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CASE REPORT

Skin Eczema Limited to Transplanted Hand

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Abstract: Hand transplantation is a vascularized type of composite tissue allotransplantation (CTA), involving the transfer of heterogeneous tissues such as skin, fat, bones, muscles, and nerves. Even with modern immunosuppression protocols, rejection remains a major obstacle in this field. We report the first documented case of eczema limited to the skin of a transplanted hand in a 38-year-old male born without a left hand. The patient underwent hand allotransplantation in December 2016 from a deceased donor with complete HLA mismatch and remained on stable triple immunosuppressive therapy. Six years post-transplantation, erythematous macules, papules, scaling, and increased keratosis appeared exclusively on the dorsal and palmar aspects of the grafted hand, involving approximately 80% of its skin surface, without lesions elsewhere. Histopathological examination confirmed subacute eczema, with no signs of acute or chronic rejection. Topical mometasone furoate ointment combined with an increased dose of oral prednisone (from 5 mg/day to 10 mg/day) resulted in marked improvement within two weeks, followed by complete resolution after several weeks of regular emollient use. No recurrence was observed during six months of follow-up. This case highlights the importance of differentiating between rejection and other dermatological conditions, such as eczema, in limb transplant recipients. Because eczema can closely mimic rejection, it may complicate post-transplant care and lead to unnecessary changes in immunosuppressive therapy if misdiagnosed. Accurate diagnosis is essential for appropriate management and graft survival.

Keywords: hand transplantation, hand eczema, case report

Introduction

Hand transplantation is a form of vascularized composite tissue allotransplantation (CTA), defined as the transfer of heterogeneous tissues (skin, fat, bones, muscles, nerves, etc). Dr. Robert Gilbert performed the world's first hand transplant in Ecuador in 1964; however, the graft was rejected and had to be amputated three weeks later. The first hand transplantation to succeed under contemporary immunosuppression was achieved in 1998 by Dr. Jean-Michel Dubernard's team in Lyon, France.[1] Although hand transplantation is the most common CTA, only less than 100 cases were reported until 2022 worldwide.[2]

Despite immunosuppressive efforts, rejection is still the most important complication. Clinically, rejection manifests initially as a local or diffuse erythematous or maculopapular eruption on the skin. To the best of our knowledge, there are no reports of eczema in CTA that may look clinically similar to graft rejection. The histopathological examination is decisive.

In acute skin rejection following vascularized composite allotransplantation, histopathology typically reveals a dense perivascular and interstitial lymphocytic infiltrate involving both the dermis and epidermis, often with exocytosis, basal cell vacuolization, and adnexal involvement, sometimes accompanied by necrotic keratinocytes. In contrast, subacute eczema demonstrates marked spongiosis, irregular acanthosis, parakeratosis, and a mixed superficial perivascular infiltrate, frequently with eosinophils, but without the basal vacuolar changes or adnexal damage characteristic of

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rejection. Understanding these differences is essential for timely and accurate differential diagnosis in hand transplant recipients.[3,4]

Hand eczema is frequently aggravated by external exposures that impair epidermal integrity. Repeated contact with soaps, detergents, sanitizers, or occupational chemicals leads to cumulative barrier disruption and facilitates the development of irritant contact dermatitis. These environmental influences interact with individual susceptibility factors, underlining their central role in the multifactorial pathogenesis of eczema, even in patients with concurrent immunosuppression.[5]

Here, we present the first case of eczema limited to the skin of the transplanted hand.

Case Report

Currently, 38-year-old male with no relevant medical history was born with the left upper extremity terminating at the level of the wrist. He is a right-handed person working as a museum curator. In December 2016, the patient received a hand allograft from 46-year-old deceased male donor. Recipient's immune risk was low; however, allograft was fully incompatible with HLA matching – the 6 out of 6 mismatches (A,B,DR). The pretransplant CDC cross-match was negative in both T and B cells. The total cold ischemia time was 12 hours. Immunosuppressive management began with basiliximab induction, followed by maintenance using tacrolimus, corticosteroids and mycophenolate mofetil. There were no surgical complications after transplantation, but the early postoperative course was complicated by multiple acute rejection episodes treated with methylprednisolone, thymoglobuline and extracorporeal photopheresis. Two years after transplantation, the patient showed no signs of rejection and presented good motor function of the allograft. Chronic immunosuppression consisted of tacrolimus with trough levels approx. 8 ng/mL, prednisone 5 mg per day and mycophenolate mofetil 1250 mg per day.

In September 2022, the patient developed skin lesions strictly limited to the graft skin (erythema, pink macules, papules, desquamation, increased keratosis of the hands), accompanied by moderate itching (Figures 1 and 2). Dermoscopy showed red dots and yellow scales consistent with eczematous lesions (Figure 3). The patient associated the appearance of the lesions with more frequent hand washing during the COVID-19 pandemic. There were no allergic incidents in the patient or in family anamnesis. There were also no data on allergic diseases in the donor. The clinical diagnosis of hand eczema was confirmed by histological examination. The epidermis demonstrated moderate hyperkeratosis with patchy parakeratosis, slight hypergranulosis and marked irregular acanthosis with focal spongiosis. In the upper dermis, there was a rather sparse mixed infiltrate, predominantly lymphocytic, with single eosinophils, mainly perivascular, with notable exocytosis into the epidermis. The histopathological features are consistent with subacute

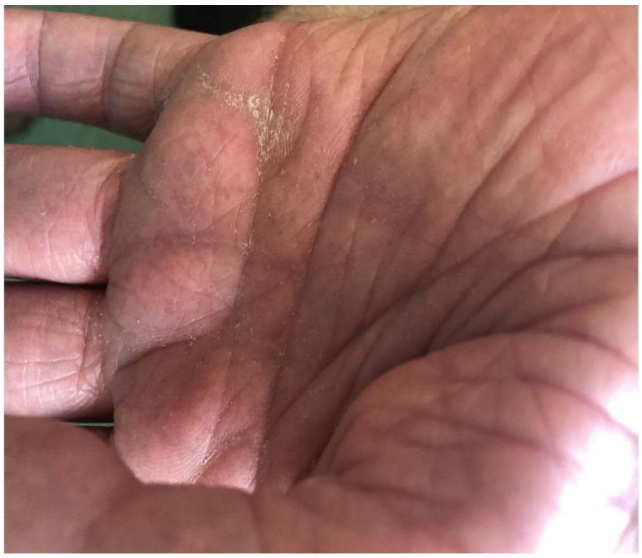

Figure 1 Eczematous lesions on the transplanted hand.

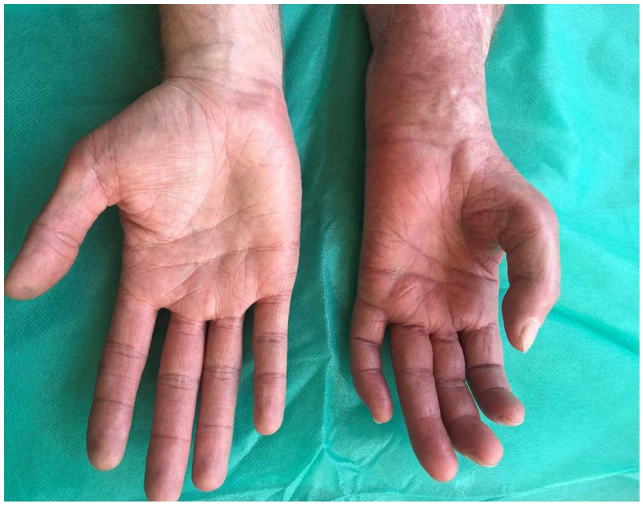

Figure 2 Comparison of clinical manifestation of hand eczema on the transplanted left hand and right clinically normal hand.

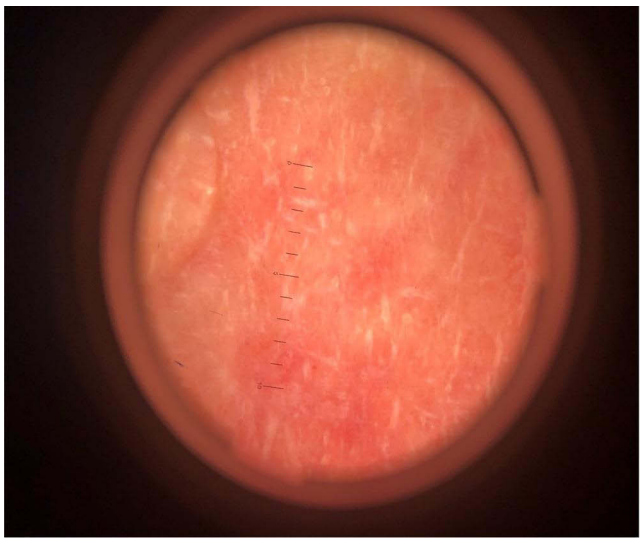

Figure 3 Dermoscopic findings within transplanted hand showing typical features of eczema including red dots and yellow scales.

eczema, and no signs of graft rejection were noted. After topical application of a medium-strength glucocorticoid ointment (mometasone furoate) and an increase in the oral dose of prednisone to 10 mg/day, improvement was achieved within 2 weeks. The patient was suggested to use emollients over the next few weeks. Follow-up performed 6 months later did not reveal any lesions.

Discussion

The paper presents the first case report of eczema limited to the skin of the transplanted hand in a patient who was born without a left hand. Among the causes of congenital defects/underdevelopment of limbs, apart from genetic (endogenous) factors, external (exogenous) factors also often play a role, most often fibrous amniotic bands occurring in the sequence of amniotic bands, causing amputation of fetal limbs, and teratogenic compounds (eg thalidomide, ethyl alcohol, valproic acid).[6] In the discussed case, the reason for the absence of a hand with the remaining part of the upper limb being normal was amputation through the amniotic band constriction, which is not uncommon, but asymmetrical amputation of one hand only is rare.[7]

Skin represents the most immunogenic component in CTA, which significantly limits the expansion of such procedures in humans.[1] Experimental studies have shown that immune tolerance can be achieved for all CTA components, with the exception of skin. In a swine model,[1] a 12-day cyclosporine regimen in all six miniature swine led to indefinite tolerance of the vascularized musculoskeletal components of their allografts, whereas the skin survived only temporarily due to a selective immune response, especially against the epidermis. Eczema (or dermatitis) is defined as any superficial inflammatory disorder primarily involving the epidermis, initially manifesting as redness, pruritus, small papules or vesicles, and exudation, followed by scaling, lichenification, and hyperpigmentation, typically flaring periodically. Eczema is primarily driven by a combination of genetic predisposition and environmental triggers. Various dermatologic disorders are present with eczematous features, such as atopic dermatitis, contact eczema (allergic and irritant), seborrheic dermatitis, nummular eczema, lichen simplex, stasis dermatitis, and dyshidrosis.[8] The term "eczema" is nowadays frequently used synonymously with atopic eczema, its most common subtype. While diagnosing eczema is straightforward, identifying the specific subtype and trigger can be challenging, and the same patient may present with more than one type. In our case, the eczema most probably resulted from more frequent hand washing and disinfectant use during the COVID-19 pandemic, consistent with irritant contact eczema. It is notable that eczema developed despite immunosuppressive therapy and was confined exclusively to the transplanted hand.

Despite immunosuppression, rejection remains the most important complication of hand transplantation. The first symptom is a local or diffuse erythematous or maculopapular eruption on the skin. Edema and desquamation can accompany the rash, potentially progressing to ulcerative or necrotic changes. In less typical cases, early signs may be restricted to the palms and nails.[1] Due to clinical overlap, late rejection can initially be mistaken for eczema. Acute skin rejection in vascularized composite allotransplantation is typically mediated by activated T lymphocytes, predominantly CD4+ and CD8+ cells, producing a dense perivascular and interstitial infiltrate that extends into the epidermis and adnexal structures. Histopathologically, basal cell vacuolization, apoptotic keratinocytes, and adnexal epithelial damage are characteristic, often accompanied by endothelial swelling.[3] In contrast, subacute eczema features marked spongiosis, irregular acanthosis, parakeratosis, and a mixed superficial perivascular infiltrate composed mainly of lymphocytes with variable numbers of eosinophils, but without basal vacuolar change or adnexal destruction.[4] Recognition of these cellular and structural differences is essential for distinguishing eczema from rejection in hand transplant recipients, guiding appropriate treatment, and preventing unnecessary intensification of immunosuppression.

Although eczema is not reported as a complication in hand transplantation, rare cases have been described in other types of skin-containing grafts. For example, eczema occurred in autologous full-thickness skin grafts[9] and split-thickness skin grafts,[10] sometimes without identifiable allergens. Experimental models suggest that grafted skin may exhibit a lower frequency of eczema due to immunologic modifications such as reduced Langerhans cell density, elevated IL-10 levels, and increased regulatory T-cell activity.[11] Conversely, certain types of organ or cell transplantation appear to increase eczema risk. In a study by Fatobene et al,[12] recipients of umbilical cord blood hematopoietic cell transplants had a significantly higher 2-year risk of eczematous dermatitis than other donor types. Similarly, infants undergoing heart transplantation demonstrated a higher incidence of atopic dermatitis than older transplant recipients or controls.[13] Isolated reports describe a paradoxical onset of eczema during systemic tacrolimus therapy after pediatric heart transplantation, resolving upon dose reduction or immunosuppressant change.[14]

In clinical practice, differentiating eczema from acute rejection of the transplanted hand should combine careful clinical assessment with histopathological confirmation. Eczema often develops gradually, is pruritic, and may follow identifiable irritant or allergic exposures, whereas acute rejection usually presents as a more rapidly progressive erythema, sometimes with edema and tenderness, and lacks external triggers. The histological distinctions between the two conditions, outlined above, remain the most reliable diagnostic tool and should guide management decisions to avoid both undertreatment of rejection and unnecessary escalation of immunosuppression.

Given the wide spectrum of possible complications and the serious implications of graft rejection, any skin lesions on a transplanted hand—including those with eczematous morphology—should undergo prompt and thorough evaluation, including mandatory histopathological examination, to ensure timely and appropriate management.

This report is limited by its single-case nature, which precludes broader generalization, and by the absence of allergen patch testing, which would have been useful to definitively exclude allergic contact eczema as a contributing factor. Nevertheless, the clear clinicopathological correlation and resolution with appropriate therapy support the diagnosis of irritant contact eczema confined to the grafted skin.

Informed Consent

The consent was obtained from the patient to publish the case details and accompanying images. Institutional approval is not required for this case study.

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Disclosure

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