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ОПИСАНИЕ КЛИНИЧЕСКОГО СЛУЧАЯ ТЕРАПИИ АДАЛИМУМАБОМ И СЕКУКИНУМАБОМ ПАЦИЕНТКИ С ПСОРИАТИЧЕСКИМ АРТРИТОМ

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Description of the Clinical Case of Adalimumab and Secukinumab Therapy of a Patient with Psoriatic Arthritis

Резюме

В данной статье рассмотрена актуальность лечения псориатического артрита генно-инженерными препаратами (адалимумабом и секукинумабом), а также проведен ретроспективный анализ истории болезни пациентки, получавшей данную терапию.

Ключевые слова: *Псориатический артрит, генно-инженерная терапия, адалимумаб, секукинумаб*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

This article considers the relevance of treating psoriatic arthritis with genetically engineered drugs such as adalimumab and secukinumab. Also, it conducts retrospective analysis of the medical history of the patient, who had this therapy.

Key words: *psoriatic arthritis, genetically engineered drugs, adalimumab, secukinumab*

Conflict of interests

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ADA — adalimumab, GEBD — genetically engineered biological drugs, IL — interleukin, LF — leflunomide, MT — methotrexate, PsA — psoriatic arthritis, TNF-α — tumor necrosis factor alpha

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Introduction

Today, genetically engineered biological drugs (GEBD) play an important role in the management of rheumatic diseases, especially when it comes to severe patients with poor response to conventional therapy with disease-modifying anti-inflammatory drugs. Psoriatic arthritis (PsA) is a complex immuno-inflammatory disease that affects the spine, joints and entheses [1]. It significantly worsens the quality of life of patients and the fact is that one person often may have several immuno-inflammatory diseases. For example, according to the literature, PsA is observed in about 30% of patients with psoriasis. This is because these disorders have similar genetic and immunological factors of development, specifically, genetic polymorphism of interleukin (IL) 23R, which determines the IL 12/23 signaling pathway of immunopathogenesis. This is the same reason why PsA and psoriasis may be concomitant with many other immuno-inflammatory diseases, in particular, inflammatory bowel diseases, thereby worsening the quality of life of patients and their prognosis for both work and life. Along with late detection and incorrect therapy, all this leads to a high level of disability among these patients [2]. Inhibitors of tumor necrosis factor alpha (TNF-α) are widely used in the management of PsA [3]. However, as mentioned above, entheses are often involved in the process in the cases of PsA. The activation of the IL 23/IL 17 axis is known to play a critical role in the development of enthesitis. It should be noted that the enthesitis of certain localities, for example, calcaneal enthesitis, seriously limits motor activity, and therapy with synthetic disease-modifying anti-inflammatory drugs in these conditions has shown to be ineffective. In such cases, an IL-17A inhibitor — secukinumab — is successfully used [4]. As for TNF-α inhibitors, it should be noted that immunogenicity is a property of proteins affecting immune response manifested in the formation of antibodies to the drug (ABD) and/or immune complexes. Decreased immunogenicity in cases of combination therapy with TNF-α inhibitors and methotrexate (MT) is observed in comparison with GEBD monotherapy, while the administration of a therapeutic dose of MT allowed reducing to a greater extent the incidence of antibodies to TNF-α inhibitors. As for adalimumab (ADA), in a number of studies, immunogenicity against ADA was observed at the early stages of treatment: in 67% of cases in patients positive for ABD, it developed in the first 280 weeks of therapy [5].

Objective

To evaluate the effectiveness of therapy with genetically engineered biological drugs in a female patient with psoriatic arthritis.

Materials and Methods

A retrospective analysis of the patient's medical records was carried out, as well as follow-up in the genetic engineering biological therapy room of the rheumatology center of Voronezh Regional Clinical Hospital No. 1.

Patient K, female, 22, was on an outpatient visit at the rheumatology center of VRCH No. 1 with a diagnosis of: Psoriatic arthritis, chronic asymmetric polyarthritis of the joints of hands, Rg stage 1–2; of feet, Rg stage 2; erosive, bilateral sacroiliitis, Rg stage 2 on the left, 1–2 on the right; coxarthrosis, Rg stage 1; arthritis, secondary arthrosis of right elbow joint, Rg stage 2–3; flexion contracture of right elbow joint, activity 2–3 on CEBD (adalimumab). Functional disorders 2–3. Psoriasis, remission.

The patient complained of constant pain in all joints, numbness of fingers, feet, swelling of 1, 3 left metacarpophalangeal joints, pain in cervical and lumbosacral spine, inability to move without assistance, morning stiffness that does not stop without taking non-steroidal anti-inflammatory drugs (NSAIDs). At the time of examination, she could move on her own with difficulty.

Medical history revealed that she considers herself ill since 2013 when the first symptoms of disease appeared. Psoriasis since 2012. In November 2012, she was diagnosed with juvenile chronic (psoriatic) oligoarthritis. Until the age of 18, she underwent regular inpatient treatment at Voronezh Regional Children's Clinical Hospital No. 1. From 2012 to 2016, she received methotrexate (MT) at a dose of 15 mg per week. Significant deterioration since January 2017, when pain and swelling in the joints intensified, and pronounced morning stiffness appeared. NSAIDs did not reduce the activity of disease, significant pain and joint dysfunction persisted. In March 2017, due to MT intolerance (severe nausea, vomiting after administration), she was switched to leflunomide (LF) at a dose of 20 mg per day. In April 2017, sulfasalazine (SF) was added to the treatment at a dose of 2 g per day. From 9 to 18 October 2017, she was hospitalized in the rheumatology department at VRCH No. 1. It was recommended that the patient should be referred to a commission for the selection of treatment with genetically engineered biological drugs (GEBD). On November 28, 2017, based on the decision of the medical commission of VRCH No. 1, taking into account the high activity of psoriatic arthritis and the ineffectiveness of the previous disease-modifying therapy (MT, LF, SF), as well as generalized enthesopathy, the patient was prescribed adalimumab (ADA) at a dose of 40 mg once every 2 weeks subcutaneously. Treatment was adjusted: ADA 40 mg once every 2 weeks, SF 2.0 g/day before the first administration of ADA, LF 20 mg/day for a long time. In February 2018, at the visit to rheumatologist, the

patient complained of the absence of a positive effect of ADA. In May, July, and September, during planned outpatient appointments, the patient also noticed no positive changes from the therapy.

Physical examination results: General condition is satisfactory. There are multiple tattoos on skin, psoriatic rashes on scalp. On auscultation, vesicular breathing over lungs, no crackles. Respiratory rate 15 per min. Heart rate is regular, 68 beats/min, blood pressure 110/70 mm Hg on both hands. Abdomen was soft and painless during palpation. Liver is not enlarged. Stool was regular and formed. Urination was without abnormalities. Status localis: pain on palpation and moderate deformity of wrist joints, swelling of 1, 2 metacarpophalangeal joint on the right. Movement in wrist joints is limited. A positive symptom of lateral compression of hands and feet. Palpation of right elbow is painful. Pain on palpation of the sacroiliac joints on both sides. Flexion contracture of the right elbow up to 30 degrees. Flexion in the right elbow is also limited. Range of motion in the spine, in hip joints in full. 4th and 5th toes of the left foot are painful and hammer-shaped, it is painful to stand on toes. Achilles tendons swollen, painful on palpation.

The patient was recommended to take a referral to a medical commission to resolve the issue of further treatment approach. On October 09, 2018, a commission was convened at VRCH No. 1. Given the high activity of the process, the ineffectiveness of treatment with ADA at a dose of 40 mg s/c once every 2 weeks and disease-modifying drugs (MT, LF, SF), it was recommended to switch the patient to an interleukin-17 inhibitor — secukinumab — at a dose of 150 mg s/c once a month (including induction treatment at a dose of 150 mg s/c on week 0-1-2-3-4). On January 09, 2019 — maintenance treatment at a dose of 150 mg s/c once a week.

On October 03, 2019, patient K. visited the rheumatology center of VRCH No. 1 on an outpatient basis to assess the effectiveness of therapy with secukinumab. The patient noted a stable state of health, morning stiffness for 5–10 minutes, pain in hip joints during exercise, when the weather changes, more on the left, periodic numbness in the neck in the morning. Physical examination: The condition is satisfactory. She moves on her own, without support. Palpation of right elbow joint, left sacroiliac joint is painful. Other joints are painless. Flexion contracture of the right elbow up to 30 degrees. Flexion in the right elbow is also limited. 4th and 5th toes on the left foot are hammer-shaped. Achilles tendons are painless on both sides, not swollen. Blood tests on September 30, 2019: hemoglobin 130 g/l (120–140 g/l), erythrocyte sedimentation rate (ESR) 6 mm/h (0–11 mm/h), C-reactive protein (CRP) 2.26 mg/l (0–5 mg/l). It is recommended to continue the ongoing therapy.

Discussion

In this clinical case, the tactic of replacing a genetically engineered biological drug from the group of tumor necrosis factor alpha inhibitors — adalimumab with an interleukin 17 inhibitor — secukinumab, was chosen. As a result of the therapy, the patient saw positive changes. In the clinical picture: stable state of health, morning stiffness for 5–10 minutes, severity of peripheral arthritis decreased, range of motion in the spine increased, pain in the hip joints during exercise and when the weather changed, more on the left, periodic numbness in the neck in the morning. There are no psoriatic rashes at the time of examination. The number of painful joints (NPJ) decreased from six to one, the number of swollen joints (NSJ) from four to one; there is a decrease in the disease activity score (Disease Activity Score 28 — DAS 28) — from 5.3 points to 2.2 (which corresponds to low disease activity). Laboratory parameters returned to normal: ESR — from 48 mm/h (September 03, 2018) to 6 mm/h (September 30, 2019), CRP — from 11.9 mg/l (September 03, 2018) to 2.26 mg/l (September 30, 2019). An effective and quick response to therapy was observed: after the first injection of secukinumab, the patient felt improvement (during the following week, she did not take NSAIDs). Quick response to therapy in this patient matches the data of randomized controlled trials [6]. It should be emphasized that for ten months of treatment, no adverse reactions that would require interruption of therapy were observed. The lack of effect on therapy with TNF-α inhibitor adalimumab may be associated with both primary and secondary inefficiency [7]. Risk factors for primary inefficiency are the following: female gender, prevalence of other inflammatory cytokines in the pathogenesis of the disease, pharmacokinetic characteristics of the drug, genetic predisposition. Mechanisms of secondary inefficiency include immunogenicity that depends on the state of the body's immune system. Due to MT intolerance in this patient, it was impossible to prescribe combination therapy with MT+ and TNF-α, and it should be noted that the apparent ability of methotrexate to prevent the formation of ABD was not found in leflunomide, which is indirectly confirmed in this case by the absence of effect from combination therapy LEF + ADA. Given the patient's medical history, young age, high activity of the disease, as well as the presence of enthesitis, it was decided to switch the patient not to another drug from the TNF-α-i group but to a drug from the group of IL 17 inhibitors. This approach had a positive result: the activity of the disease decreased, the patient's quality of life improved significantly, and her ability to work was restored. Secukinumab demonstrates a favorable safety profile in actual clinical practice in patients with psoriatic arthritis, and in clinical studies. According to the literature, in patients with PsA, secukinumab

provides a rapid clinical effect after the first week of treatment, prevents the progression of structural damage to joints, and promotes active regression of enthesitis [8].

Conclusion

This case demonstrates compliance with the golden rule in modern rheumatology «treat to target» — treatment to achieve the goal. The presented clinical case demonstrated high clinical efficacy of secukinumab in the treatment of patients with severe PsA, who are resistant to standard methods of treatment with disease-modifying drugs and the ineffectiveness of monoclonal antibodies to TNF-α. Results of this clinical case indicate the positive effect of secukinumab on the primary signs of PsA: arthritis, enthesitis, dactylitis, functional abilities, skin manifestations. An important condition for the development of such a treatment strategy is a timely response to the ineffectiveness of therapy, as well as obtaining information about the immunogenicity of various TNF-α inhibitors and improving test systems for determining the concentration of the drug and antibodies to the drug (ABD) and/or immune complexes.

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