Letter to the Editor

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Highly Resistant Acrodermatitis Continua of Hallopeau and Pustular Psoriasis

John W. Frew Dedee F. Murrell

Department of Dermatology, St George Hospital, and University of New South Wales, Sydney, NSW, Australia

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Acrodermatitis continua of Hallopeau · Atypical mycobacteriosis · Generalized pustular psoriasis

Dear Editor,

We present the case of an 82-year-old Caucasian female who was evaluated in 2009 with an 18-month history of purulent nailbeds of the bilateral great toes and thumbs. She reported a history of hypertension, non-insulin-dependent diabetes mellitus (NIDDM), and pernicious anaemia. She denied recurrent fevers, arthritis, or a family history of pustular psoriasis. Her medications included lisinopril, frusemide, potassium, and metformin. She reported allergies to codeine and erythromycin, and no new medications in the past 3 months. Previous biopsies for H&E and immunofluorescence demonstrated subcorneal cavities filled with polymorphonuclear neutrophils in combination with a moderate lymphohistiocytic infiltrate and upper dermal oedema with no granulomatous inflammation or acid-fast bacilli identified. Previous management (Table 1) of her psoriasis and nails had included systemic antibiotics, whole-body NB-UVB phototherapy, hand and foot PUVA, and vitamin D supplementation with little benefit. Sequential trials of methotrexate 5 mg once per week, acitretin 25 mg daily, and cyclosporine 100 mg b.i.d. resulted in limited improvement but worsening of her pre-existing hypertension. The left great toe was amputated in September 2008 on suspicion of osteomyelitis due to persistent positive culture specimens for *Mycobacterium fortuitum* despite antibiotic therapy with cephalexin, flucloxacillin, and a 6-month course of doxycycline (doxycycline-sensitive isolate). After amputation she was referred to our clinic for ongoing management. On examination, pustules were concentrated on the fingertips and toes, particularly the right thumb. There was complete absence of the nail plate with diffuse pustular exudate (Fig. 1). She had scattered pustules on the extensor upper limbs and reported previous involvement of the lower limbs and trunk. There was no evidence of psoriatic arthritis on physical examination. The principal diagnosis was acrodermatitis continua of Hallopeau (ACH)/pustular psoriasis with a differential diagnosis of subcorneal pustular dermatosis (Sneddon-Wilkinson syndrome).

Table 1. Summary of treatments, response, and adverse effects in our case report

Date	Treatment	Response	Adverse effect
2008	Oral antibiotics (cephalexin/doxycycline/flucloxacillin)	No response	–
2008	Whole-body NB-UVB 3× weekly Hand and foot PUVA	No effect on nail lesions	–
2008	Methotrexate 7.5 mg/week (+5 mg folic acid on the following day) (for 8 weeks)	Thumb lesion recalcitrant	Nausea, elevated transaminase, and serum creatinine
2008	Acitretin 25 mg daily (for 12 weeks)	Thumb lesion recalcitrant	Lower back pain (resolved upon self-cessation)
Sept. 2008	Cyclosporine 100 mg b.i.d. (2.5 mg/kg/day) (for 5 months)	Mild improvement of the toe lesion	Hypertension, renal impairment (toe amputation)
Feb. 2009	Adalimumab 40 mg fortnightly (for 8 weeks)	Thumb lesion recalcitrant	–
2009	Thioguanine 40 mg b.i.d.	Thumb lesion recalcitrant	–
2009	Cyclosporine 100 mg b.i.d.	Thumb lesion recalcitrant	Hypertension, renal impairment
2009	Methotrexate 7.5 mg/week (+5 mg folic acid on the following day)	New lesions on 3rd and 5th digits of the right hand	Nausea
2010	Ustekinumab 45 mg/12 weekly	No effect on nail lesions (PASI score 16)	–
2010	Cyclosporine + prednisolone	No effect on nail lesions	Hypertension, renal impairment
2010	Thalidomide 50 mg b.i.d.	Ceased due to cost	
2010	Infliximab 5 mg/kg 8 weekly	Not administered due to transport/mobility issues	
Feb. 2011	Ustekinumab + cyclosporine + prednisolone	No effect on nail lesions (PASI score 2.7)	Hypertension, renal impairment
June 2012	Intravenous immunoglobulin 0.4 g/kg for 3 days then monthly infusions	2 doses administered, not continued due to transport/mobility issues	

E-Mail karger@karger.com
www.karger.com/sad

Prof. Dedee F. Murrell
Head, Department of Dermatology
James Laws House, St George Hospital
Kogarah, Sydney, NSW 2217 (Australia)
E-Mail d.murrell@unsw.edu.au

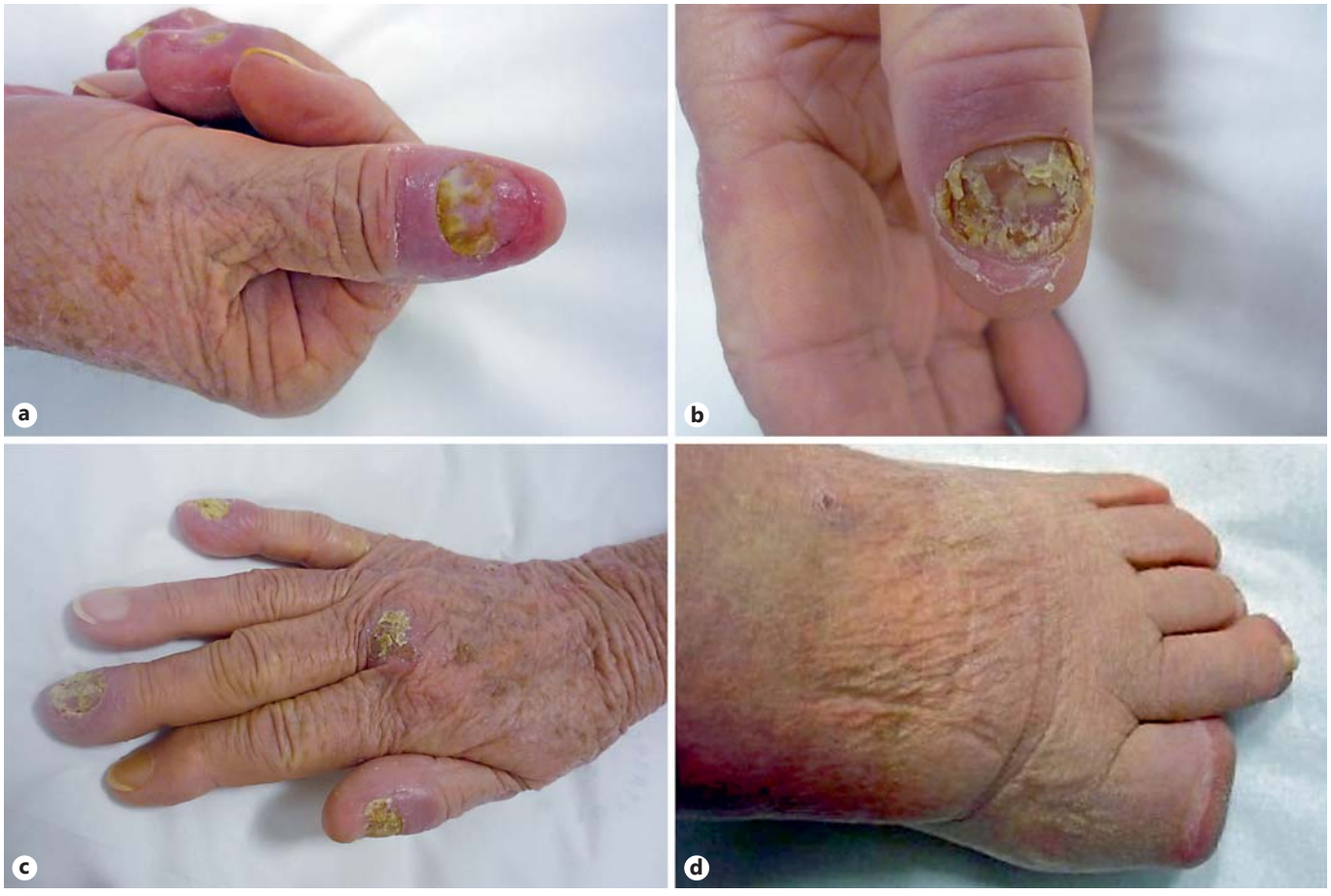

Fig. 1. a–d Inflamed, purulent, dystrophic nails of the right hand, with relative sparing of the second and fourth digits and a psoriatic plaque over her third metacarpophalangeal joint are shown (**a–c**). The amputated great toe of the right foot (**d**) due to misdiagnosis of chronic atypical mycobacterial infection is presented.

Clinical presentation at the time of referral is shown in Figure 1. Adalimumab was commenced (40 mg subcutaneously every fortnight) on a compassionate use basis for a 12-week trial (Table 1). Limb plaques improved, however, the thumb remained recalcitrant and new pustules appeared by week 8 of therapy. Thioguanine 40 mg b.i.d. was trialled for 4 weeks; however, due to further deterioration, the patient requested resumption of cyclosporine at 300 mg/day. Worsening hypertension along with creatinine elevation necessitated cessation of cyclosporine and replacement with oral methotrexate and prednisolone whilst awaiting application for compassionate use of ustekinumab. Three doses of ustekinumab 45 mg were approved with minimal improvement (PASI score 16). Cyclosporine 100 mg b.i.d. was subsequently restarted with no impact upon nail disease. Blood pressure and eGFR remained within the normal range. Adjuvant topical therapies included miconazole 2% solution, calcipotriol/betamethasone dipropionate ointment, and saturated solution of potassium iodide. No repeat isolation of *M. fortuitum* was identified during the period of treatment. Thalidomide was commenced at 50 mg b.i.d. with moderate improvement of nail symptoms, unfortunately treatment was discontinued due to cost. A significant flare (PASI score 27) resulted in resumption of cyclosporine and application for infliximab. Worsening mobility meant that regular attendance for infusions was impractical. Combined ustekinumab 45 mg, cyclosporine 200 mg b.i.d., and prednisone 7.5 mg/day commenced in July 2011 with rapid improvement (PASI score 2.7 at 4 weeks) but resistant nail disease. After 12 months, 2 infusions of intravenous immunoglobulin 0.4 mg/kg were administered, with no benefit to the nails. The patient was lost to follow-up and passed away after an intracranial haemorrhage, still on cyclosporine.

Discussion

ACH is a chronic, recalcitrant disease with a predisposition to elderly females [1], is considered an acral variant of pustular psoriasis [2], and shares a common pathogenesis with DITRA (deficiency in interleukin-1 receptor antagonist) [2–4]. Physicians unfamiliar with the disease can misdiagnose it as a chronic infection through identification of commensals (such as *M. fortuitum*) on culture specimens. Reports of a Lebanese family with a common

IL-36RN mutation presenting as both ACH and GPP raises questions as to the epigenetic or environmental cues that may result in different phenotypes [2], progression from one to the other [5], or manifestations of both, as seen in our case. It is also unclear why, if the conditions are related, such contrasting responses to treatment are seen within the same individual and why long-term remission often remains elusive [6]. While secondary infection of the nailbed can occur in ACH, it is not known to contribute to the activity of disease. The use of biologic agents is variable in efficacy [6] with the IL-1 antagonists Anakinra and Gevokizumab [4], as well as the IL-17 antagonists Secukinumab and Ixekizumab [7] showing future potential.

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Statement of Ethics

The patient presented in this article has given her informed consent for the publication of the case report.

Disclosure Statement

The authors have no conflicts of interest to declare.

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