

Serpentine supravenuous hyperpigmentation (SSH) in nasopharyngeal carcinoma patient on docetaxel and carboplatin chemotherapy: a case report

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ABSTRACT

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Serpentine supravenuous hyperpigmentation (SSH) is a rare but unique side effect of intravenous anticancer. It manifests as linear hyperpigmentation eruption on the skin that radiates along the superficial vein accompanied by mild pain and/or itch. This SSH does not cause systemic alterations, however, most patients complained about its cosmetic effects. The diagnosis of SSH can be made clinically, although histopathological examinations can aid in excluding differential diagnoses. We reported a case of SSH found in a nasopharyngeal cancer patient during docetaxel and carboplatin chemotherapy. It is a potentially alarming interface dermatitis that is not lot reported in the literature. It was reported, the patient tolerated the second and third cycles well with less severe side effects when premedicated with 250 mL NaCl 0.9% bolus intravenously before and after chemotherapy sessions, 10 mg cetirizine every 24 hr orally, and desoximetasone cream 0.25% every 12 hr topically added.

ABSTRAK

Hiperpigmentasi supravenuous serpentine (HSS) adalah efek samping antikanker intravena yang jarang terjadi namun unik. Manifestasi HSS berupa erupsi hiperpigmentasi linier pada kulit yang menyebar sepanjang vena superfisial disertai nyeri ringan dan/atau gatal. Efek samping ini tidak menyebabkan perubahan sistemik, namun sebagian besar pasien mengeluhkan efek kosmetiknya. Diagnosis SSH dapat ditegakkan secara klinis, meskipun pemeriksaan histopatologi dapat membantu menyingkirkan diagnosis banding. Kami melaporkan kasus SSH yang ditemukan pada pasien kanker nasofaring selama kemoterapi docetaxel dan carboplatin. Ini adalah dermatitis antarmuka yang berpotensi mengkhawatirkan dan tidak banyak dilaporkan dalam pustaka. Dilaporkan, pasien mentoleransi siklus kedua dan ketiga dengan baik dengan efek samping yang tidak terlalu parah bila diberikan premedikasi dengan 250 mL NaCl 0,9% bolus intravena sebelum dan sesudah sesi kemoterapi, 10 mg cetirizine setiap 24 jam secara oral, dan krim desoximetasone 0,25% setiap 12 jam ditambahkan secara topikal.

Keywords:
docetaxel;
carboplatin;
nasopharyngeal
carcinoma;
serpentine supravenuous
hyperpigmentation;
side effects

INTRODUCTION

Serpentine supravenuous hyperpigmentation (SSH), also known as serpentine supravenuous dermatitis (SSD) or persistent supravenuous hyperpigmentation (PSSH) is a term used to describe skin morphology of

linear hyperpigmentation eruption which is along the superficial veins. This rare phenomenon is related to the use of intravenous anticancer therapy. The SSH was first described by Hrushesky in 1976 to describe peculiar cutaneous-manifesting side effects after intravenous 5-fluorouracil (5-FU) administration.

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Even though SSH does not cause systemic alterations, the majority of the patients complained about its cosmetic effect.¹

Nasopharyngeal carcinoma is a rare malignant case that originates from the nasopharyngeal epithelium. The incidence of nasopharyngeal carcinoma varies based on its geographical distribution. In Indonesia, nasopharyngeal carcinoma came in fourth as the most common malignancy, treated with either radiotherapy and/or chemotherapy.^{2,3} However, the use of anticancer puts a variety of side effects at risk. These side effects are dependent on the type of anticancer used. On the other hand, administration, and dosage of the medications also correlate to the side effects. The side effects may manifest in every organ system, for instance, the cardiovascular, respiratory, gastrointestinal, nervous, and immune systems. Some side effects may also manifest in the skin with distinctive clinical manifestations. Serpentine supraparaveneous hyperpigmentation is considered one of the unique and distinctive side effects manifestations in the skin.⁴

The side effects during chemotherapy must be taken into consideration when deciding the management options for cancer patients, from dosing to further treatment planning. Furthermore, this side effect can dominantly affect the life quality of the patients. Hence, physicians need to know, distinguish, and diagnose the commonly found reactions, so that prevention and also comprehensive early management can be addressed for these specific patients.

In this case report, we reported one case of docetaxel and carboplatin-induced SSH. This report was made to increase the knowledge about one of the side effects of chemotherapy agents manifesting in the skin, along with establishing a diagnosis, an etiology investigation, and management planning for the patient.

CASE

A 48 y.o. male from the Ear, Nose, and Throat (ENT) Outpatient Care was consulted to the Department of Dermatology and Venereology (DV), Sanglah General Hospital with 5 d history of linear, erythematous, and pruritic eruption on his right lower arm without systemic symptoms, 2 d after receiving chemotherapy infusion at this location. His past medical history was remarkable for a recent diagnosis of nasopharyngeal carcinoma. He had his first cycle of chemotherapy with 100 mg of docetaxel in 500 mL NaCl 0,9% infused over 6 hr followed by 400 mg of carboplatin in 500 mL NaCl 0,9% infused over 2 hr, with premedication of 10 mg of dexamethasone intravenously, 10 mg of diphenhydramine intravenously, along with 100 mL of NaCl 0.9% 20 drops per min. After the chemotherapy session was conducted, another 100 mL of NaCl 0.9% (20 drops per min) along with 8 mg of ondansetron 2 x daily, 20 mg of omeprazole 2 x daily, 500 mg of paracetamol 3 x daily, and vitamin B complex once daily were prescribed. He was known to have no drug allergies. He had no other medical conditions and took no regular medications, vitamins, or supplements. His social and family histories were non-contributory. On dermatologic examination, he had multiple erythematous macules to patch, a well-defined margin, annular to linear shaped by the vein tracks, with the size of 0.5 cm x 0.5 cm to 1 cm x 22 cm, linear in configuration, locally distributed on his right upper and lower arm (FIGURE 1A and 1B). The patient was suggested for a biopsy examination, but the patient refused. Based on the clinical pattern, a diagnosis of SSD was made. The patient was discharged home with a prescription for a 5 d course of 10 mg of cetirizine 10 mg intraorally, desoximetasone 0.25% cream applied to the affected areas 2 x daily for 7 d.

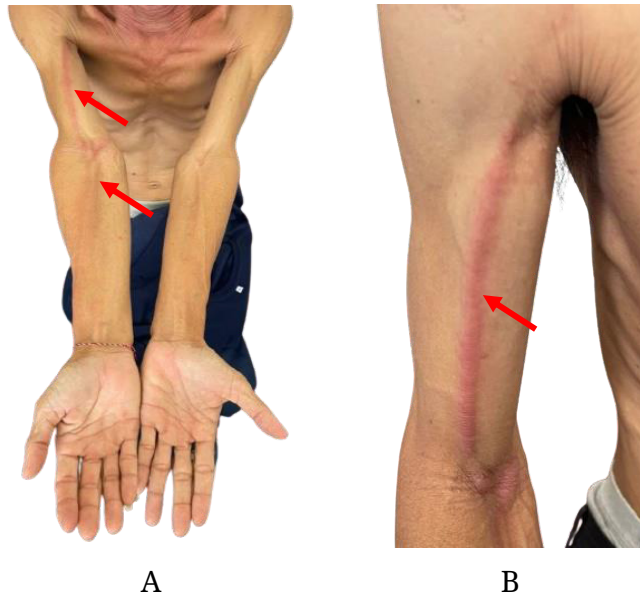


FIGURE 1. Multiple erythematous macules to patch (red arrow) characterized by well-defined margin, annular to linear shaped by the vein tracks (A and B).

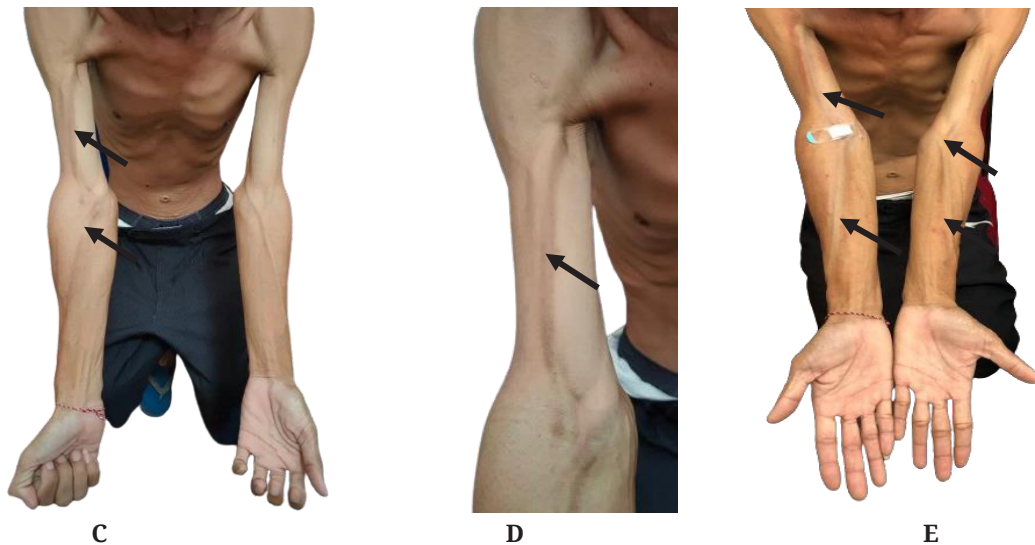


FIGURE 2. Multiple hyperpigmented patch (black arrow). The first visit to the DV outpatient care (C and D) after receiving 1 wk treatment from the DV outpatient care. The third visit to the DV outpatient care after receiving second and third session of chemotherapy (E).

A week later, his lesion had significantly improved when he arrived for DV outpatient therapy (FIGURE 2A and 2B). He was scheduled for a second chemotherapy session with the same regimen the next week. For the next

chemotherapy session, he was suggested to receive premedication of 250 mL of NaCl 0.9% bolus intravenously before and after the administration of the chemotherapy agent and communicate with the ENT department. He tolerated

his second and third cycles with milder adverse events. The linear, erythematous-hyperpigmented, and slightly pruritic eruption appeared on his left and right arm and lower arm after receiving the second and third cycle chemotherapy infusions (FIGURE 2C). The eruption slowly disappeared after a few days.

DISCUSSION

Serpentine supravenuous hyperpigmentation rarely happens to patients on anticancer therapy. There have been several reports of SSH cases globally, but the exact incidence is unknown. Some anticancers susceptible to inducing SSH include fluorouracil, taxanes, vinca alkaloids (vincristine and vinorelbine), proteasome inhibitors, methotrexate, dacarbazine, actinomycin, docetaxel, doxorubicin, daunorubicin, cyclophosphamide, cisplatin, fotemustine, nitrogen mustard, nitrosoureas, and carboplatin. The majority studies reported that most of the SSH occurred during chemotherapy sessions using multiple treatment regimens at the same time.⁵⁻¹⁰

The exact pathophysiology of SSH is yet to be known, thus additional studies are still needed to understand more about this phenomenon. Currently, two hypotheses try to explain this phenomenon. The first one is the direct cytotoxic effect of anti-cancer medications on endothelial cells causing increased permeability. Thus, the medications extravasate to the nearest epidermal cells. Hence, the extravasated medications will cause toxic effect on the nearest melanocytes and keratinocytes, ultimately causing hyperpigmentation throughout the blood vessels.⁶ The second hypothesis is the accumulation of anti-cancer medications in the skin around the blood vessels can cause local and generalized hypersensitivity reactions followed by hyperpigmentation.^{9,11}

Serpentine supravenuous

hyperpigmentation clinically manifests as hyperpigmented macule lesions, and/or linear- or serpentine-shaped erythema across the cutaneous veins. In some cases, these lesions can manifest as purpuric papules with hyperpigmentation or erythema. It is distributed locally to the skin blood vessels which provide access for anti-cancer drugs. The lesion will first show in the proximal area where the intravenous medication administration is located, then it slowly extends to distal areas. In some cases, SSH can be preceded by some lesions in the other parts of the body, for example, the back of the neck and the thorax.¹² SSH lesions may or may not be preceded with erythematous lesions. The lesions usually show in 24 hours up to 15 days after exposure to the causative agent(s).^{6,11,12} Regardless, one study has reported that there was a unique SSH patient who slowly began to manifest 1-6 mo after the exposure. This opens up the possibility of the mechanism of delayed reaction causing SSH.^{5,11} Most of the patients complained of itch on the lesions. Systemic symptoms are never found on SSH.⁸

Most cases of SSH do not need additional diagnostics because of their pathognomonic clinical manifestation. The only additional examination which can distinguish SSH from other conditions (even without the presence of the pathognomonic sign) is histopathology examination.^{7,9} On histopathology examination, the lesion typically shows basement layer degeneration, pigment incontinence, melanophages, focal band-like infiltrates, and perivascular mononuclear infiltrates.⁹ Some histopathological examinations will also show acanthosis, hyperkeratosis, and necrotic keratinocytes.¹² Some differential diagnosis that can be considered include thrombophlebitis, cutis marmorata, erythema ab igne, livedo reticularis, and linear lichen planus which manifests across the

superficial cutaneous veins.¹³

Several precautions that can be taken by patients who will undergo anti-cancer therapy to help reduce the risk of SSH. Applying moisturizing cream to the arms and legs regularly can help repair the skin barrier. In addition, avoiding irritants such as alcohol and tight clothing, extreme temperatures (too cold or too hot) and friction on the skin are also recommended.⁸ Several studies have also shown that exposure to sunlight can increase the risk of developing SSH. Therefore, patients should use anti-UV creams and avoid excessive sun exposure.^{4,8,12} In acute cases, several studies recommend the administration of moderate potency topical steroids plus oral glucocorticoids. One study used oral prednisone at a dose of 20 mg per day (for 7 d) along with betamethasone valerate 0.1% cream (14 d) with favorable outcomes.¹² Another study used oral dexamethasone at a dose of 20 mg for 3 days.¹⁴ Fernandes *et al.*⁶ used methylprednisolone once daily for 7 d on two SSH patients with different outcomes. Several studies support the administration of corticosteroids before and after therapy to suppress the inflammatory response.⁶ Hossain *et al.*¹² gave dexamethasone 2 mg orally for 3 d to patients who had just undergone a second chemotherapy after experiencing SSH on their first chemotherapy. In this patient, no further side effects were found.¹² To avoid further reactions, the intravenous infusion of the drug should be given at a slower rate. In addition, administration of the drug should be initiated and terminated with a bolus of normal saline (250 mL initially, 500 mL at the end) to remove residual toxic metabolites from the vasculature. Bolus administration should be considered in patients who can not tolerate fluid overload.⁶ For longer therapy sessions (>1 hr), central venous access may be a better option than peripheral access. Cold compresses can be applied to the

infusion site to cause vasoconstriction in the veins and degradation of drug metabolites. In addition, cold compresses can also be used during acute reactions to reduce pain and inflammation.^{6,12} To treat pruritic complaints, antihistamines, for instance, cetirizine or loratadine can be used.¹⁴ The interruption of chemotherapy or modification of the standard dose of the chemotherapeutic drug is not indicated.

Resolution of the lesions generally happens spontaneously, after the patient stops the exposure to anti-cancer drugs.¹³ The duration of resolution varies from person to person, ranging from weeks to years. However, these post-inflammatory hyperpigmented lesions persist in a minority of patients.^{6,12,14}

CONCLUSION

We reported a case of SSH found in nasopharyngeal cancer patient on docetaxel and carboplatin chemotherapy. Diagnosis of SSH is made based on the clinical findings of linear, erythematous, and pruritic eruption at the location used to receive chemotherapy infusion. The patient is given a premedication of 250 mL of NaCl 0.9% bolus intravenously before and after the chemotherapy session, 10 mg of cetirizine every 24 hr orally, and desoximetasone 0.25% cream every 12 hr topically. The patient tolerates his second and third cycles well with milder adverse events.

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