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Case Report

Novel Biological Drug Helped Young Female with Severe Atopic Eczema Attend School after Two Years of Sick Leave

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Abstract

Dupilumab is the first biological drug approved for the treatment of atopic eczema in adults. The drug inhibits Th2 mediated inflammation by blocking IL-4 and IL-13 pathways. We present a case-report involving a 17-year old female with severe atopic eczema who responded quickly on dupilumab injections. Prior to treatment she was on sick-leave for two years. One week after her first injection she could attend school. According to calculations made by Swedish medical authorities, approximately 1% of the Swedish population could potentially benefit from dupilumab.

Introduction

During the past two decades, biological drugs have revolutionised the treatment of psoriasis and other autoimmune diseases. The allergic conditions that belong to the category of atopy, i.e. allergic asthma, rhinoconjunctivitis, food allergy and atopic eczema have another immunological dysfunction. In March 2017 the first biological drug, dupilumab, has been approved by the US Food and Drug Administration (FDA) for treatment of atopic eczema. Dupilumab was approved by the European Medicines Agency (EMA) in September 2017 and is expected to be available on the European market in 2018.

Atopic eczema is a common disease in the industrialised world, occurring in at least 20 % of the children and 2-10 % of adults [1]. Local treatments with steroids, tacrolimus and emollients help the majority of patients but occasionally UVAB/UVB treatment may be required. The most severely affected patients require systemic treatment with peroral steroids, azathioprine, methotrexate or ciclosporin. Occasionally even this treatment is inadequate or causes severe side effects. Dupilumab is the first biological drug for atopic eczema, approved in March 2017 by FDA and in September 2017 by EMA. The atopic inflammation is driven via Th2-cells and their messengers IL-4 and IL-13. Dupilumab entails monoclonal antibodies to the IL 4-receptor. Phase 3 studies have shown that almost 40% of the included patients with moderate to severe atopic eczema healed compared to 10% of patients in the placebo group [2,3].

Case Description

A 17-year old female patient, without any known comorbidity had previously presented mild atopic manifestations of the skin and mucous membranes. Her father and aunt had atopic eczema. During the first year of upper secondary school she developed a severe itching and widespread eczema that made school attendance impossible. The eczema worsened notably from stress, heat and perspiration. The itching impaired sleep and concentration and the scratching resulted in repeated skin infections and aesthetic concerns. Through her general practitioner she was given local treatment with steroids, tacrolimus, emollients, and peroral steroid regimens with insufficient or transient effect. The patient also tried a complementary UVAB-light for three consecutive months, subsequently in combination with peroral steroids.

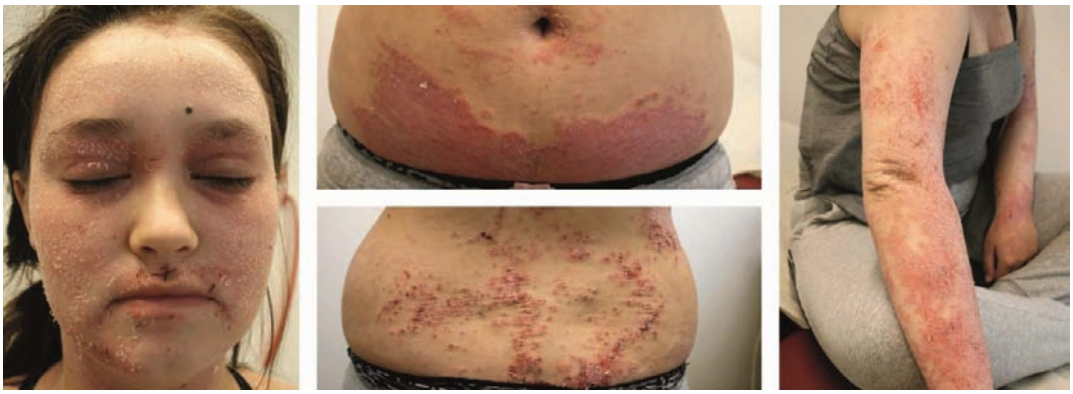

Figure 1: Clinical status prior to first injection with dupilumab. Despite the usage of potent topical steroids and ciclosporine the eczema is widely spread, lichenified and scratched. The patient cannot attend school. Eczema Area and Severity Index (EASI) is 39,7 and Dermatology Life Quality Index (DLQI) is 29. These scores indicate a severe eczema with an immensely effect on quality of life.

On our first encountering with the patient, the eczema was widespread and intensely pruritic, covering large parts of the body, with secondary infection. Temporary improvement was achieved

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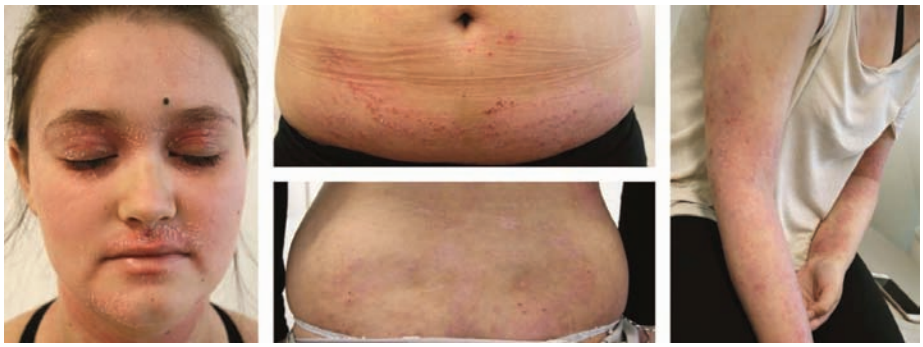

Figure 2: Clinical status 7 days after the first subcutaneous injection of 600 mg dupilumab. Complementary treatment with emollients and topical steroid is used. The itching has greatly decreased and an objective clinical improvement of the eczema is observed.

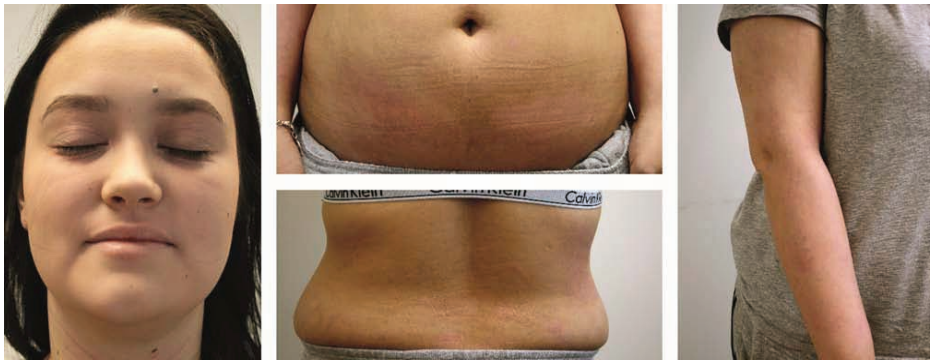

Figure 3: After 28 days on dupilumab treatment. The first subcutaneous injection of dupilumab 600 mg was continued with 300 mg/weekly. EASI score is 1,1 and DLQI is 0, indicating a great improvement in quality of life. After two years of sick-leave the girl attended school and was involved in outdoor and social activities. Follow-up after 9 months showed a sustainable positive outcome.

with oral antibiotic (flucloxacillin) along with oral and local steroids. Within a couple of weeks signs of rebound phenomena and adverse side effects were seen with a flare up of eczema and cushingoid weight gain. Fluconazole 50 mg peroral, was taken continuously twice a week in order to minimise the effect of Malassezia furfur on the eczema.

The treatment was altered from peroral steroids to ciclosporin (2.5 mg/kg) with insufficient effect. When we started treatment with dupilumab, the situation was critical, quality of life severely affected, and the eczematous spread extensive (Figure 1). Subcutaneous injections of dupilumab were initiated with 600 mg the first week followed by 300 mg once weekly. The itching decreased evidently within a day, followed by a reduction in scratching and eczematous spread (Figure 2). The patient went from absent from school for two years to normal school attendance within one week after initiating injections with dupilumab. After 28 days (Figure 3), the eczema was under control with a certain need of local treatment with steroids and emollients. The extent of eczema was improved from EASI 39,7 to 1,1, and life quality from DLQI 29 to 0, after 4 weeks on dupilumab. The only reported side effect during the first 9 months was a bacterial conjunctivitis that responded to antibacterial eye drops.

Discussion

For our patient, inhibition of IL-4 and IL-13 with dupilumab was sufficient to eliminate the itching within a week and subsequently, the eczema a few weeks later. The effect was sustainable after 9 months follow-up. For more than 2 years, the patient had developed a scratching behaviour during daytime as well as in asleep. Treating atopic eczema is a "two-party solution" where we as medical professionals are responsible for reducing the itching, and the patient is responsible for minimizing the scratching. Long-term scratching leads to neurodermatitis and prurigo nodularis. Becoming free from eczema has been an immense transformation for the patient, from having to stay at home, to go back to school, making up for missed schooling, taking greater responsibility at home, socially, etc. As with all eczema treatments, dupilumab is symptomatic, and the need to minimise water contact, to use emollients and to reduce scratching prevails. Thus, as clinicians, it is important to follow up a potent life-changing treatment with support regarding lifestyle.

Initially, the itching returned 6 days after the dupilumab injection, later only after 10 days, i.e. injections were initiated weekly, later to be phased out. Dupilumab is approved for patients over 18 years of age with atopic eczema and is administered every other week. At the same time, dupilumab is also being studied in children from 6 years of age [4] and administered once a week [2], which justified our treatment strategy.

Like psoriasis, atopic eczema is increasingly characterized as a systemic disease. The association with mucosal atopy and food allergy is well-known, but other comorbidity has been further described where evidence of the link to ADHD is the strongest one [5]. Both atopic eczema and psoriasis have a strong hereditary element, where the early acute manifestations have different immunological characteristics in the skin, but where the chronic atopic neurodermatitis plaque resembles psoriasis, both immunologically and clinically. Trials have therefore been conducted with biological drugs for psoriasis as well as for atopic eczema, with varying rates of success [6]. In addition to a reactive immune system with the dominance of Th 2 cells and its signalling with e.g. IL-4 and IL-13, there is also a barrier dysfunction with increased frequency of mutation in the important filaggrin gene, and an increased number of IgE mediated contact eczema against common antigens such as yeast fungi, bacteria and airway allergens [4].

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Filaggrin is an important protein that enables the keratinocytes in the stratum corneum to be packed optimally with the water-proof protein keratin. A single mutation in the filaggrin gene results in symptoms corresponding to dry atopic skin, and a mutation in both genes results in the skin disease ichthyosis vulgaris which is associated with the eczema. IL-4 and IL-13 reduce gene expression of filaggrin, involucrin and other important proteins for adequate barrier function [7]. Consequentely, inhibition with dupilumab not only reduces the excessive Th2 inflammation, but also improves the barrier function [8,9].

Atopic eczema is associated with IL-5 activation and increased IgE production, but at the same time, the biological drugs for the treatment of asthma and urticaria, anti-IL 5 (mepolizumab) and anti-IgE (omalizumab) have had dubious effect on atopic eczema [9,11,12]. Additional biological drugs are currently being tested and could possibly gain approval in the near future [10]. For local treatment, FDA has recently approved crisaborole, a phosphodiesterase-4 inhibitor, as a complement to local steroids and tacrolimus [13]. Crisaborole is expected to be approved for the treatment of eczema in Europe in 2018. The Swedish municipalities and county councils have estimated that up to 1% of the Swedish population with moderately to severe atopic eczema may benefit from dupilumab [14,15]. If the eczema can be healed in 40,000 of these patients and alleviated in a further significant number, this would mean a medical breakthrough for a severely affected patient group.

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