatotoxicity [10]. This association may be relevant because a number of case reports summarized by Devarbhavi et al. [11] reported that patients with drug-induced liver dysfunction and SJS have poorer outcomes. These findings were especially prevalent in patients taking antiepileptics, antiretrovirals, and sulfonamides. Although it is unknown whether liver dysfunction predisposes patients to SJS, there appears to be an association that should be noted by physicians.

### 4. Conclusion

We recognize that a number of other authors have encountered apparent docetaxel-induced SJS and our report adds to the growing body of knowledge of this detrimental relationship. We encourage clinicians that employ the use of this medication to be cognizant of the risk of SJS and to treat this condition early and aggressively.
Disclosure

The details of this manuscript were presented as a poster presentation at the 2016 Association of Veteran Affairs Hematology Oncology (AVAHO) annual meeting on 09/24/2016 at the Renaissance Hotel in Dallas, Texas.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] C. Moisidis and V. Möbus, “Erythema multiforme major following docetaxel,” *Archives of Gynecology and Obstetrics*, vol. 271, no. 3, pp. 268–270, 2005.

[2] C. Elm'hadi, R. Tanz, M. R. Khhamouche et al., “Toxicities of docetaxel: original drug versus generics—a comparative study about 81 cases,” *SpringerPlus*, vol. 5, no. 1, p. 732, 2016.

[3] N. Frey, J. Jossi, M. Bodmer et al., “The epidemiology of Stevens-Johnson syndrome and toxic epidermal necrolysis in the UK,” *Journal of Investigative Dermatology*, vol. 137, no. 6, pp. 1240–1247, 2017.

[4] J. A. Schneider and P. R. Cohen, “Stevens-Johnson syndrome and toxic epidermal necrolysis: a concise review with a comprehensive summary of therapeutic interventions emphasizing supportive measures,” *Advances in Therapy*, vol. 34, no. 6, pp. 1235–1244, 2017.

[5] S. P. Dourakis, V. A. Sevastianos, A. Alexopoulou, M. Deutsch, and N. Stavrianes, “Treatment side effects: case 2. toxic, epidermal, necrolysis-like reaction associated with docetaxel chemotherapy,” *Journal of Clinical Oncology*, vol. 20, no. 13, pp. 3030–3032, 2002.

[6] F. Arshad, T. Bhat, and A. Lone, “Docetaxel induced Lyell’s syndrome: a rare life threatening cause of dermatitis medicamentosas,” *Journal of Cancer Research and Therapeutics*, vol. 10, no. 3, pp. 742–744, 2014.

[7] Y. Sawada, K. Sugita, R. Kabashima, M. Nakamura, and Y. Tokura, “Docetaxel-induced Stevens-Johnson syndrome with regenerating epidermis composed of atypical keratinocytes,” *Journal of the European Academy of Dermatology and Venereology*, vol. 23, no. 11, pp. 1333–1335, 2009.

[8] C. H. Ohlmann, S. Kohlmergen, D. Sahi, U. Engelmann, and A. Heidenreich, “Letaler ausgang einer chemotherapie mit docetaxel,” *Der Urologe*, vol. 46, no. 10, pp. 1425–1427, 2007.

[9] J. G. Kattan, F. S. Farhat, G. Y. Chahine et al., “Weekly docetaxel, zoledronic acid and estramustine in hormone-refractory prostate cancer (HRPC),” *Investigational New Drugs*, vol. 26, no. 1, pp. 75–79, 2008.

[10] Z. Wang, X. Liang, J. Yu et al., “Non-genetic risk factors and predicting efficacy for docetaxel-drug-induced liver injury among metastatic breast cancer patients,” *Journal of Gastroenterology and Hepatology*, vol. 27, no. 8, pp. 1348–1352, 2012.

[11] H. Devarbahi, S. Raj, V. H. Aradya et al., “Drug-induced liver injury associated with Stevens-Johnson syndrome/toxic epidermal necrolysis: patient characteristics, causes, and outcome in 36 cases,” *Hepatology*, vol. 63, no. 3, pp. 993–999, 2016.