



# Pachyonychia Congenita Project

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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: Therapeutic and Immunologic Aspects

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**Abstract:** A 4-year-old girl with pachyonychia congenita was followed from birth. During childhood, slow progression of the nail hypertrophy was seen because she was not willing to have the nails ground or cut. After grinding of her nails under general anesthesia, the child has had acceptable nail thickness, and continued regular grinding without anesthesia. The child had recurrent oral and cutaneous candidiasis. Investigations showed a weakly positive response to *Candida albicans* in the lymphocyte transformation test, and absence of a delayed hypersensitivity skin test response to *Candida*. The secondary infection due to *Candida* seemed to prevail because of an immune defect.

In 1906 Jadassohn and Lewandowsky described a genodermatosis characterized by hypertrophy of the nail bed, oral leukokeratosis, palmoplantar hyperkeratosis, follicular hyperkeratosis, and blistering of the feet. Since then numerous reports have been published and different treatments have been used, but as yet no effective treatment is available for the thickened nails and the palmoplantar hyperkeratosis. In some patients the abnormal oral mucosa may predispose to the development of chronic oral candidiasis. Furthermore, disturbances in the cellular immune response to *Candida* have been found (1) that might indicate an associated selective, immune deficiency in some cases.

We present a patient who underwent successful treatment of nail hypertrophy, and who demonstrated absence of the delayed hypersensitivity to *Candida*.

## CASE REPORT

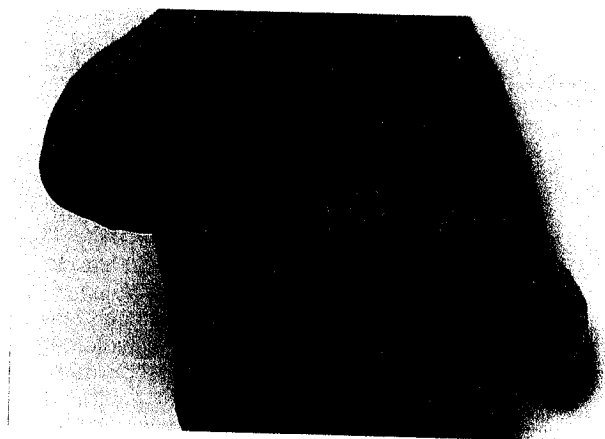
The patient was a 4-year-old girl who had thickened fingernails and toenails since birth. She was the first

child of a healthy, nonconsanguineous couple. Her nails were curved from side to side and their color was yellow to green. She also had leukokeratosis of the tongue that was refractory to antimycotic treatment. At age 6 months the patient developed a marked, recurrent diaper dermatitis with secondary *Candida* infection. Later, in early childhood, follicular hyperkeratosis was found at the neck, thighs, and knees. Bullous eruptions and increased palmoplantar hyperkeratosis developed.

The oral leukokeratosis was complicated by marked angular cheilitis due to *Candida* infections. Local antimycotic treatment had only a partial, temporary effect on the oral and skin lesions. Therefore the child's immune response to *Candida* was tested.

During early childhood, slow aggravation of the nail hypertrophy occurred, leading to functional and cosmetic complaints (Fig. 1). The child would not accept cutting or grinding of the nails, and treatment with 40% urea ointment was inadequate. When she was 3½ years old, the nails were ground and milled under general anesthesia with the use of

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**Figure 1.** The patient's hypertrophic fingernails before they were ground under general anesthesia at age 3½ years.

a grinding machine (Maniquick, Maniquick Denmark APS, Brønshøj, Denmark). Since then more acceptable nail thickness (Fig. 2) has been maintained by regular grinding with the machine without anesthesia (Fig. 3).

#### LABORATORY DATA

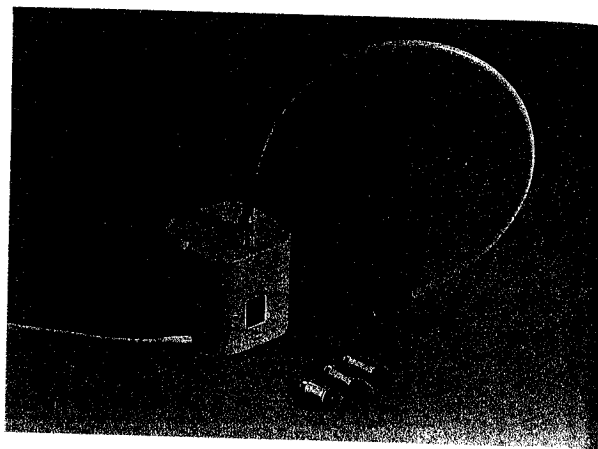
Several cultures from the oral mucosa, angular cheilitis, and pustular lesions in the diaper area showed *Candida albicans* and on some occasions, group A hemolytic streptococci as well.

The total leukocyte and differential counts were normal. Lymphocyte function tests at ages 2 and 2½ years showed normal lymphocyte counts, and the numbers and distribution of CD3, CD4 and CD8 cells were normal, as was the CD4:CD8 ratio (2.3).

Lymphocyte transformation tests with mitogens (PHA, ConA, PWM) and antigens purified protein



**Figure 2.** The patient's fingernails after grinding under general anesthesia, age 3 years, 10 months.



**Figure 3.** The grinding machine.

derivative (PPD), *C. albicans*, *Escherichia coli*, and streptococcal antigen (Varidase) showed a slightly decreased proliferative response to the mitogens compared with healthy adults. Antigen stimulation showed a negative response to streptococcal antigen, *E. coli*, and PPD, and a weakly positive response to *C. albicans* ( $3.8 \text{ cpm} \times 10^3$ ) compared with healthy adult controls. Serum IgG, IgA, IgM, and IgE levels were normal.

Delayed hypersensitivity skin testing was carried out using Multitest CMI (Institut Merieux, France) and read at 48 hours. Positive reactions to tetanus and diphtheria were found, consistent with previous vaccinations, but skin reactions to *Streptococcus*, *Candida*, tuberculin, *Trichophyton*, and *Proteus* were absent.

#### DISCUSSION

Pachyonychia congenita has been described in more than 150 patients. Familial cases show an autosomal dominant inheritance. Four clinical types have been delineated (2); our patient seems to be compatible with type II.

Treatment of the dystrophic nails is still far from satisfactory. It is difficult to keep the nails well trimmed with the use of clippers, and young children may protest against the procedure. The dystrophy can be so distinct that removal of the nails and nail matrix may be considered. Such a surgical approach may be cosmetically desirable (3).

In our patient the nail hypertrophy was so aggravated that she had considerable physical and cosmetic complaints. Thus, at age 3½ years thorough grinding of all nails was performed under general anesthesia.

Aromatic retinoids have been effective in pa-

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tients with pachyonychia congenita (4), but in our opinion they are contraindicated due to considerable toxicity when used in long-term treatment.

Oral leukokeratosis is often mistaken for oral candidiasis, but treatment with antimycotics is fruitless. As seen in our patient, however, remarkable, recurrent oral candidiasis as well as skin infections due to *Candida* may occur due to an immune defect (2,5). Lymphocyte stimulation by *Candida* and delayed hypersensitivity skin reactions to the organism were absent in one reported patient (1). Similarly, in our patient anergy to *Candida* was found by skin testing, but lymphocyte stimulation with *Candida* antigen was weakly positive. Furthermore, this child had a negative response to streptococcal antigens in spite of the fact that she had had streptococcal skin infections. However, no signs of a more profound immune deficiency state were evident clinically or in the immunologic tests.

Our case provides further evidence for the opinion that immune defects comparable to those in patients with chronic mucocutaneous candidiasis (CMC) may be present in patients with pachyonychia congenita. In many cases of CMC there are narrow abnormalities in cell-mediated immunity (6) that lead to a selective deficiency in the recognition and processing of *Candida*, although the handling of other antigens is intact, as in our patient. The inherited abnormality of the oral mucosa in pachyonychia congenita may predispose to infection with *C.*

*albicans* in early infancy, and hence the absence of a normal cellular response to *Candida* (1). Furthermore, structural or functional abnormalities in the skin and mucous membranes might prevent appropriate induction of delayed hypersensitivity, even in the presence of a normal immune system. Thus, more detailed studies are required to elucidate the apparent minor dysfunction of the immune system as part of the pachyonychia congenita syndrome.

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