



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.

LETTERS TO THE EDITOR

Pachyonychia congenita and hidradenitis suppurativa: no response to infliximab therapy

Editor

Pachyonychia congenita (PC) is a rare genodermatosis affecting the nails, skin, oral mucosae, larynx, hair and teeth. There are two subtypes of PC: PC-1 (or Jadassohn-Lewandowski type) and PC-2 (or Jackson-Lawler type). Both types show hypertrophic nail dystrophy, focal palmoplantar keratoderma and follicular keratoses of the elbows, knees and hips. The clinical discrimination between PC-1 and PC-2 usually depends on more prominent oral leukokeratosis in PC-1, or, conversely, in findings of steatocystomas/pilosebaceous cysts, vellus hair cysts, hair abnormalities and natal teeth in PC-2. Pathogenic mutations in keratins K6a or K16 are associated with the PC-1 phenotype, whereas K6b and K17 mutations are associated with the PC-2 phenotype.¹ This entity is usually a therapeutic challenge because there is no available effective treatment.

We have been following a 36-year-old woman with a PC type I due to a heterozygous missense mutation 1390A→C in exon 7 of the *KRT 6A* gene. As we have reported previously,² she had been suffering from whitish plaques on the buccal mucosa, thickened toenails and fingernails and recurrent blistering and crust formation on the soles of her feet, followed by gradual development of thick plantar keratoderma, making walking very difficult, especially during summer (fig. 1). Keratosis follicularis was observed at clinical examination. She had no family history of similar findings. Since our report,² she developed lesions compatible with hidradenitis suppurativa in axillary regions and groins (fig. 2) that did not resolve after several systemic antibiotic treatments (cloxacillin, tetracycline or clindamycin). The patient did not accept hormonal therapy. Several treatments for her PC had been tried without any success. Topical treatments (lubricants, emollients, keratolytics such as salicylic acid, antibiotics, antiseptic wet dressings, hydrocolloid dressings, chromium mercury solution, corticosteroid cream, retinoid cream and coal tar) and systemic treatments (etretinate, vitamin A and erythromycin) had very limited effect. Some transient improvement was seen with the use of oral corticosteroids and non-steroidal anti-inflammatory drugs.

Infliximab is an inhibitor of the pro-inflammatory cytokine tumour necrosis factor- α (TNF- α). Good results in hidradenitis suppurativa have been published.^{3,4} On the other hand, it has been shown that keratinocytes become activated in wound healing and many pathologic conditions, like psoriasis or PC. This process, named keratinocyte activation cycle, is orchestrated by growth factors (chemokines and cytokines) and leads to changes in the keratin profile of the cell. In fact, keratins K6 and K16 are up-regulated during this active state. Moreover, the cytokine TNF- α is one of the most important molecules involved in the maintenance of activation.⁵ We hypothesized that if we could inhibit TNF- α , we could inhibit the keratinocyte activation cycle, down-regulating keratin K6 and therefore improving the clinical conditions of our patient.

We started treatment with intravenous infliximab 5 mg/kg. Infusions were performed at 0, 2 and 6 weeks. Four weeks after the last infusion, we could not observe



fig. 1 Keratoderma of the plantar surfaces with severe fissures.



fig. 2 Inflammatory abscesses and nodules of hidradenitis suppurativa on the left groin of our patient.

any improvement on the hidradenitis suppurativa nor the PC lesions. The patient even referred a slight worsening on her palms and soles due to the development of new painful keratosis. The patient has refused further treatment.

There are currently no specific treatments for PC.⁶ To our best knowledge, this is the first case reported of PC and hidradenitis suppurativa treated with infliximab,

although in our case, it was ineffective. On the other hand, we have found a series of PC type II in which five of the six members also had varying degrees of hidradenitis suppurativa.⁷ No treatment was reported. The case of McDonald *et al.*⁸ could be another example of this association. Nevertheless, we have not found any report of PC-1 associated with hidradenitis suppurativa.

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