UNUSUAL SIDE EFFECTS OF SYSTEMIC 5-FLUOROURACIL

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A 55-year-old male having adenocarcinoma of the caceum developed photosensitivity and temporary nail pigmentation following use of systemic 5-fluorouracil. The lesions disappeared following withdrawal of the drug, but recurred when the drug was started again.

Key words : 5-Fluorouracil, Photosensitivity, Nail pigmentation.

Fluorouracil is a fluorinated analogue of pyrimidine. Use of 5-FU in the form of a 5% cream or a 25% solution in propylene glycol is well established for the treatment of multiple solar keratoses, Bowen's disease, warts, erythroplasia of penis and basal cell carcinoma.[1] Besides skin conditions, systemic administration is most effective for the treatment of carcinoma of stomach, colon, rectum, breast, ovaries, cervix and liver. The drug is toxic to both bone marrow and the alimentary epithelium. Side effects include transient conjunctival irritation, corneal erosion, erythema and crusting in the skin folds and creases, erosion of the lower lip, alopecia and seborrhoeic dermatitis of the face and scalp.[2,3] Allergic contact and photosensitivity reactions[2,4] and onycholysis following application around nails[5] and eczema[6] have been reported. A patient who developed photosensitivity and temporary pigmentation of the nails is reported herewith.

Case Report

A 55-year-old male, underwent emergency laparotomy in March 1983. Perforated appendix with a small portion of the small intestine, caecum and ascending colon were removed and right hemicolectomy was performed. The histopathological report of the excised tissue was adenocarcinoma arising from the caecum. Intravenous injection of 5-FU, 500 mg twice a week was started on 14 April, 1984. In the third week of May 1984 he started developing erythema over the sun-exposed areas i.e. face, front of neck, dorsal aspects of both hands and both forearms. Erythema was followed by a few papulo-vesicular eruptions. Maximum effect was noticed on the face. Clinically, a diagnosis of photosensitivity following use of systemic 5-FU was made. Every time 5-FU was injected intravenously, the patient developed diarrhoea lasting for 2 days. A month and a half later, the patient noticed pigmentation of all the nails of his hands and feet. On examination, all the nail plates of hands and feet were bluish-black. The pigmentation was more marked on the finger nails. Due to the problem of diarrhoea following 5-FU injection, an alternative regimen of mitomycin 6 mg, once a week intravenously was started. A week later, the manifestations of photosensitivity started improving and complete clearance of photosensitivity except residual pigmentation was observed at the end of 2 months of stoppage of 5-FU. The nail pigmentation also gradually cleared up along with growth of the nails. Patient developed similar type of photosensitivity reactions when 5-FU was given again after 3 months, requiring complete stoppage of treatment with 5-FU.

Comments

Systemic photosensitivity is often caused by drugs such as sulphonamides, sulphonylureas, chlorthiazides, demethylchlortetracycline, phenothiazines, griseofulvin, isoniazid, diphenhydra-

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mine, psoralen etc.[7] 5-FU under occulsive dressing produces erosions and pigmentation of normal skin.[8] Photosensitivity following systemic use of 5-FU is uncommon. Falkson and Schulz[3] investigated the skin changes in patients with advanced carcinomatosis and found photosensitivity manifested in the form of either erythema, pigmentation and polymorphic light eruption. They also noticed that in all these cases when therapy was discontinued, photosensitivity disappeared.

The exact mechanism of the enhanced reaction to light is not known. Sweat glands excrete urocanic acid which has protective action on human skin exposed to sunlight.[9] The decrease in excretion of urocanic acid during 5-FU therapy occurs. However, according to Falkson and Schulz,[3] alterations in the epidermal RNA and possibly DNA are also responsible for the great enhancement of erythema and direct and indirect variety of pigmentation from sunlight.

Nail pigmentation has been noticed following prolonged treatment with tetracycline,mepacrine, chloroquine and inorganic arsenicals and argyria. Falkson and Schulz[3] and Staley et al[6] had noted diffuse melanosis of the nail following systemic 5-FU therapy. They have also reported in a few patients, transverse melanotic striations of the nail plate corresponding to the periods of growth during 5-FU therapy.

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