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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
Pachyonychia Congenita


A 10-year-old Malay girl whose parents were second cousins, presented with a history of long, thickened nails present since 8 months of age. Initially, she had had episodes of inflammatory swellings of the nail beds of both fingers and toes followed by recurrent shedding of the nails. This process ceased after a short while and was replaced by hard and thickened nails. Some of these nails grew perpendicular to the nail bed. The nails grew rapidly and needed trimming at 3-day intervals, but soon trimming became impossible. There was no history of similar nail changes in the family.

Physical examination showed that she was normal for her race, sex, and age. There were no systemic abnormalities; the main changes were in the nails and skin.

All nails were involved, the fingernails more than the toenails. They were hard, thick, and cylindrical and had a yellowish discoloration. There was evidence of subungual hyperkeratosis in some nails (Fig. 1). On her skin she had fine horny papules of the central area of the face, buttocks, and legs. The rest of the skin was normal (Fig. 2). There was no evidence of palmar–plantar hyperkeratosis, hyperhidrosis or mucosal lesions. Her hair, teeth, eyes, and tongue were normal.

Discussion

The term *pachyonychia congenita* was first used by Jadassohn and Lewandowski\(^1\) to describe a case in which there were dystrophic nails, palmar and plantar hyperkeratosis, blisters of the feet, and leukokeratosis of the tongue. There have been numerous reports in the literature on families with some of these features. There are different syndromes, all inherited as an autosomal dominant.

There are probably four different syndromes, the classical type 1 being the case described by Jadassohn. In type 2, the nail thickening is uniform and is associated with chronic candidiasis of the mouth.

Keratoses are less severe. Type 3 is the most interesting. Affected children have erupted teeth at birth. Hyperkeratosis is insignificant, and nail thickening is much less severe. The characteristic feature of type 4 is a widespread macular pigmentation affecting the neck and axillae. Nail changes and hyperkeratosis are of moderate severity.

The present case is of interest because there were only two features of the syndrome, the nail changes and the presence of horny papules of the skin of the face, legs, and buttocks. The other interesting feature was the lack of a family history. The possibility of a mutant gene cannot be excluded.

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*Address for correspondence: A. Sivasundram, M.B.B.S., Department of Dermatology, General Hospital, Kuala Lumpur, Malaysia.*

*Fig. 1. Abnormalities of the fingernails.*
The Development of Chemotherapy

It is also necessary to look at the role of dyes in the brilliant development of chemotherapy by Ehrlich. Soon after Ehrlich had observed the power of methylene blue to stain nerve cells selectively, he found the same dye would colour malaria parasites. In 1891, he and Guttmann found the dye effective in human tertian malaria, although not nearly as good as quinine. Absence of knowledge at that time about malaria in species other than the human prevented exploitation of this piece of information.

Ehrlich established associations with dyestuff chemists, particularly with Ludwig Benda, chemist of the Farbeweke Cassella Co., Frankfurt, and also with hematologists and immunologists to whose sciences he made such contributions, and with many other biological and chemical investigators. The breadth of these connections and of his interests enabled him to advance and elaborate arguments for what he called the side-chain theory. He postulated affinities of chemicals attaching themselves to a pathogen by side-chains in a reaction similar to the affinity of dyes for textiles fibres. The chemicals attaching themselves to a pathogen by means of a side-chain were thought to be able to interfere with the pathogen’s metabolism. Methylene blue’s dyeing of malarial parasites was the first example of chemotherapy. Mice and rats proved susceptible to the trypanosomal parasites and Trypan red, a dye, proved to have antitrypanosomal properties. Further studies were then immediately possible.

In this work on anti-trypanosomal entities containing arsenic, Ehrlich declared the principle of the therapeutic index. This very important therapeutic indicator may be defined as:

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\text{therapeutic activities} = \frac{\text{desirable biological activity against uneconomic species (cells)}}{\text{undesirable biological activity against economic species (cells)}}
\]

He observed the occurrence of resistance, and drew conclusions about 20 dyes and arsenic-containing compounds on the basis of periodic table relationships between nitrogen and arsenic, and by reason of trivalent arsenic’s therapeutic activity in the As = As linkage, an analogue of the azo structure found in dyes. Thus began the search for therapeutically effective organic arsenicals, synthesized to order by dye manufacturers. These effective substances were tested against trypanosomes in mice and rats, and against the syphils organism in rabbits. Compounds were found with acceptable therapeutic indices and desirable antisyphilitic activity, particularly No. 606 (arsphenamine or Salvarsan) in 1909.—Paterson GR. Relationship between synthetic dyes and drug entities. Can Bull Med Hist. 1984;1:15.

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References