



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.

include erythema, pruritus, pain, and oedema and do not necessitate discontinuation of therapy. Etanercept has also been associated with drug-induced systemic lupus erythematosus, which resolved following discontinuation of biological therapy. Anti-double-stranded DNA antibodies and antihistone antibodies have been detected in these etanercept-treated patients.⁴ Erythema multiforme has also been described in association with etanercept therapy in a patient with rheumatoid arthritis.⁵

Although this patient has no history of atopy, it is possible that etanercept has disrupted the T-helper 1/T-helper 2 balance by down-regulating T-helper 1 cytokines, thereby favouring the development of eczematiform reaction. There are reports of development of atopic dermatitis in patients undergoing infliximab therapy.⁶

To our knowledge, this patient has not taken any unprescribed nonsteroidal anti-inflammatory drugs, which could have caused a drug rash, thereby misleading evaluation of drug side-effects. A rechallenge with etanercept would be ideal.

Physicians should be aware of this newly described etanercept-induced rash as increasing uses are being found for this drug namely in psoriasis, psoriatic arthropathy and other autoimmune diseases.

J Lai-Cheong,*† R Warren,† R Bucknall,‡ R Parslew†
 †Department of Dermatology, Royal Liverpool and Broadgreen University Hospital NHS Trust, Thomas Drive, Liverpool L14 3LB and ‡Rheumatic Diseases' Unit, Royal Liverpool and Broadgreen University Hospital NHS Trust, Prescot Street, Liverpool L7 8XP, UK, *Corresponding author, Department of Dermatology, Royal Liverpool and Broadgreen University Hospital NHS Trust, Thomas Drive, Liverpool L14 3LB, UK, tel./fax 020 7064 4887; E-mail: jelai_cheong@hotmail.com

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Pachyonychia congenita: treatment of the thickened nails and palmoplantar circumscribed callosities with urea 40% paste

Pachyonychia congenita (POC) is an autosomal dominant disorder of keratinization, which is characterized by pachyonychia, hyperkeratosis of palms and soles and follicular keratosis. POC is resistant to therapy. Urea 40% cream was found to be effective in the removal of dystrophic nails, callosities, and necrotic eschars; accordingly, we decided to use this preparation for the control of excessive nail thickness and circumscribed palmoplantar hyperkeratosis of a 27-year-old male patient having POC type II.

POC is an autosomal dominant disorder of keratinization in which deletion/insertion mutations affect the genes of keratin types 6, 16 and 17. POC is characterized by pachyonychia, hyperkeratosis of palms and soles, and follicular keratosis.¹

Although POC is resistant to therapy, some studies report unpredictable response to systemic retinoids^{2,3} and phenytoin.⁴ However, systemic therapy is mostly not helpful for the pachyonychia and the thick hyperkeratosis. Other measures such as nail grinding and electrofulguration of the nail matrix were tried,^{5,6} but both methods are traumatizing and have a temporary effect.

Urea 40% cream was found to be effective in the removal of dystrophic nails, callosities, and necrotic eschars.⁷ Accordingly, we used this preparation for the control of excessive nail thickness and circumscribed palmoplantar hyperkeratosis of a 27-year-old male patient having POC type II (fig. 1). This patient was born with natal teeth and the skin lesions started shortly after birth with history of blisters on the trunk. The patient received neotigason in a dose of 25 mg three times daily, topical keratolytics (salicylic acid 6% and topical retinoids) and underwent nail paring, but these gave little improvement. So, we applied 40% urea paste for the thickened nails and circumscribed callosities. To prepare 40% urea paste, we used the compounding presented in Table 1.

The application of 40% urea paste to the treated areas involved six key steps as recommended by Michelle and Fred⁷:

- 1 Cloth tape (0.5 inch thickness) was applied to outline the nails as well as the thick keratotic lesions and protect the surrounding skin.



fig. 1 Circumscribed hyperkeratotic plaques on the sole before treatment.



fig. 2 Improvement of hyperkeratotic plaques after application of 40% urea paste.

Table 1 40% urea paste preparation

Urea crystals	48 g
Anhydrous lanolin	24 g
Paraffin wax	6 g
White petrolatum	42 g
Total	120 g

- 2 40% urea paste was applied liberally (0.5 inch thickness) over the entire treated areas.
- 3 A liquid adhesive (Mastisol; Ferndale Laboratories Inc., Ferndale, MI, USA) was applied (0.5 inch frame) around the cloth tape.
- 4 Polyethylene film (Saran Usap plastic film; Dow Chemical Company, Midland, MI, USA) was cut and applied to adhere to the liquid adhesive.
- 5 Cloth tape (1 inch thickness) was applied to fix the polyethylene film margins.
- 6 Elastoplast tape was applied over the entire dressing.

The dressing was removed after 72 h followed by immediate cutting of the hyperkeratotic lesions and paring of the nails (within a maximum of 3 min). In case of the hyperkeratotic lesions, the softened tissue could be gently elevated and excised. This procedure was performed

every 2 weeks, until both pachonychia and hyperkeratosis were satisfactorily reduced in size. Thereafter it was repeated every month to obtain the desired effect. After 3 months, the patient showed marked improvement of both pachonychia and palmoplantar hyperkeratosis (fig. 2) with no side-effects.

Urea (10–25%) is both a moisturizer and skin softening agent. Most effective skin softening properties are achieved with the 40% concentration.⁷ The rapid action of urea results from its strong osmotic effect on the skin. With diffusion in and around corneocytes, urea disturbs hydrogen bonding and thereby exposes water-binding sites. Urea rehydrates the stratum corneum by drawing water from deeper epidermal and dermal tissues. The humectant property explains its ability to soften hard, devitalized tissues. Conversely, after removal of the urea paste from the skin, exposure to air rapidly reverses its humectant effect.⁸ That is why removal of the keratotic tissues soften by urea 40% should be done within 3 min of removal of urea dressing. We recommend the use of urea 40% in the

treatment of both thick nails and circumscribed palmo-planter hyperkeratosis in POC and consider this method safe, effective and non-invasive.

MA El-Darouti,* SA Marzouk, N Nabil, MRE Abdel-Halim, MHM El-Komy, M Abdel-Latif
Department of Dermatology Faculty of Medicine–Cairo University, Kasr Al-Aini hospitals, El-manial, Cairo, Egypt,
 *Correspondence author, 47 El-Falaki St., Bab El-louk 11461, Cairo, Egypt, tel. (00202) 7962509; E-mail: mkomy@hotmail.com

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Aspirin-induced unilateral angioedema of the tongue

Angioedema of the tongue due to drugs, especially aspirin, is a well-known entity and has been reported several times. But unilateral angioedema of the tongue is rarely reported. There are only two case reports of unilateral angioedema of the tongue and both of them are related with enalapril. We report a case of 40-year-old male patient admitting with unilateral angioedema of the tongue 12 h after aspirin usage. To the best of our knowledge this is the first case of unilateral angioedema of the tongue related with aspirin.

A 44-year-old male patient was admitted to our emer-

gency service with a swelling in the left part of his tongue, which suddenly occurred and increased during the last 2 h. In his personal history there was an aspirin ingestion for an occasional headache 16 h ago. There was no history of intolerance to aspirin or other drugs previous to this. The patient denied changing any habits such as toothpaste use or food intake. His family history revealed no abnormality. On the physical examination, the patient had a diffuse, soft and nontender swelling in the left side of the tongue. He had no pain, stridor, respiratory difficulties or fever. His arterial blood pressure was 130/75 mmHg. He had no cutaneous lesions of urticaria. The patient otherwise was found to be healthy. In laboratory tests, IgE and total eosinophil count were within normal limits. Diagnosis was compatible with angioedema. As treatment, epinephrine (0.5 mg subcutaneously), methylprednisolone (60 mg intravenous infusion) in association with chlorphenoxamine HCl (20 mg intravenous infusion) were administered. He improved within 2 h. On follow-up at 1 and 10 days, the patient was totally normal. Unfortunately the patient did not accept to further oral challenge tests.

Urticaria/angioedema and anaphylactoid responses to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) occur in approximately 1% of individuals in an outpatient population. Aspirin intolerance manifests itself as urticaria/angioedema and/or bronchial asthma in otherwise normal individuals. Clinical manifestations may appear from 15 min to 20 h after ingestion. Although urticaria/angioedema may accompany rhinorrhoea, flushing, and asthma, it may occur independently as well. Prick skin testing is of no diagnostic value, passive transfer reactions are negative, and neither IgG nor IgE antibodies have been associated with clinical disease. Oral challenge test is the only definitive diagnostic test for aspirin intolerance irrespective of the presenting clinical symptoms.¹ Although oral challenge test could not be performed in our patient, aspirin seemed to be the only possible agent causing angioedema as there was neither a history of any other drug or food intake, nor trauma.

The interesting part of this patient's angioedema was the unilateral and localized nature. Unilateral angioedema of the tongue is rarely and only reported related with ACE inhibitors.^{3,4} We did not find any report of localized unilateral angioedema of the tongue related with aspirin. Such localized reactions due to aspirin are very rare. To our knowledge, there are only two previous reports of localized angioedema seen in the periorbital region after aspirin ingestion.²

The mechanism for aspirin intolerance is unclear. Mast-cell degranulation has been shown to occur in aspirin-induced angioedema and urticaria. Mast cells may be activated by 5-lipoxygenase products or by aspirin directly to release inflammatory mediators including tryptase and histamine.