

CYCLOPHOSPHAMIDE NAIL PIGMENTATION

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SYNOPSIS

Two Chinese patients with histiocytosis developed cyclophosphamide induced nail plate pigmentation, probably the first report in this ethnic group. The mechanism of the pigmentation is discussed. This is probably a drug reaction in certain genetically determined individuals rather than a pharmacological toxic reaction.

INTRODUCTION

Discoloration of the nail plate has been caused by drugs such as chloroquine (Tuffanelli et al., 1963), metals such as arsenic and may be a feature of systemic disease such as hepato-lenticular degeneration (Bearn and McKusick, 1958). The damage probably starts in the nail matrix and becomes visible initially in the region of the lunula of the nail plate. As the plate progresses distally with the growth, the pigmented part of the nail plate moves towards the free edge of the nail plate.

This report describes purple to brownish band of discoloration of the nail plates, probably caused by the cyclophosphamide in two Chinese patients who had malignant histiocytosis (non-Hodgkin's lymphoma) presenting with skin deposits.

MATERIAL AND METHODS

Case 1

A 68 year old Chinese female presented with lumps on the skin which was diagnosed as histiocytic lymphoma (non-Hodgkin's) without systemic involvement. After receiving a total dose 7400 mg. of cyclophosphamide and eight weeks from the initial day of therapy, a curvilinear purplish brown pigmentation of the distal edge of the lunulae was seen in the big toe of both feet (Fig. 1) and all the fingers of both hands (Fig. 2) with prominence in the medial three fingers. As the patient succumbed not much later, the distal progress of the pigmentary band could not be observed.

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Figure 1. Big toe-nail of both feet with band of pigmentation. Case 1.



Figure 2. Finger nails of the left hand. Pigmented band is seen in all the nails. Case 1.

Case 2

A 25 year old Chinese male developed nodules on the skin and investigation lead to diagnosis of malignant histiocytosis with systemic involvement. He was treated with 'CHOP' regime (intermittent) which included cyclophosphamide, adriamycin, vincristine and prednisolone. After a total dose of 4000 mg. of cyclophosphamide and 8 weeks after the initial therapy, the patient developed purplish brown pigmentation of the entire lunulae with the distinct distal dark border in the thumbs (Fig. 3) and the fingers of both hands. The toes were not affected. During the period of his stay in the ward the pigment was found to progress distally.

DISCUSSION

Both Amar Inal Singh (1972) and Harrison and Wood (1972) suspected that cyclophosphamide may induce nail pigmentation. However a definite aetiological relation between the drug and the nail change was proposed by Shah et al, (1975). The initial reluctance to attribute the cause of pigmentation to cyclophosphamide was because the patients, most of whom had malignancy, received additional therapy such as adriamycin or radiation, both of which are known to cause pigmentation. However observation of pigmentation in patients who received cyclophosphamide alone including one of the patients in this report,



Figure 3. Thumb nails of both hands with diffuse pigmentation of the lunulae with distinct distal border. Case 2.

disappearance of the pigmentation following withdrawal of the drug (Harrison and Wood, 1972) and development of multiple bands of pigmentation in patients with intermittent therapy, together suggest an aetiological role to the drug.

Though the shade of the discoloration reported here varied from purplish to brown it is due to melanin, as it is known that melanin deeper to the basal layer in a keratinising epithelium appears purplish to blue on the surface as seen in such conditions as lichen planus and Mongolian blue spot. This physical phenomenon tends to be more distinct in non-dark skinned individuals.

Where the racial origin of the patients with this complication was mentioned in reports, it was the East Indians and the American Blacks who developed the pigmentation. The present observation of pigmentary change in Chinese is probably the first of its kind. Though there are reports of concurrent discoloration of the palmar creases and the gum, majority of the patients like the two described here, had their pigmentary change confined to the nails.

The mechanism of pigmentation is not clear. Increase in the number of melanosomes and or dispersal of aggregated melanosomes is usually responsible for the pigmentary change but this is difficult to reconcile with the fact that the change was confined to the nails only or predominantly in the nails. From personal observation of the absence of similar change in the majority of patients who receive cyclophosphamide and from a handful of patients with this pigmentary change recorded in the literature, it is probable that this discoloration is a drug-reaction manifested in certain genetically determined individuals rather than a pharmacological toxic reaction.

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