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Iloprost administration in acrodermatitis of Hallopeau complicated by acquired toes syndactyly: a case report and review of the literature

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Abstract. – OBJECTIVE: Acrodermatitis Continua of Hallopeau (ACH) is a variant of pustular psoriasis often very difficult to treat. Secondary syndactyly, also called "pseudosyndactyly", is rare and can be a complication of burns, dystrophic epidermolysis bullosa or trauma. If left untreated, joint complications and definitive functional impairments may occur.

CASE REPORT: We report a case of a 74-year-old man with acrodermatitis continua of Hallopeau involving the toes and complicated by syndactyly. ACH regression following Iloprost administration was also observed.

DISCUSSION: Published studies are mainly limited to case reports only, due to the rarity of the disease. Therefore, there are no clear-cut therapeutic management guidelines available for this chronic and sometimes debilitating disease. ACH is often recalcitrant to the available therapies. Topical and systemic treatments have been described in literature with no long-lasting results.

CONCLUSIONS: To our knowledge, this is the first report of foot syndactyly associated to ACH. In our patient, ACH symptoms regressed with Iloprost administration: this finding has never been previously described in literature. If confirmed by other clinical experiences, Iloprost could be a further therapeutic option in ACH.

Key Words:
Syndactyly, Acrodermatitis of Hallopeau, Iloprost.

Introduction

Acrodermatitis continua of Hallopeau (ACH), also known as Acrodermatitis continua suppurative or perstans[1], is a variant of pustular psoriasis often very difficult to treat. Typical clinical findings are sterile 1-3 mm pustules surrounded by erythematous skin at the tips of the fingers and, less frequently, the toes. The onset is characterized by painful, sharply bordered erythematous plaques in the nail region that rapidly evolve into pustules[2]. The plaques may extend proximally and fuse together to form small lakes of pus. Digital tips may become pruriginous, puffy and swollen with pain and impaired use of the involved digits[3]. Moreover, osteoporosis or loss of bony structures can complicate this clinical framework[4]. Histopathologic examination shows unilocular pustules with neutrophils seeping through the dermis[3].

Syndactyly is the fusion of one or more fingers. It is classified in complete syndactyly with bone finger fusion or partial syndactyly with only skin fusion. In most cases, it is congenital. Secondary syndactyly, also called "pseudosyndactyly", is rare and can be a complication of burns, dystrophic *epidermolysis bullosa* or trauma[5,6].

We report a case of acrodermatitis continua of Hallopeau involving the toes and complicated by syndactyly. We also report ACH regression following Iloprost administration. The literature about clinical approach and therapeutic management is reviewed.

Case Report

A 74-year-old man was referred to our Department for ulcerative lesions involving the dorsal surface of the right first toe and the plantar surface of the distal third of the foot associated with painful pustules localized on the lateral and proximal nail fold of the same toe. Co-morbidities included a 20-year history of psoriatic arthritis (previously treated, during the acute phases, with topical cortisone cream) hypertension and aortic aneurysm (treated one year earlier with the placement of an endoprosthesis). Firstly, ACH and/or

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vascular ulcer were suspected. Microbiological examination resulted negative for any bacteria. A color Doppler ultrasound study and a CT-scan with contrast were performed to evaluate limb perfusion: popliteal and femoral arteries presented a partial flow reduction bilaterally but with no evidence of severe vascular obstruction. One pustule was biopsied. Despite the clinical suspect of ACH, immunosuppressive and corticosteroid therapies were not administered before having the histological report, due to the risk of infection and the hampering effect on tissue healing. Meanwhile, the patient was treated with polyurethane foam dressings changed every other day. In spite of this treatment the ulcers did not improve and the de-epithelized area extended to the lateral surfaces of all toes with fusion of the soft interdigital tissues, thus resulting in secondary syndactyly (Figure 1A; Figure 1B). Moreover, further painful pustules developed, involving the dorsal surface of all toes. The histological report of the earlier biopsy referred neutrophils infiltrating the dermal layer. As a consequence, considering the previous clinical finding of sterile pustules, the diagnosis of ACH was made. A further microbiological examination was performed, reporting local infection sustained by *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Achromobacter denitrificans*. Corticosteroid or immunosuppressive therapies were therefore contraindicated and the patient was started on systemic antibiotics (Piperacillin/Tazobactam 2 g and Ciprofloxacine 500 mg twice a day, according to the antibiogram) and on vasodilation therapy (Iloprost 1 vial 0.05 mg slow infusion 35 ml/h five days a week for 4 weeks). Two weeks later, the wound presented no purulent secretions with pustules still present on the dorsal surface of all toes. Microbiological examination showed no bacterial overgrowth: as a consequence, antibiotic therapy

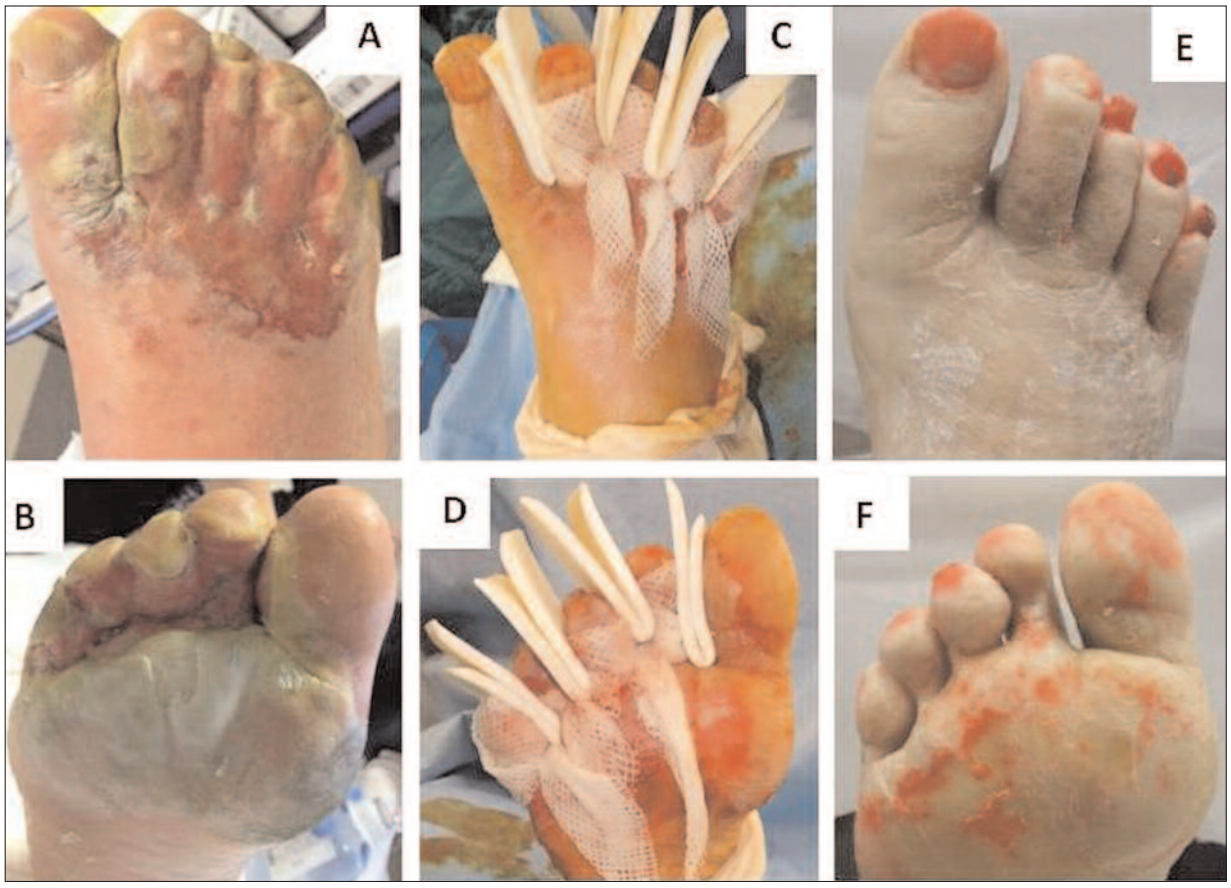

Figure 1. Pre-operative view: acquired skin syndactyly of the right foot: ***(A)*** dorsal and ***(B)*** plantar view. Intra-operative view ***(C, D)***: gauzes with hyaluronic acid and silver sulfadiazine were placed around the toes following surgical debridement. Polyurethane foam sheets where placed into the inter-digital spaces to avoid tissue adhesion. 2 months post-operatively: complete re-epithelization has been achieved: ***(E)*** dorsal and ***(F)*** plantar view.

was discontinued. Two further weeks later (4 weeks after the start of Iloprost therapy), the patient presented with no pain, no pustules, no clinical signs of infection and partial re-epithelialization of the ulcerative lesions. X-rays of the feet showed neither osteoporosis nor bone erosive lesions. We therefore decided to perform surgical debridement of the inter-digital spaces to correct syndactyly and avoid deeper interdigital fusion and joint impairment (Figure 1C; Figure 1D). At 2-months follow-up no complication was experienced, with complete regression of pustules and re-epithelization of ulcerative lesions (Figure 1E; Figure 1F).

Discussion

Acrodermatitis continua of Hallopeau is a localized, rare variant of pustular psoriasis. Tipical clinical findings are sterile 1-3 mm pustules surrounded by erythematous skin at the tips of the fingers and, less frequently, the toes. It may complicate with pruritus, pain, impaired use of the involved digits and, in severe cases, with osteoporosis and loss of bony structures[7]. To our knowledge, published studies are limited to case reports only, due to the rarity of the disease. As a consequence, there are no clear-cut therapeutic management guidelines available for this chronic and sometimes debilitating disease. Moreover, ACH is often recalcitrant to the available therapies[8-19]. Topical treatments have been previously described in literature. White and Main[8] reported the regression of oral cloxacillin resistant ACH with an association of clobetasol propionate and neomycin sulfate, while Piquero-Casals et al[9] described a case of sulfasalazine refractory ACH responding to topical betamethasone cream after one week of therapy. The successful outcome of topical cytostatic agents, such as fluoro-uracil[10,11] and tacrolimus[12], has also been reported. Two studies described the therapeutic effect of psoralen combined with ultraviolet A (PUVA) photochemotherapy[13] and ultraviolet B (UVB) phototherapy[14], with no relapse during the follow-up period. Intra-lesional and systemic corticosteroids or immunosuppressive agents have been shown to achieve contrasting results in ACH. Calkins et al[15] reported no effect following 300 mg of cortisone local injection but some studies reported a partial response after corticosteroids local injections[16,17]. Promising results have been described with the systemic use of methotrexate in association with propylthiouracil. Nevertheless, the long-term intake of these drugs implies the risk of pancytopenia or idiosyncratic side effects, which may lead to discontinuation[18]. Cyclosporine A is a rapid-acting systemic drug used in the treatment of psoriasis; Zachariae and Thestrup-Pedersen[19] reported the first successful use of cyclosporine A in a case of 10-year multiresistant ACH. Biologic drugs have also been used in the treatment of ACH. Anti-TNF-α human monoclonal antibodies, such as adalimumab, infliximab and etanercept, were proposed to treat patients with acrodermatitis of Hallopeau resisting to topical and/or systemic therapies or in association with systemic therapies[20].

In our patient, presenting with cutaneous ulceration and ACH, both local and systemic immunosuppressive or corticosteroid therapies were contra-indicated because of the risk of infection and the hampering effect on tissue healing. As a consequence, the patient was firstly treated with advanced medications and then with iloprost, in order to improve local tissue conditions and vascularization, respectively. Iloprost is a prostaglandin I2 analogue used in the treatment of severe vascular stenosis but also in immune-mediated diseases like systemic sclerosis[21]. In our case, after 4 weeks of iloprost administration, the patient presented with complete regression of pustular lesions as well as of pain and swelling. This result may be a consequence of the anti-inflammatory and immunomodulating effects of this drug recently demonstrated by D'Amelio et al[22]. Iloprost has been shown to reduce the TNF-α produced by T-cells, to enhance self tolerance by modulating T-regulator cells and to increase IL2 serum level with a control on T-cell regulation and development.

Acquired sindactily rarely complicates burns, dystrophic *epidermolysis bullosa* or trauma. Digital fusion secondary to blistering and scarring has been also described in patients with Kindler syndrome[23]. If left untreated, joint complications and definitive functional impairments may occur.

Psoriasis is not usually associated with skin scarring. Kirkup et al[24] firstly described a case of secondary hand syndactyly due to acrodermatitis of Hallopeau; in their patient the fusion of adjacent fingers developed after many years of not pharmacologically controlled systemic psoriasis. In our case, the loss of the interdigital epidermal layer secondary to ACH and infection, lead to an abnormal healing with fusion of adjacent tissues that needed surgical intervention.

Conclusions

ACH is a chronic, relapsing condition that involves hands in most cases. Actually, there are no management guidelines. We described a case of ACH of the foot complicated by secondary partial syndactyly. To our knowledge, this is the first report of foot syndactyly associated to ACH. Moreover, in our patient, ACH symptoms regressed with Iloprost administration: this finding has never been previously described in literature. If confirmed by other clinical experiences, iloprost could be a further therapeutic option in ACH. By providing both immunomodulation and vascular improvement, this drug could be a valuable option in cases of infection or when vascular comorbities associate and overlap to ACH. We would like to encourage further studies on the use of iloprost in ACH management.

Conflict of Interest Disclosure Statement

Neither the author or the co-authors have any conflict of interests to disclose.

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