

CASE REPORT

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Vinorelbine Induced Serpentine Supravenous Hyperpigmentation

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ABSTRACT Serpentine supravenous hyperpigmentation (SSH) is a rare complexity arising from antineoplastic therapy. Vinorelbine, a chemotherapeutic drug that is frequently used for the treatment of breast and lung cancer, contributes to the etiology of SSH. A 54 years old male patient was being treated for lung adenocarcinoma. An intravenous (IV) infusion of vinorelbine was administered in the distal dorsal vein of the left forearm. Erythematous hyperpigmentation at the infusion area was observed a week after the administration of the chemotherapeutic drug. The initial symptoms of SSH usually appear between 1 to 15 days post IV administration of a cytotoxic drug, and it spontaneously becomes hyperpigmented within 1-3 weeks. However, these local reactions can be prevented by applying IV infusion for a short period (15-30 min) along with adequate venous irrigation (75-124 mL) instead of bolus administration. The termination of the drug can also be considered.

Keywords: Vinorelbine; adenocarcinoma of the lung; hyperpigmentation

Serpentine supravenous hyperpigmentation (SSH) was first described by Hrushesky as a side effect of intravenous 5-fluorouracil in 1975.¹ SSH mostly affects men. The condition usually afflicts people between 7 and 85 years (but mostly occurs in people in their mid-forties). It is most frequently seen on the forearm and rarely on peripheral areas such as the torso, back, hip, back femoral, and the popliteal fossa.² SSH develops on the superficial venous plexus, usually starting at the infusion site of a drug. These lesions develop as red or purple papules and plaques with erythematous lines following the superficial venous network in a linear or serpentine pattern. It can appear within 24 h or may take up to 15 days after the intravenous cytotoxic drug administration; it spontaneously becomes hyperpigmented within 1-3 weeks.³ After repeated intravenous injections of the drug, these rashes may reappear along with hyperpigmentation. However, the symptoms of SSH closely resemble that of other conditions, in-

cluding cutis marmoratus telangiectatica, congenital eritema abigne, and livedo reticularis-disorders related to congenital or acquired skin variance. These diseases must be excluded (differential diagnosis) for proper diagnosis and treatment of SSH.²

CASE REPORT

A 54-year-old male patient was diagnosed with lung adenocarcinoma and was getting treated at the medical oncology clinic. The patient had been taking cisplatin and pemetrexed for the past 12 weeks. In his last visit, vinorelbine [25-30 mg/m² intravenous; 60 mg/m² oral dose (day 1-8) q3w] was prescribed due to the disease progression. The drug was administered in the distal dorsal vein of the left forearm as an intravenous infusion. Infusion was followed by a 100 cc 0.9% saline flush.

The patient was admitted to the outpatient clinic with the complaint of a rash at the site of the injection

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after the first dose of vinorelbine was administered. Erythematous hyperpigmentation had appeared at the infusion area a week after chemotherapy. Skin examination revealed linear and serpiginous erythematous lesions over the superficial venous plexus of the left forearm (Figure 1). However, no other adverse condition such as axillary lymphadenopathy, superficial venous thrombosis, thrombophlebitis, or extravasation was observed. The patient consulted a dermatologist and a topical steroid treatment was suggested and followed up.

Histopathological examination was not considered because the appearance of the lesions and the patient's history were typical. The patient was informed that the lesion was benign and that it would limit itself and regress over time. As the lesions regressed completely with the topical medication, vinorelbine treatment was recommenced. Fortunately, the lesions did not recur. The total dose of vinorelbine given to the patient was 1,580 mg. We specifically report this case to emphasize that the use of vinorelbine (a commonly used chemotherapeutic agent) may lead to the occurrence of SSH even with the intravenous first dose of this drug. Informed consent of the patient was obtained while preparing this case report.

DISCUSSION

The pathogenesis of SSH remains unclear. In contrast to superficial venous thrombosis or Thrombophlebitis, veins remain intact in SSH.^{4,5} Some of the known drugs that contribute to the etiology of SSH include 5-fluorouracil, daunorubicin, vinorelbine, vinblastine, vincristine, nitrogen mustard, 6-



FIGURE 1: Serpentine supravenuous hyperpigmentation of the left arm of the patient.

mercaptopurine, bleomycin, dacarbazine, docetaxel, and paclitaxel.⁵

Vinorelbine is a chemotherapeutic drug used commonly in the treatment of breast and lung cancers. It may cause serious local damages leading to extravasation injury. Some of the side effects of bolus injection include skin irritation and phlebitis. The molecular mechanism of SSH associated with this drug is also unclear. Several theories suggest that the drug might impart a direct toxic effect on the vascular endothelium, where it induces loss of vascular integrity and promotes vascular permeability.

It can be surmised that the toxicity of the drug induces extravasation injury, which in turn stimulates the surrounding epidermal melanocytes resulting in hyperpigmentation.⁴ Venous insufficiency can be the reason for vascular endothelium damage.^{4,6} The local reactions can be prevented by terminating the use of medications that causes serious side effects or by a short intravenous infusion (15-30 min) along with adequate venous irrigation (75-124 mL) instead of bolus administration of drugs. There is no specific treatment for SSH, and topical steroids are only partially effective. We propose that copious venous irrigation after each chemotherapeutic infusion may prevent micro thrombus formation or the occurrence of SSH. Once the SSH lesions regress in patients, the treatment can be resumed, but close clinical monitoring of the patient is required.

Vinorelbine-associated SSH cases are rarely reported.⁶⁻¹⁰ This case report aims to raise awareness and add to the current understanding of chemotherapeutic drug-related rare side effects.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Ahmet Dirican, Atike Pınar Erdoğan; **Design:** Ahsen Duygu Yetut, Ferhat Ekinici; **Control/Supervision:** Atike Pınar Erdoğan; **Data Collection and/or Processing:** Ahsen

Duygu Yetut; **Analysis and/or Interpretation:** Ahmet Dirican; **Literature Review:** Semra Taş; **Writing the Article:** Ahsen Duygu Yetut; **Critical Review:** Ferhat Ekinici; **References and Findings:** Cumali Çelik; **Materials:** Semra Taş, Ahsen Duygu Yetut.

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