Supravenous Hyperpigmentation Induced by Vinorelbine

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Antiblastic chemotherapeutic agents may induce well-recognized pigmentary changes involving the skin, mucosa and epidermal appendages [1].

We describe a localized supravenous hyperpigmentation induced by a vinca alkaloid, vinorelbine.

Case Report

A 60-year-old man affected with inoperable squamous cell carcinoma of the left lung (stage IV) underwent a monochemotherapeutic cycle with vinorelbine (5'-noranhydro-vinblastine). The treatment regimen consisted of a 25 mg/m² intravenous injection of vinorelbine once weekly. The drug was administered through a brief vein infusion (15-20 min) in a 150-ml isotonic sodium chloride solution, followed by an abundant washing of the injected vein.

Three days after the third infusion, the patient developed a supravenous, streaky, dark-brown hyperpigmentation at the sites of the vinorelbine injections on the left cubital fold. No drug infusion was performed on the right forearm.

Further venous injections increased the hyperpigmentation, with a more evident streaked and serpiginous aspect.

There was no other mucocutaneous hyperpigmentation. Histopathology revealed an increased melanization of the basal cell layer and within melanophages in the upper dermis, without evidence of dermal inflammatory infiltrate.

Discussion

Our patient showed a localized hyperpigmentation developing in the supravenous skin after vinorelbine infusions. Pigmentary changes were not preceded by any evidence of skin inflammation or thrombophlebitis and did not appear in a sun-exposed area. In addition, the patient denied any exposure to any UV source. A streaked hyperpigmentation overlying the arm veins, defined as 'serpentine supravenous hyperpigmentation' has been previously reported after intravenous injection of 5-fluorouracil [2-4].

More recently, Claudy et al. [5] have reported 2 cases of supravenous hyperpigmentation after fotemustine administration. The mechanism of fotemustine pigmentation is not well defined, but a depletion of reduced thioredoxin resulting in a tyrosinase stimulation has been postulated [6]. Vinorelbine is a cytostatic agent of the vinca alkaloid family that has been recently introduced in the chemotherapy of non-small cell lung cancer [7].

Skin side effects include alopecia, local irritation and phlebitis, with sclerotic evolution, at the site of injection, mainly after bolus administration [7]. Extravasation may produce severe local

injury. These local negative reactions may be prevented by a brief intravenous infusion (15-30 min) instead of bolus administration [7].

To our knowledge, no previous report of localized hyperpigmentation occurring in the area of vinorelbine infusion has been reported.

The mechanism of vinorelbine toxicity is unknown. A direct stimulation of melano-cytes or a depletion of tyrosinase inhibitors, resulting in the observed hyperpigmentation, as suggested for busulfan [8] or fotemustine [5, 6], may be occurring.

Because vinorelbine has been recently introduced in cancer chemotherapy, further clinical experience will be necessary to establish the true incidence of this cutaneous side effect.

References

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