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The use of adalimumab in children with complicated psoriasis: review of clinical cases

V.P. ADASKEVICH[1], V.E. SPIRIDONOV[2], V.V. SALAREV[2]

[1]Vitebsk State Medical University, Vitebsk, Republic of Belarus; [2]Vitebsk Regional Clinical Center of Dermatovenereology and Cosmetology, Vitebsk, Republic of Belarus

The study was aimed at assessing clinical efficacy of treatment of complicated forms of psoriasis (erythroderma, arthropathy) in children administered with combination therapy including the immunobiological drug adalimumab. The efficacy was evaluated based on the clinical index PASI (Psoriasis Area and Severity Index) and mean remission time analysis. Short-term results of treatment were evaluated in 3 months. The aggregate data were indicative of stabilization of the psoriatic process. The results of the overall evaluation of long-term results (in 1 year) were clearly indicative of stable remission.

The results of the study led to conclusion that adalimumab is highly effective in treatment of psoriatic erythroderma in children. The use of a standard dose of adalimumab provides quite rapid clinically significant decrease in PASI, which is indicative of positive effect on the severity of erythroderma and dissemination of the psoriatic process. This drug is safe for children subject to a standard screening procedure.

Keywords: *psoriatic arthritis, psoriatic erythroderma, children, adalimumab, complex therapy.*

Psoriasis is one of the most significant medical and social problems [1]. This is due to the huge and increasing number of patients with early onset of clinical manifestations, persistent and recurrent course, resistance to therapy, and the severity of the disabling complications [2]. Psoriatic arthritis (PA) and psoriatic erythroderma (PE) are the most important and threatening complications of psoriasis. Children with this pathology often develop arthropathies resistant to conventional therapy despite the treatment. It has been established that PA is diagnosed in 5—7% of in children with the duration of psoriasis of more than 5 years and in 13—16% of cases with the duration of psoriasis of more than 10 years [2]. Aggressive course of psoriasis and development of complications that worsen life expectancy dictate the need for timely administration of effective targeted therapy. Taking into account the key role of tumor necrosis factor-alpha (TNF-α) in the development of psoriasis and its complications, active immunobiological therapy aimed at both suppressing TNF-α and modifying the course of psoriasis and reducing the risk of serious complications plays an important role in the treatment.

To date, the choice of TNF-α inhibitors in Europe, Russian Federation, and the Republic of Belarus is limited to four registered drugs: infliximab (remicade, flammegis), adalimumab (humira), and ustekinumab (stelara), etanercept (enbrel).

Objective — the study was aimed at assessing the clinical efficacy of the combination therapy with the immunobiological preparation adalimumab in the treatment of complicated forms of psoriasis (erythroderma, arthropathy) in children.

Material and methods

Two children, patient L.A. (13 years) and patient S.M. (14 years), were followed at the clinic of the Vitebsk Regional Clinical Center for Dermatovenerology and Cosmetology (VRCCDC).

Patient *L.A.*, 13 years old, was admitted to the clinic with the diagnosis of psoriatic erythroderma, grade I—II psoriatic arthropathy, joint incompetence. Disease duration was 5 years. He was treated as an outpatient with temporary improvement. Previous therapy included methotrexate at a dose of 0.3 mg/kg for 8 months, basic conventional therapy (30% solution of sodium thiosulfate, antihistamines for 7—15 days, enterosorbents), class I—III topical glucocorticoids for 10—14 days (lotions, creams); 0.5—2% salicylic ointment, non-steroidal anti-inflammatory drugs, detoxification therapy, vitamin therapy (B_1, B_6, E), and general UV therapy after determining the bio-dose (no more than 1—2 courses per year). At admission, the involved area was 94%.

Pediatric patient *S.M.*, 14 years old, suffers from psoriasis for 9 years. He was followed by a dermatovenerologist at the regional center at the place of residence. He received an outpatient treatment. The patient noted worsening of his condition during 6 months after viral infection. He was admitted to the clinic with the diagnosis of psoriatic erythroderma, progressive stage, persistent and recurrent course. Psoriatic arthropathy. Psoriasis of the scalp. Psoriatic onychodystrophy. Lymphadenopathy. The area of involved skin was 97%.

We studied medical history of both children, analyzed the genetic maps for the presence of psoriasis in the

[1]e-mail: uladas@hotmail.com
[2]e-mail: vokvd@vitebsk.by

nearest relatives. An objective status of patients was assessed. Paraclinical examination included analysis of general clinical laboratory tests: general blood analysis, biochemical blood parameters (total protein, protein fractions, urea, creatinine, cholesterol, C-reactive protein), and clinical urine analysis. X-ray examination of the lungs and Mantoux test were carried out for subsequent consultations (rheumatologist, pediatrician, phthisiotherapist). The severity of psoriatic skin lesions was assessed using PASI index (before drug administration, on day 14 and 30).

Ultrasound (US) examination of the child L.A. before treatment showed the thickness of the dermis of 2.9 mm, infiltration of the dermis, and decrease in the acoustic density. After treatment, the thickness of the dermis was 1.8 mm, normal echogenicity of dermal layer and distinct skin layers were observed.

US examination of the child S.M. before treatment showed dermal layer thickening to 3.5 mm, decrease in the acoustic density of all dermal layers, and hyperechoic band in the projection of the epidermis and dermis. After treatment, echogenicity of skin layers was close to normal, thickness of the dermis was up to 2 mm, there were hyperechoic areas in the dermis.

Patients' skin was assessed using ultrasonography at the dermatological department of the center on the Sonoscape SL1000 instrument using a linear sensor with a frequency of 7.5 MHz and scanning depth of 10 to 20 mm in order to obtain reliable image of morphological skin lesions before and after therapy. Epidermis, dermis, and subcutaneous adipose tissue were visualized. Additionally, the thickness of each visualized skin layer was measured and characteristics of their boundaries were determined, including the level of echogenicity. All structural changes in the skin detected at the examined area were diffuse and/or focal and were described according to the conventional US protocol. In most cases, the scans of pathologically altered skin areas were compared to those of contralateral or adjacent apparently healthy skin areas. The dimensions (thickness) of the observed skin structures were measured in millimeters (1 mm = $1 \cdot 10^3$ m) according to the following US criteria: the hyperechoic epidermal band and the hypoechoic cone, thickened dermal layer, hypoechoic region in the projection of the papillary dermis (in the acute phase) and the presence of fibrous inclusions in the dermis.

The efficacy of adalimumab was assessed based on PASI (Psoriasis Area and Severity Index) and mean remission time. Depending on the score, the severity of psoriasis was considered as severe (PASI of more than 30 points); moderate (PASI of 11—30 points); mild (PASI of 6—10 points); remission (PASI of 5 points or less).

Results and discussion

The children manly complained of permanent migrating itching, exfoliation, knee joint pain, and mood lability during the day. Analysis of the medical history showed that psoriasis initially manifested in children in the form of classical symptoms (erythema, infiltration, exfoliation), the onset of the disease was associated with a viral disease, psychoemotional trauma, and positive family history for psoriasis. In children, psoriasis was characterized by persistent and recurrent course and resistance to previous combination therapy. Characteristic features of the clinical picture of the disease were also identified, including pronounced erythroderma, nail plate lesions («thimble pitting» and «oil stain» symptoms) **(Table 1)**.

When assessing the parameters of physical development, it was found that all children had average physical development parameters. Objective data analysis also showed that both children had biliary dyskinesia, changes in large joints with grade 2 joint disfunction.

We applied a complex step-by-step approach to treat persistent recurrent PE, which includes three stages. At the first stage (during 7 days), a complex clinical and laboratory examination of children was carried out aimed at possible prescription of the immunobiological drug adalimumab according to the current guidelines and with obligatory informed consent of one of the parents, as well as the approval of the local ethical committee of the VRCCDC. We selected this drug due to the fact that patients previously received long-term conventional systemic treatment, phototherapy, class I—III topical corticosteroids, as well as cytostatic antimetabolites, namely methotrexate at age dose (10—15 mg/m^2/week) in combination with folic acid, and resistance to these treatments was observed [2]. Before treatment with adalimumab, US examination of the skin showed pronounced thickening of the epidermis with uneven echolucency and hypoechoic sites (parakeratosis, hyperkeratosis, acanthosis, microabscesses). The hypoechoic region was detected under the epidermis, indicating the development of papillomatosis and perivascular infiltration of the upper dermal layers. Significant increase in the thickness of the dermis and uneven decrease in its echogenicity compared to healthy skin was observed, which is due to erythroderma, i.e. edema and perivascular infiltration of the dermis.

Table 1. **Clinical and demographic characteristics of patients with psoriasis who received adalimumab**

Patient	Age, years	Sex	Age of onset, years	Duration, years	Diagnosis	Family history	Rash	L. nodes	Joints	Nails	Fever
L.A.	13	Male	8	5	PE	+	+	+	+	-	+
S.M.	14	Male	4	10	PE	+	+	+	+	+	+

Table 2. **Assessment of PASI in patients during treatment**

Patient	PASI, points		
	before treatment	after the 1st injection	after the 2nd injection
L.A.	33.3	27.8	11.4
S.M.	48.6	35.2	27.4

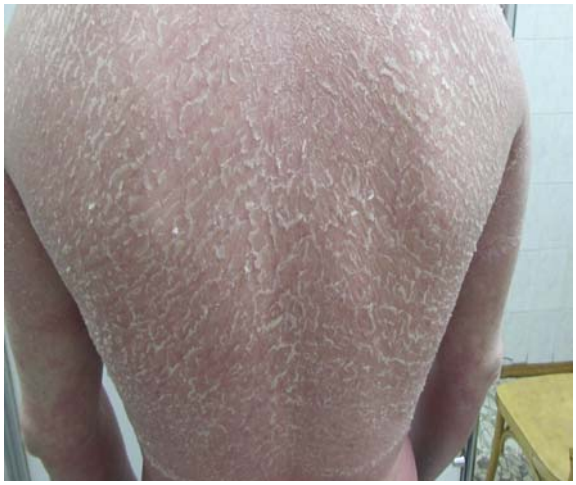

Fig. 1. **Patient *S.M.* before drug injection, PASI was 33.3 points.**

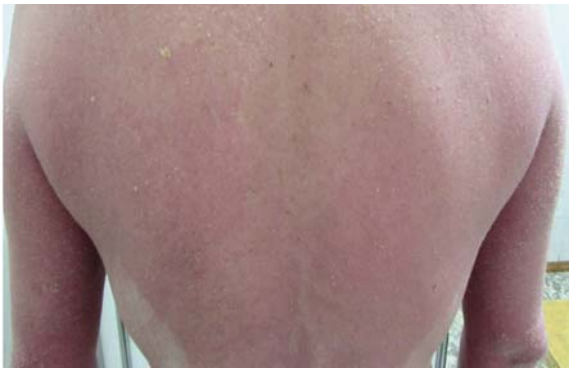

Fig. 2. **The same patient 7 days after drug administration, PASI was 27.8 points.**

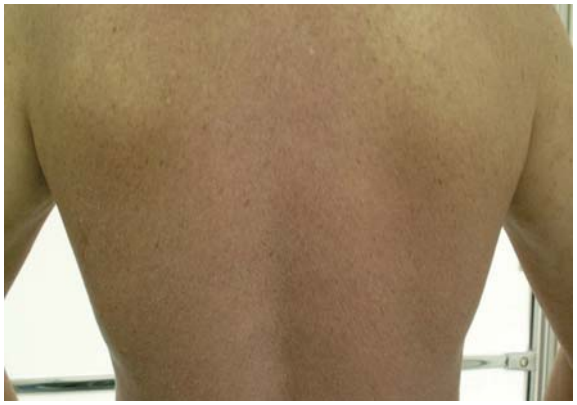

Fig. 3. **The same patient after the 2nd injection (day 30), PASI was 11.4 points.**

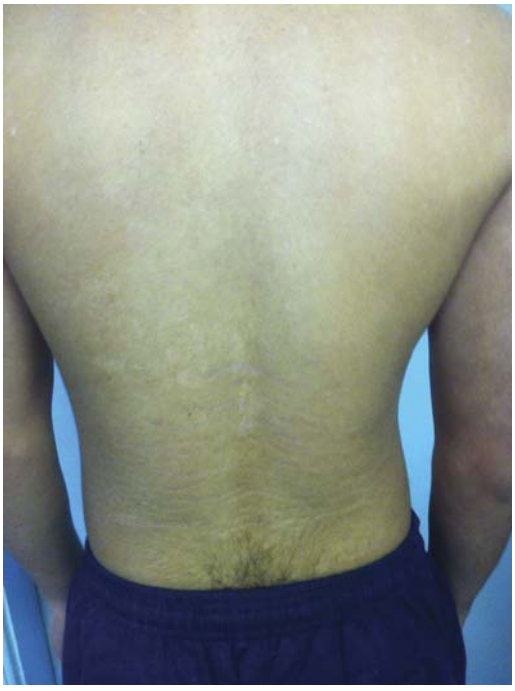

Fig. 4. **The same patient after one-year-long follow-up, PASI was 5 points.**

At the second stage after the consultation involving the staff of the department of the Vitebsk State Medical University, a medication (0.8 ml of adalimumab solution) was administered according to the following regimen: the initial dose was 40 mg (day 1) followed by subcutaneous injection of 40 mg in 2 weeks (day 15). Injection of 40 mg once per 2 weeks (subcutaneously) was used as a supporting therapy.

Complete inpatient treatment course (stage II) was followed by clinical (according to PASI) **(Table 2)** and instrumental examination of children, as well as skin examination using ultrasound. The results of ultrasonography showed statistically significant decrease in the thickness of the epidermis, dermis and a number of values comparable to intact skin. It was found that administration of this biological agent resulted in complete reduction of inflammatory changes in the epidermis and dermis, as well as normalization of keratinization processes in the epidermis.

Two injections were followed by an outpatient stage of treatment (stage III) under the supervision of a dermatovenerologist at the place of residence. The patients were thoroughly followed for 12 months, when they received injections of the drug according to the conventional procedure.

The short-term results of treatment were evaluated in 3 months based on PASI index and the results of the clinical and laboratory examination. The results were virtually unchanged and matched the values obtained at discharge from the hospital. The psoriatic process was at the stage of stabilization. The overall assessment of long-term outcomes (in 1 year) clearly showed stable remission, PASI did not exceed 5 points, which is indicative of clinical remission **(Fig. 1—4)**.

Conclusions

The positive outcomes of the reported cases, where the immunobiological drug was used in the treatment of psoriatic erythroderma in children, suggest that adalimumab is highly effective in treatment of psoriatic erythroderma in children. The use of the standard dose of adalimumab of 40 mg and treatment regimen of 0.8 ml per 2 weeks subcutaneously (when body weight is at least 30 kg) provides quite rapid clinically significant decrease in PASI, which is indicative of a positive effect on the severity of erythroderma and dissemination of the psoriatic process. This drug is safe for children subject to a standard screening procedure.

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