Linear Hyperpigmentation of the Left Hand Following Chemotherapy

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CASE REPORT

A 48-year-old female had been diagnosed with Paget's disease of the right breast in 1992 and had received a modified radical mastectomy. She had also received adjuvant chemotherapy with 12 courses of single daily 5-fluorouracil (5-FU) therapy, docetaxel for 5 years, two courses of vinorelbine, and one course each of cisplatin and etoposide. Asymptomatic linear hyperpigmentation along the superficial veins of the dorsal left hand and wrist was present for at least 6 months (Fig. 1). There was no history of extravasation or phlebitis preceding the hyperpigmentation.
**DIAGNOSIS:** Chemotherapy-induced Serpentine Supravenous Hyperpigmentation

**DISCUSSION**

It is well known that chemotherapeutic drugs may induce various patterns of hyperpigmentation of the skin, mucosa, and epidermal appendages. For example, 5-FU-induced hyperpigmentation occurs in 42% of Caucasian patients. In a recent study, skin hyperpigmentation occurred in 26% of biliary tract carcinoma patients following weekly 24-hour infusions of high-dose 5-FU and leucovorin. However, linear hyperpigmented streaks over the arm veins used for injections without previous erythematous changes have rarely been reported.

Serpentine supravenous hyperpigmentation (SSH) is a peculiar, linear pigmentation pattern localized to the skin overlying veins that is observed following intravenous cytotoxic drug administration. Persistent supravenous hyperpigmentation following 5-FU injection has also been described by Hrushesky, who suggested the term "serpentine supravenous hyperpigmentation." These lesions usually develop after several infusions, and while 5-FU is the most frequently incriminated agent, isolated cases of SSH following fotemustine, vinorelbine, triazinate and other polychemotherapy regimens have been reported.

The time of onset is variable and the pigment aberrations may persist for more than 1 year after chemotherapy. Histopathologic findings of SSH have primarily revealed basal hyperpigmentation and pigment incontinence, while inflammatory changes are usually not present. The pathogenesis of SSH has not been well clarified. Possible hypotheses include: ① subclinical thrombophlebitis-induced postinflammatory hyperpigmentation of the overlying skin; ② promotion of melanin synthesis via removal of inhibitors of tyrosinase by certain drugs, such as busulfan; and ③ direct stimulation of melanocytes by fotemustine.

Persistent supravenous erythematous eruption (PSEE) may evolve into hyperpigmentation. SSH and PSEE cannot be distinguished by the time required for the reaction pattern to appear. The only difference in clinical manifestation is that the latter lesion is associated with previous erythematous inflammatory eruption.

In our patient, the lesions developed slowly over at least 6 months. During this period, she completed docetaxel and high-dose 5-FU treatment, and due to disease progression with lung metastasis, two courses of vinorelbine and one course of cisplatin/etoposide were given via peripheral lines. Skin pigmentation persisted for additional 2 months, when the patient expired with respiratory failure. It is difficult to clarify the relationship between the time course of chemotherapy and the onset of skin lesions. In addition, we do not know which drug is responsible for the observed hyperpigmentation. According to the literature, 5-FU and vinorelbine are the most likely culprits.

There is no specific treatment for SSH, although they may disappear gradually. Central venous access routes could potentially be used to protect the skin overlying the peripheral veins from darkening.

**REFERENCES**