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Trichochromes in Human Malignant Melanoma

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Abstract. Decarboxytrichochromes B and C were isolated from a melanoma metastasis in a red-haired man, indicating the presence of trichochromes B and C in the tissue. Trichochromes E and F were not detected.

Trichochromes are pigments of low molecular weight present in certain red hair and feathers (3, 4). Two of them, trichochromes B and C, have been detected in the urine of some patients with widespread melanoma metastases (1, 6).

Trichochromes E and F, however, reported to be present in red feathers (3), have not been detected in red human hair (2) or in melanoma urines (1, 6).

Trichochromes are insoluble at neutral pH. It seems likely that, if formed in human melanoma, trichochromes E and F would be excreted in the urine in the same way as trichochromes B and C. No study on trichochromes in melanoma tissue has

been performed previously, and we now report an investigation on trichochromes in a human melanoma metastasis.

MATERIAL AND METHODS

Melanoma tissue was obtained at necropsy of a 41-year-old man with red hair. A few weeks before death he had shown excretion of large amounts of 5-S-cysteinyl-dopa (123 mg/24 h) and of trichochromes B and C (29 mg/24 h).

1.94 g of a liver metastasis was homogenized in 10 ml 0.1 M NaOH, oxidized for 15 hours in oxygen current to destroy any 5-S-cysteinyl-dopa and then analysed for trichochromes as previously described (6).

RESULTS AND COMMENTS

Thin-layer chromatography showed decarboxytrichochromes B and C, indicating the presence of trichochromes B and C in the melanoma metastasis. No trichochrome E or F could be detected. The quantity of trichochromes was calculated, on the basis of the molecular absorption of decarboxy trichochrome C, to be 4.8 µg/g melanoma tissue.

Although the total tumour mass was not calculated in our patient the content of trichochromes in the tumour and in the urine shortly before death indicates rapid excretion of trichochromes from the tumour tissue. The absence of detectable amounts of trichochromes E and F indicates that these compounds are formed in melanoma either in very small amounts or not at all.

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Subhydroxylated Collagen in Scleroderma

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Abstract. In sclerodermal skin, the values for proline (Pro), hydroxyproline (Hyp) and hydroxylysine (Hyl) are lower than in normal skin. The molar ratio Hyp to Hyl is lowered. The molar ratio Pro to Hyp was found to be elevated, while that of Pro to Hyl was like that of normal skin. It was concluded that in scleroderma the hydroxylation of Pro to Hyp is incomplete, resulting in an abnormal collagen.

Key words: Proline; Hydroxyproline; Hydroxylysine; Collagen; Subhydroxylated proline

In sclerodermal skin, the dermis is thickened and hypertrophic, while the epidermis is thin and atrophic. Both light- and electron microscopy demonstrate the dermal thickening to be due to increased quantities of collagen fibres (7).

Hydroxyproline (Hyp) and hydroxylysine (Hyl) are the two amino acids which specifically characterize the collagen molecule, and, in chemical analysis of tissue, they are generally used to indicate collagen. The molar ratio of Hyp to Hyl in normal, dry, defatted skin varies very little from person to person (unpublished data on 212 control skin samples). The two amino acids are produced by hydroxylation of certain residues of proline (Pro) and lysine (Lys) incorporated in procollagen. De-

terminations of procollagen proline hydroxylase in sclerodermal skin have given varying results (10). An increased rate of collagen formation is indicated by an increased urinary output of certain high molecular Hyp- and Hyl-containing peptides in active progressive scleroderma (3).

Several authors have found a low Hyp content per weight unit of sclerotic skin in comparison with normal skin (4, 6, 8).

The morphological and the chemical findings could be explained by the production of excess, partly subhydroxylated collagen, as well as non-collagenous material in sclerotic skin.

In a recent study (5) we showed a highly significant decrease in the contents of hydroxyproline (Hyp) and hydroxylysine (Hyl) per weight unit of dried defatted skin of patients suffering from scleroderma. The Hyp to Hyl molar ratio was lower than in normal skin. The possibility of incomplete hydroxylation of proline (Pro) was postulated.

MATERIAL AND METHODS

Four mm punch biopsies of wrist skin were taken from 17 patients with active, progressive generalized scleroderma of the acrosclerosis type and from 7 healthy individuals. All samples were analysed for Pro, Hyp and Hyl. One of the patients had been successfully treated for generalized scleroderma with dimethylcysteine, an inhibitor of collagen synthesis, and was now cured. The Mann-Whitney test was used to assess the difference between the contents of Pro, Hyp and Hyl in the skin biopsies.

Pro was determined by a modification of the Troll & Lindsley procedure (9), which is not interfered with by either lysine or by ornithine (unpublished data). Hyp was assayed by the method of Blumenkrantz & Asboe-Hansen (1), and Hyl by a method developed by the same authors (2).

RESULTS

The results of all analyses and the calculated molar ratios Pro to Hyp and Pro to Hyl appear from Table I. When comparing the values for Pro, with the exception of the patient who experienced complete regression, we found a significantly lowered content in the scleroderma group ($p < 0.001$), and the values of Hyp were even further depressed ($p < 0.001$) as compared with the controls. Consequently, the ratio Pro to Hyp was significantly higher in scleroderma than in control skin ($p < 0.001$). In contradistinction, the ratio Pro to Hyl did not differ from that of skin of normal controls (Table I).