Dear Editors,

There is a dearth of literature regarding the treatment of atopic dermatitis (AD) in patients with organ transplants. Despite the immunosuppressive regimens in the post-transplant population, de novo development of atopic diseases is a well-documented phenomenon, particularly in liver transplant recipients, with frequencies of 27.6 % in children and 10.3 % in adults [1]. We report a case of dupilumab treatment in an orthotopic liver transplant (LT) patient with AD.

A 38-year-old Caucasian woman presented with severe AD and recurrent erythroderma under immunosuppressive therapy with tacrolimus 5 mg per os daily for an LT. At the age of 22 years, she had received an orthotopic LT because of acute liver failure due to Wilson’s disease. Post-transplantation immunosuppressive regimens included tacrolimus and cyclosporine A (CyA), the latter having been discontinued due to deterioration of renal function. Her personal and family histories were negative for atopy. There was no information on atopic diseases of the liver donor.

Nine months post-transplantation, the patient developed AD, fulfilling the Hanifin and Rajka diagnostic criteria with respect to chronic pruritic eczematous skin, flexural eczema, lichenification and elevated total serum immunoglobulin E (IgE), as well as palmar hyperlinearity. She also started to suffer from food allergy to hen’s eggs and fish. Atopic dermatitis treatment included topical glucocorticosteroids and calcineurin inhibitors as well as basic treatment with emollients, UVA1 phototherapy and repeated systemic glucocorticosteroids as recommended in the guideline [2], but without sustained improvement. Physical examination at presentation showed multiple excoriated papules, nodules and deep excoriations (Figure 1), with an atopic dermatitis score (SCORAD) of 81. Laboratory investigations revealed elevated levels of IgE (> 5000 kU/l) and eosinophil cationic protein (69.4 μg/l, normal range 11.1–13.3 μg/l), and a slight increase in eosinophil counts (0.61 × 10^9/l, normal range < 0.50 × 10^9/l). No other laboratory abnormalities were found, particularly regarding hepatic and renal panels. Following intense and lengthy interdisciplinary evaluation, the patient was started on dupilumab at 600 mg subcutaneously on day 0, followed by 300 mg subcutaneously every two weeks. No modifications were made regarding the post-transplantation immunosuppressive regimen with tacrolimus (5 mg per os). A rapid improvement was noted reaching a SCORAD of 25 after four weeks of dupilumab treatment, which has now been stable for five months (Figure 2). The hepatic function panel was monitored every two weeks, and a liver ultrasound was performed three months after initiation of dupilumab treatment, with neither showing any abnormalities. However,

Figure 1  Multiple excoriated papules and nodules over the entire body, massive xerosis with a corresponding atopic dermatitis score (SCORAD) of 81 at week 0 of dupilumab treatment.
the patient developed persistent moderate conjunctivitis four weeks after the initiation of dupilumab treatment; this required lubrication and intermittent treatment with glucocorticosteroid-containing eyedrops (Figure 3) as previously recommended [3].

Liver recipients have a significantly higher risk of post-transplant allergy, autoimmunity and immune-mediated (PTAA) disorders than other recipients of solid organ transplants [4]. Multiple pathogenic mechanisms have been proposed [5]. Firstly, PTAA disorders have been closely linked to immunosuppressive treatment with tacrolimus, which inhibits the formation of interleukin (IL)-2, causing a shift toward a Th2 cytokine profile, increased IgE and eosinophilia via IL-5 [6–9]. However, the low rates of de novo food allergies in non-liver transplant recipients treated with tacrolimus argue against a sole role of tacrolimus in the pathogenesis of PTAA [5, 6]. Secondly, hematopoietic lymphoid tissue is transplanted during bone marrow, liver, and small bowel transplants, with passive transfer of leukocytes that may promote or produce IgE antibodies in the recipient following organ transfer [5, 7, 10]. However, results of microchimerism testing for the presence of donor-origin cells in the blood and skin of recipients were inconclusive [10]. Thirdly, antigen-specific IgE antibodies, possibly membrane-bound on basophils and mast cells, are transferred passively during liver transplantation and may mediate a temporary de novo allergy [5].

To our knowledge, this is the first published case showing the effectiveness and safety of dupilumab in treating severe AD in an orthotopic liver transplant recipient in the setting of post-transplantation immunosuppressive therapy with tacrolimus. To date, there is no reason according to preliminary study data and the literature to assume any negative influence on liver transplant tolerance and function by inhibiting IL-4 and IL-13 signaling (via blockade of the shared alpha subunit of the IL-4-receptor component of
type I and type II receptors). Nevertheless, the decision to initiate a dupilumab treatment in transplant recipients must be made interdisciplinary, carefully considering the individual risk-benefit prospects together with the patient. Larger series of patients with longer follow-up periods are required to estimate the risk-benefit ratio of dupilumab treatment in transplant recipients.

Conflict of interest
None.

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