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Case report

Bullous vesicant-type reaction to docetaxel along the venous tract: A case report

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ABSTRACT

Docetaxel is an anti-neoplastic agent commonly used to treat major solid tumors. Common toxicities of docetaxel include neutropenia, alopecia, nausea and vomiting. While docetaxel is typically considered an irritant, we present the case report of a 54-year-old female with high-grade undifferentiated uterine sarcoma who experienced a standard infusion reaction during a docetaxel infusion, followed by an atypical, delayed vesicant-type reaction, without a clear extravasation history.

1. Introduction

High grade undifferentiated uterine sarcoma is a rare, aggressive malignancy and data on its management is limited. In this report, we present a case of a bullous vesicant-type reaction to docetaxel, received in combination with gemcitabine, an accepted first- or second-line chemotherapy regimen for the treatment of high-grade uterine sarcomas. Docetaxel (Taxotere) is a semi-synthetic taxoid anti-neoplastic agent which disrupts the assembly of cellular microtubules. Typical side effects to docetaxel include neutropenia, fluid retention, neuropathy, hypersensitivity reaction, alopecia, mucositis or nail changes (Moisidis and Möbus, 2005; Ener et al., 2004).

Most chemotherapy agents are classified as vesicants, irritants or non-vesicants. Vesicants have the ability to induce the formation of blisters and/or cause tissue destruction while irritants can cause pain at the injection site or along the vein with/without an inflammatory reaction. Irritants do not typically cause soft tissue ulcers unless a large quantity of the drug is inadvertently extravasated (Ener et al., 2004). Extravasation is the accidental direct infiltration of chemotherapy into the tissues surrounding the intravenous site (Boschi and Rostagno, 2012). Extravasation of anti-neoplastic agents can potentially cause tissue necrosis and functional impairment (Boschi and Rostagno, 2012).

2. Case presentation

A 54-year-old post-menopausal Filipino woman was diagnosed with a 16 cm undifferentiated uterine sarcoma, first presenting with hemorrhagic degenerating fibroids the largest of which measured 14.8 × 10.2 cm and a hemoglobin of 43 g/L. Accordingly, she was transfused 4 units of blood and underwent a total abdominal hysterectomy, bilateral salpingo-oophrectomy. She was diagnosed with a high grade undifferentiated uterine sarcoma, stage pT1bNXM0. Pathology revealed that the tumor infiltrated through the myometrium with extension to the serosal surface focally. There was no cervical, fallopian tube or ovarian involvement. The margins were negative. Past medical history was unremarkable and gynecologic history was significant for two vaginal deliveries and menopause at age 48.

The patient recovered well from surgery. Her case was discussed at the gynecologic oncology multi-disciplinary cancer case conference, and consensus was for no adjuvant therapy. Clinical follow-up took place every 3 months with computed tomography scans every 6 months. Eight months after surgery, an 8.8 cm left pelvic cystic and solid mass extending to the left pelvic sidewall, with involvement of the proximal internal iliac vessels, was identified on imaging. There was a second mass involving the left vaginal apex. The mass was not palpable on abdominal exam, but the patient had some mild abdominal tenderness.

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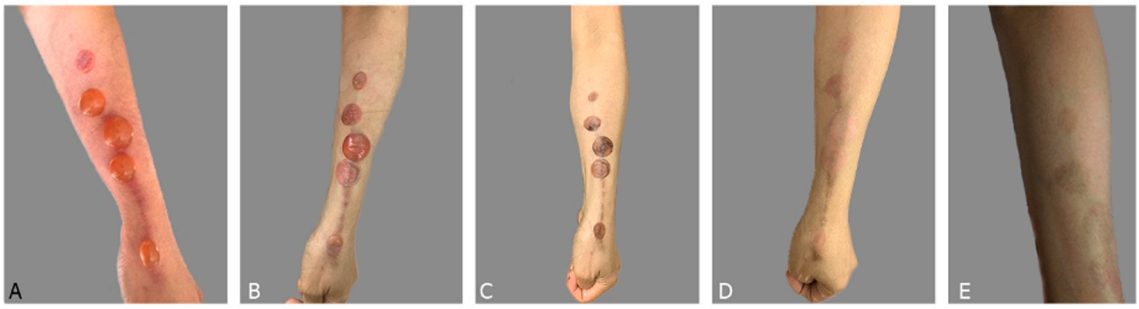

Fig. 1. Left arm tense bullae following a linear distribution of the cephalic vein on day 9 post infusion (A), on day 13 (B), on day 20 (C), on day 27 (D), and on day 60 post infusion showing patches of post-inflammatory hyperpigmentation (E).

The vaginal apex mass was palpable on recto-vaginal examination.

Based on the imaging results, the patient was prescribed gemcitabine and docetaxel chemotherapy. She received intravenous gemcitabine on day one as per protocol and presented for day 8 intravenous docetaxel and gemcitabine infusion with pre-medication including dexamethasone 8 mg orally, prochlorperazine 10 mg orally and diphenhydramine 50 mg orally. Upon initiation of docetaxel (1.7 mL) the patient developed generalized erythema with a sensation of heat and flushing. The infusion was discontinued. Symptoms included mild chest tightness, increased work of breathing and a localized urticaria developed over the left forearm at the time of infusion. No clear extravasation was noted. The patient received 50 mg of intravenous diphenhydramine and 8 mg of intravenous dexamethasone, after which her clinical condition returned to baseline over 30 min. She was re-challenged and completed the infusion of docetaxel and gemcitabine without any further adverse reactions.

Nine days later the patient presented to the emergency department with a bullous reaction of the skin along her left arm with 5–6 bullous lesions following the tract of the vein into which the chemotherapy agents were infused. The bullae were tense, large (2–3 cm in diameter), and filled with serous fluid on a non-erythematous base. The patient described pain but denied pruritis at the reaction site and the blisters were dressed with Polysporin and gauze. She was prescribed prednisone and topical hydrocortisone. She had no associated systemic symptoms. She was found to be neutropenic with a white blood cell count of 1.9×10^9/L and an absolute neutrophil count of 0.2×10^9/L. The bullae on her arm healed over the course of two weeks and there was no extension of inflammation. The prednisone was subsequently tapered down. There were residual patches of post-inflammatory hyperpigmentation at the sites where the bullae resolved (see Fig. 1). Following this reaction, docetaxol/gemcitabine was discontinued and the treatment was changed to single agent doxorubicin, which was tolerated well and achieved a partial response.

3. Discussion

This unique case shows a classic chemotherapy infusion reaction followed by a vesicant-type reaction. This patient had a standard infusion reaction characterized by flushing, chest tightness, increased work of breathing and localized urticaria. Bullous eruption at and proximal to her infusion site occurred nine days later which is in keeping with other reports of extravasations involving a small amount of vesicant leakage, after which dermatological findings developed in the following days or weeks (Raley et al., 2000; Una Cidon et al., 2011). It is possible the erythema and dysaesthesia attributed to her standard infusion reaction masked symptoms of a small amount of extravasation followed by delayed bullae formation. Also notable was that the bullae were non-inflammatory; there was a lack of surrounding erythema aside from the linear erythema following the distribution of the cephalic vein into which the docetaxel was infused. This is compared to other cases of cutaneous reactions to docetaxel describing inflammatory bullae with a significant background of erythema (El Saghir and Otrock, 2004; Ascherman et al., 2000; Chang et al., 2014; Ho et al., 2003).

There is no consensus whether taxanes are vesicants or irritants. Generally, they cause mild self-limiting reactions. Docetaxel has been reported to have a low incidence of infusion-site reactions (<1%) (Barbee et al., 2014), and to have low vesicant potential (Ener et al., 2004). Only 5 cases have been reported with bullae formation after docetaxel infusion (Raley et al., 2000; Una Cidon et al., 2011; El Saghir and Otrock, 2004; Chang et al., 2014; Ho et al., 2003; Uña et al., 2009). Paclitaxel, another taxane chemotherapy agent, has an incidence of 1.6% injection site reactions including those secondary to extravasation (Barbee et al., 2014). Based on the few reports of docetaxel extravasations, different treatments have been proposed, including warm compresses, elevation, range of motion exercises, topical steroids and antibiotics (Ascherman et al., 2000; Chang et al., 2014). Hyaluronidase has also been suggested as an antidote which should be injected subcutaneously in a pinwheel fashion into the affected area (Kreidieh et al., 2016). Gemcitabine, which was received on the same day, has never been described to cause vesicant-like reactions.

Systemic reactions to taxanes infusion are common. It is uncertain whether taxanes or the vehicles in which taxanes are dissolved are responsible for the majority of infusion reactions. In the case of docetaxel, the vehicle polysorbate 80 is suspected to be a trigger for histamine release and cause infusion reactions but the pathophysiology of this remains unclear (Fossella, 1994).

4. Conclusion

This case report presents a rare case of standard infusion reaction followed by a vesicant-type reaction to docetaxel infusion. This unusual clinical presentation suggests that practitioners should carefully monitor skin reactions in the days and weeks following any infusion reaction. Patients should be carefully educated about the risks and side effects of extravasation so that they may receive prompt treatment and avoid subsequent sequelae.

Author contribution

JS and LB conceived the project, collected the data, wrote the original draft and approved the final version. AN prepared the visual data. SC, AN, HH and LE contributed data, edited the manuscript and approved the final version.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Ascherman, J.A., Knowles, S.L., Attkiss, K., 2000. Docetaxel (Taxotere) extravasation: A report of five cases with treatment recommendations. Ann. Plast. Surg. 45, 438–441.

Barbee, M.S., Owonikoko, T.K., Harvey, R.D., 2014. Taxanes: Vesicants, irritants, or just irritating? Therapeut. Adv. Med. Oncol. 6, 16–20.

Boschi, R., Rostagno, E., 2012. Extravasation of antineoplastic agents: Prevention and treatments. Pediatr. Rep. 4.

Chang, P.H., Wang, M.T., Chen, Y.H., Chen, Y.Y., Wang, C.H., 2014. Docetaxel extravasation results in significantly delayed and relapsed skin injury: A case report. Oncol. Lett. 7, 1497–1498.

El Saghir, N.S., Otrock, Z.K., 2004. Docetaxel extravasation into the normal breast during breast cancer treatment. Anticancer Drugs 15.

Ener, R.A., Meglathery, S.B., Styler, M., 2004. Extravasation of systemic hemato-oncological therapies. Ann. Oncol. 15, 858–862.

Fossella, F.V., et al., 1994. Phase II study of docetaxel for recurrent or metastatic non-small-cell lung cancer. J. Clin. Oncol. 12, 1238–1244.

Ho, C.H., Yang, C.H., Chu, C.Y., 2003. Vesicant-type reaction due to docetaxel extravasation. Acta Dermato-Venereol. 83, 467–468.

Kreidieh, F.Y., Moukadem, H.A., El Saghir, N.S., 2016. Overview, prevention and management of chemotherapy extravasation. World J. Clin. Oncol. 7, 87–97.

Moisidis, C., Möbus, V., 2005. Erythema multiforme major following docetaxel. Arch. Gynecol. Obstet. 271, 267–269.

Raley, J., Geisler, J.P., Buekers, T.E., Sorosky, J.I., 2000. Case Report: Docetaxel extravasation causing significant delayed tissue injury. Gynecol. Oncol. https://doi.org/10.1006/gyno.2000.5873.

Una Cidon, E., et al., 2011. A silent chemotherapy extravasation as the unexpected enemy: a case report. Webmed Central Oncol.

Uña, E., Cuadrillero, F., López-Lara, F., 2009. Drug extravasation: A dreaded complication. BMJ Case Rep. 2009.