



Treating Psoriatic Arthritis By TNF – α Inhibitors: A Case Study

Zhuravleva Nadezhda Vladimirovna¹, Sharapova Olga Viktorovna^{2,3}, Gerasimova Liudmila Ivanovna^{*2,4} , Diomidova Valentina Nikolaevna¹, Smirnova Tatiana Lvovna¹, Ukhterova Nadezhda Dmitrievna¹, Karzakova Luiza Mikhailovna¹, Arkhipova Anastasia Vladimirovna¹ And Yastrebova Svetlana Alexandrovna¹

¹Internal Medicine Department of the Federal State Budgetary Educational Institution of Higher Education "I. N. Ulianov Chuvash State University", 428017, the Chuvash Republic, Cheboksary, Moskovsky prospect, 45, Russia

² Moscow State Budgetary Healthcare Institution «City Clinical Hospital named after V.V. Vinogradov», Moscow City Health Department», 117292, Vavilov street, 61, Moscow, Russia

³Medical Institute of Continuing Education at the Federal State Budgetary Educational Institution of Higher Education "Moscow State University of Food Production", 125080, Volokolamskoe Shosse, 11, Moscow, Russia.

⁴Institute of Clinical Medicine at the Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University under the Healthcare Ministry of the Russian Federation (Sechenovskiy University), 119435, Bolshaya Pirogovskaya st., 2, build.4, Moscow, Russia

Abstract: Psoriatic arthritis (PsA) is a heterogeneous seronegative chronic inflammatory spondyloarthritis associated with psoriasis. Doctors consider PsA hard in complex treatment. The purpose of the study is to perform the analysis of clinical data and to identify the features of psoriatic arthritis and selecting drug therapy. The patient's condition clinical assessment has carried out by using clinical, laboratory and instrumental methods with calculating the Psoriasis Area and Severity Index (PASI), the CASPAR diagnostic criteria and the genetically engineered biological drugs treatment. In the clinical case we studied, a patient with a history of psoriasis has first diagnosed with widespread skin psoriasis at the age of 12, when he carried out medicamentous therapy combined with PUVA. Despite the use of glucocorticosteroids, no complete regression of psoriasis has observed, and the PASI score was 35.3-36.3 points. At the age of 30, the patient developed lower back pains, enthesitis, the PASI score was of 37.1 points. Nonsteroidal anti-inflammatory drugs were added to the treatment. At the age of 42, he was diagnosed with psoriatic arthritis, activity III, stage II, dactylitis, enthesites, the PASI index was 31.3 points; right-sided active sacroiliitis - radiologically stage I (BASDAI 4.2 points), FCS 2-3". According to the CASPAR criteria, 4 points were obtained at the time of the disease diagnosis (current psoriasis - 2 points, familial psoriasis - 1 point, negative rheumatoid factor - 1 point). In 2016, at the age of 48, Adalimumab therapy has started according to the scheme in combination with Methotrexate, as a result it was possible to achieve psoriatic arthritis remission and the skin rashes' regressed and 0 PASI score. The psoriatic arthritis therapy with the use of Adalimumab - TNF- α - inhibitor contributed to the disease's long-term stable remission and completed the psoriatic skin rashes regression.

Keywords: psoriatic arthritis, psoriasis, genetically engineered biological drugs (GEBD), Psoriasis Area and Severity Index (PASI), recommendations of the European Anti-Rheumatic League (EULAR) and the American College of Rheumatology (ACR).

*Corresponding Author

Gerasimova Liudmila Ivanovna, Moscow State Budgetary Healthcare Institution «City Clinical Hospital named after V.V. Vinogradov», Moscow City Health Department», 117292, Vavilov street, 61, Moscow, Russia

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INTRODUCTION.

Psoriatic arthritis (PsA) is a heterogeneous seronegative chronic inflammatory spondyloarthritis associated with psoriasis.^{1,2} In 1964, the American College of Rheumatology (ACR) recognized PsA as a distinct disease entity. The prevalence of PsA among patients with psoriasis ranges from

six to forty-two percentage. Approximately 30% of people suffering from skin psoriasis developed an inflammatory disease of the peripheral or axial skeleton involving synovial and/or enthesis tissue in the pathological process, called psoriatic arthritis (PsA) (Table 1).

Table 1 Classification of clinical forms of PsA (Moll and Wright)

No	Form of PsA	Clinical characteristics of PsA
1.	Oligoarticular arthritis	Asymmetric <5 asymmetrically affected joints
2.	Symmetrical polyarthritis	>5 symmetrically affected joints, similar to rheumatoid arthritis
3.	Distal arthritis	Involves the distal interphalangeal joint
4.	Arthritis mutilans	A destructive form that leads to deformities
5.	Spondyloarthropathy	Affects the spine (spondylitis), sacroiliac joints (sacroiliitis) or the hip joint with or without peripheral arthritis

Psoriasis in most cases can precede the development of PsA. According to the survey, the undiagnosed PsA cases reveal among the patients. PsA diagnosis is important at its early stage to prevent joint damage and related disability. The risk factors for the disease development are infections (gram-positive bacteria, such as streptococci or retroviruses, including HIV), drug use, joint injuries, obesity and smoking. Emotional stress plays an important role as a trigger for cutaneous psoriasis and psoriatic joint damage.³ PsA is associated with the presence of the major histocompatibility complex (MHC) class allele HLA-Cw6. The frequency of concordance between monozygotic twins is 70%.⁴ The conducted studies revealed changes in both humoral and cellular components of the immune system.³ In patients, CD4+ lymphocytes predominate in the synovial fluid, while the ratio of CD4+ /CD8+ lymphocytes in the synovial fluid becomes 2:1. An in-depth study of synovial fluid revealed that CD8+ fraction lymphocytes has most often found in entheses.⁴ An active participation of T-cells in the development of psoriasis and PsA have been established. Detection of CD4+CD8+, CD4+ Th17 in the psoriatic synovial membrane indicates a significant influence of the immune system on the PsA pathogenesis. Epidermal keratinocytes release DNA that binds to the antibacterial peptide LL-37 and this stimulates plasmacytoid dendritic cells to release tumor necrosis factor- α (TNF- α). Dendritic skin cells activate, which migrate to the draining lymph nodes and trigger the differentiation of type 1 (Th1) and Th17 T helper cells. From the lymph nodes Th1 and Th17 cells migrate into the dermis and release IL-12, IL-17, IL-22 and TNF- α , which promote the proliferation of keratinocytes. The microbial intestinal dysbiosis can cause the colon's inflammation. In this case, Th17 cells are stimulated and they release IL-23. IL 23

activates Th17 cells with the further cytokines secretion. The cytokines cause the tendon's inflammation, the bone tissue erosion and the abnormal bone formation. IL-22 and other factors stimulate the mesenchymal cells' differentiation into the osteoblasts. The osteoblasts form the enthesophytes in peripheral entheses and joints. At the same time, the osteoblasts create syndesmophytes in the spine.

CLINICAL MANIFESTATIONS.

Clinically, PsA characterized by swelling, pain and stiffness of the joints, damage to ligaments and tendons. Simultaneous development of synovitis, enthesites of tendons and ligaments of one toe or finger is called dactylitis and is detected in 30% of PsA patients.⁵ Up to 20% of affected patients suffer from severe destructive and crippling (leading to disability) forms of the disease. In the clinical course of psoriatic arthritis, there are periods of exacerbation and remission. In the absence of adequate treatment during the exacerbation of psoriatic arthritis, joint destruction is possible. Skin lesions usually precede arthritis (in 75% of cases) or occur simultaneously in 10%. In the remaining 15% of cases, psoriatic arthritis may precede skin lesions. Correlation between the type or the severity of skin lesions and the presence, type or degree of joint damage is rare.¹ According to clinical observations, vulgar psoriasis detected in most PsA patients.⁶ Ninety % of PsA patients have the nails' structure changed.² In 2006, a research group, in accordance with psoriatic arthritis classification (CASPAR), established a highly sensitive (91-100%) and specific (97-99%) set of criteria for the diagnosis of psoriasis.⁷ Diagnosis of psoriatic arthritis in patients with psoriasis with signs of inflammatory joint disease is carried out based on the CASPAR criteria (Table 2).

Table 2 The CASPAR criteria for the diagnosis of PsA⁴ (Classification criteria for Psoriatic Arthritis, 2006).

No	Criteria for Psoriatic Arthritis
To meet the CASPAR criteria, a patient must have inflammatory diseases of the joints (joints, spine or intestines) with ≥ 3 points from the following categories:	
1	Evidence of current psoriasis (score 2), personal history of psoriasis (score 1) or family history of psoriasis (score 1) Nail
2	Lesions - -typical psoriatic nail dystrophy, including onycholysis, and hyperkeratosis revealed in the current physical examination (score 1)
3	Current dactylitis, or dactylitis in the anamnesis recorded by a rheumatologist (score 1)
4	A formation that manifests itself in the form of extra-articular bone proliferation near the edges of the joint (but excludes the formation of osteophytes) on radiographs of a hand or foot (score 1).
5	Negative rheumatoid factor (score 1)

Given that 10-15% of patients develop arthritis before psoriasis, another problem is the potential presence of psoriatic synovitis. In this situation, the family history of psoriasis is important; a typical damage to the musculoskeletal system and negative serology can help to differentiate PsA. Sometimes psoriasis is "hidden" in nature and does not detect in areas such as the scalp, nails, and flexor areas. Despite the fact that, the CASPAR criteria have been established in patients with long-term ongoing disease, studies have shown that they are applicable for making the diagnosis in patients with early signs of the disease.⁷ If there are complaints of joint pain, the patient must necessarily be examined by a rheumatologist to make a clinical diagnosis. Laboratory markers of systemic inflammation increased. C-reactive protein or erythrocyte sedimentation rate increased only in 50% of cases. Ten percent of the patients have low rheumatoid factor titer and anti-cyclic citrullinated peptide.

CASE ANALYSIS

The patient's examination and treatment carried out based on the budgetary institution of the Chuvash Republic "Republican Clinical Hospital" under the Public Health Ministry of the Chuvash Republic. Upon enrollment in the study, the patient signed an informed consent form. The patient's diagnosis was established according to the criteria of PASI, ACR/EULAR, CASPAR. The doctors made all the procedures in accordance with the ethical standards established by Helsinki Declaration of 1964 as amended in 2013, in accordance with the ethical standards of the Supervisory Board of the Naresuan University (IRB566/59 and Certificate of Authenticity № 573/2016). Using a hematological analyzer, we made the general blood test. The erythrocyte sedimentation rate (ESR) was determined according to the standard international Westergren method (normal value <30 mm/h). Serum concentrations of C-reactive protein (CRP), IgM of the rheumatoid factor (RF) was measured by light scattering immunoassay method on a BN ProSpec analyzer (Siemens, Germany); a highly sensitive latex test (sensitivity 0.175 mg/L) was used to assess the level of CRP. The value of C-reactive protein (CRP) in the blood serum less than 5.0 mg/l and corresponded to the normal value. According to the manufacturer's recommendations, the concentration of C-reactive protein (CRP) 15.0 IU/ml has taken as the upper limit of the IgM normal values in the Russian Federation. Quantitative determination of cyclic citrullinated peptide antibodies (anti-CCP) in the blood serum has carried out by enzyme immunoassay using commercial reagent kits (Axis-Shield, UK), with the upper limit of the normal values being 5.0 units/ml. The index of the lesion area and the effectiveness of treatment for psoriatic skin lesions were evaluated in points according to severity and prevalence - the PASI index (Psoriasis Area and Severity Index): from 0-10 points - mild form; from 20-30 points - moderate severity; severe course of the disease from 30-72 points. To classify psoriatic arthritis, the CASPAR criteria has used, according to which the diagnosis of psoriatic arthritis is made according to five criteria, the total number of points is at least three. X-ray examination of the joints has performed on a Siemens magnetic resonance tomograph (Germany) with a 1.5 Tesla field. The degree of joint damage has assessed in points according to the criteria of ACR/EULAR (American College of Rheumatology/European Alliance of Rheumatology) 2010, assuming a "treatment to goal" approach to achieve remission or low disease activity in the

patient. A visual analog scale (VAS) has used to assess the intensity of pain.

TREATMENT HISTORY

In confirmation, we provide a description of our own clinical case. The patient P., born in 1968, at the age of 12, psoriatic rashes first appeared on the skin of the extensor surfaces of the elbows, knee joints, lower legs, the scalp, behind the auricles; somewhat later, the skin rashes acquired a generalized character. The patient has the family history of psoriasis; his father suffers from psoriasis of the skin. The dermatologist consulted the patient. The diagnosis of "widespread skin psoriasis" was verified. Since that time, he followed and treated by a dermatologist. The patient carried out the therapy with intravenous infusions of sodium thiosulfate. He got the local treatment with salicylic and steroid ointments, PUVA therapy, with physiotherapy methods. In severe exacerbations of cutaneous psoriasis, the patient had the systemic therapy with glucocorticoids (Dexamethasone). However, a complete regression of psoriatic skin rashes never observed, the PASI score was 35.3-36.3 points. At the age of 30 (1998), for the first time, he noted inflammatory pains in the lower back (in the second half of the night and in the morning after waking up, decreasing against the background of physical activity). The patient had joint lesions accompanied by pronounced morning stiffness lasting up to 1-2 hours, as well as the onset enthesites in the area of the lateral condyles of the humerus, iliac wings, the great trochanter, the upper edge of the patella and the tibial tuberosity. The PASI score was 37.1 points. To relieve the pain syndrome, the patient independently administered Diprosan 40 mg intramuscularly up to 1-2 times a month. A patient is a teacher; the disease worsened his life quality and hindered his professional activity. When signs of temporary professional disability appeared, he carried out the treatment on an outpatient basis by a therapist and a dermatologist. In 2002, nonsteroidal anti-inflammatory drugs (NSAIDs) (Nimesulide 100 mg 2 times a day orally) were added to treatment due to high laboratory activity (ESR according to Westergren 43 mm / h, CRP 12.7 mg / l), the PASI score was 38.5 points (Fig. 1). While taking nonsteroidal anti-inflammatory drugs (NSAIDs), the intensity of lower back pains decreased (VAS 5 points), but enthesitis persisted. In February 2009, pains (VAS 5-6 points) appeared in the left elbow, metacarpophalangeal joint of the 3rd finger on the left hand, the right knee joint and swelling in them, which persisted for 6 months (asymmetric arthritis). At this, the PASI score was 37.1 points. In January 2010, the patient had the pain (VAS 4-5 points) in the radiocarpal, metacarpophalangeal, proximal and distal interphalangeal joints of the hands with their defiguration. At the same time, inflammatory pain in the lower back, psoriatic rashes on the skin of the chest, abdomen, and extensor surfaces of the lower and upper extremities persisted, the PASI score was 31.3 points. According to samples' results, the ESR by Westergren was 53 mm / h, CRP 22.5 mg / l, the RF was negative. In order to verify the diagnosis, he has hospitalized in the rheumatology department of the Republican Clinical Hospital under the Health Ministry of Chuvashia in the town of Cheboksary. According to the results of MRI of the sacroiliac joints, right-sided active sacroiliitis was revealed, radiological stage I. Radiography of the hands revealed changes in the form of joint space narrowings and irregularities in the contours of the distal interphalangeal joints. According to the CASPAR criteria, 4 points were

obtained at the time of the disease diagnosis (current psoriasis - 2 points, familial psoriasis - 1 point, negative rheumatoid factor - 1 point). Diagnosis: "psoriatic arthritis, activity III, stage II, dactylitis, enthesitis, the PASI score - 31.3 points; right-sided active sacroiliitis, radiological stage I (BASDAI index was 4.2 points), joint functional insufficiency (FNS) 2-3". Methotrexate added to the treatment at its initial dose of 15 mg / week, followed by an increase in the dose to 25 mg / week subcutaneously. In February 2012, due to persisted lower back pain (5-6 points by VAS), the onset of intermittent pain in the gluteal regions, most pronounced on the left, magnetic resonance imaging (MRI) of the sacroiliac joints was performed. Conclusion: bilateral active sacroiliitis - stage II on the right, stage I on the left. At this, psoriatic skin phenomena progressed in visible areas of the face, the auricles, the upper extremities, the scalp and the nails (PASI score was 34, 4 points). All this indicated the therapy ineffectiveness. Upon re-hospitalization to the rheumatology department of the Republican Clinical Hospital under the Health Ministry of the Chuvash Republic, the patient was started to receive the therapy with TNF- α inhibitor - Infliximab at the rate of 5 mg / kg of body weight according to the scheme: zero, two, six, and then - every eight weeks. Methotrexate therapy has continued; the drug has administered parenterally at the dose of 25 mg / week. As situations demanded, the patient has recommended in taking nonsteroidal anti-inflammatory drugs (NSAIDs) in average daily doses. The patient received the Infliximab treatment during 3 months period. He had the positive dynamics. The intensity of pain in the spine (3 points by VAS) decreased. The acute inflammation symptoms of the elbow, knee, and interphalangeal joints of the hands stopped. The volume of active movements in the joints increased. Morning stiffness in the joints and the spine decreased to 15 minutes. The patient had the cutaneous psoriasis manifestations regression (PASI 30.4). The enthesitis decrease. Acute-phase blood parameters normalized (ESR 15 mm per hour, CRP - 4.2 mg/l). In December 2013, the patient's condition worsened in the form of an increase in peripheral arthritis of the elbow, radiocarpal and interphalangeal joints of the hands, increased pain (6-7 points by VAS) in the lower back, & the onset pain in the thoracic and cervical spine. When examining the patient, the rheumatologist revealed disfiguration in the area of the elbow, radiocarpal and interphalangeal joints of the hands. The patient had soreness during the palpation and limited mobility in the spine, the "chin-sternum" symptom was 4 cm, and chest excursion was 1.5 cm. The Schober test was 4 cm. The Forestier test was negative. The symptoms of Kushelevsky were one, two positive, the PASI score was 33.4 points (Fig. 1). According to laboratory studies findings the ESR was 34 mm/h, CRP was 29 mg/l, the MRI of the sacroiliac joints revealed signs of bilateral active stage II sacroiliitis. In January 2014, there was a pronounced exacerbation of peripheral arthritis in the radiocarpal joint and small joints of the hand. The patient experienced significant limitations when performing his professional duties. The examination revealed tenderness during palpation, deformity in the area of the elbow joints, left radiocarpal and interphalangeal joints of the hands. The patient had limited mobility in the spine, the "chin-sternum" symptom was 4 cm, chest excursion was 2 cm, Schober test was 4.5 cm, lateral slopes of the trunk were 8 cm on both sides, the Forestier test was negative, the Kushelevsky's symptom was 1 positive. The patient had soreness during palpation in the enthesitis projection, the PASI score was 34.1 points. High laboratory activity of the inflammatory process noted in blood tests (ESR 45 mm/h,

CRP 25 mg/l). Radiographs of the joints of the hands showed joint spaces of the distal interphalangeal joints, the first metacarpophalangeal joints, the radiocarpal joints of the right and left hands was unevenly narrowed, there were bone overgrowths of the articular margins. According to the MRI examination of the sacroiliac joints, bilateral sacroiliitis has detected in the stage without signs of active inflammation. The patient underwent pulse therapy with Methylprednisolone 1000 mg per injection № 3 to reduce the intensity of joint and pain syndromes, PsA activity. In September 2015, an increase in the intensity and prevalence of skin rashes was registered; the PASI score was 44.2 points, as well as involvement of new joints in the process, and a decrease in the quality of life. The MRI of the pelvic bones and pelvis joints revealed bilateral sacroiliitis of the radiographic stage. The general blood test (CBT) found hemoglobin 149 g/l, leukocytes $4.58 \times 10^9/l$, platelets $216 \times 10^9/l$, eosinophils 2%, stab neutrophils 1%, segmented neutrophils 57%, lymphocytes 31%, monocytes 8%, ESR 7mm / hour. The common analysis of urine showed no protein, the specific gravity of 1025, the urinary sediment was unremarkable. The biochemical blood analysis found CRP 2.4 mg / l, RF 11.7 units / ml. The laboratory parameters was regarded as a manifestation of secondary resistance to Infliximab, in connection with which the patient started to receive the therapy with Etanercept at the dose of 50 mg/week in the form of subcutaneous injections, continued to be administered Methotrexate 25 mg / week intramuscularly (i. m.). The tolerability of Etanercept was satisfactory. At the beginning of 2016, a positive clinical effect of Etanercept has obtained on skin psoriasis (by the PASI index the score was 33.8 points). In August 2016, against the background of Etanercept therapy at the dose of 50 mg / week, peripheral arthritis, and enthesitis increased, a pronounced skin process has observed (the PASI score was 17.8 points) and an increased daily need for nonsteroidal anti-inflammatory drugs (NSAIDs) has noted. Laboratory findings obtained by the complete blood count (CBC) showed hemoglobin 128 g/l, leukocytes $4.69 \times 10^9/l$, platelets $201 \times 10^9/l$, ESR 39 mm / h. The common analysis of urine showed no protein, the specific gravity of 1020, the urinary sediment was unremarkable. The biochemical blood analysis revealed bilirubin 26 mmol/l, AspAT 29 units/l, ALAT 19 units/l, creatinine 84 mmol / l, CRP 9.4 mg/l. The radiograph of the joints of the hands showed negative radiological evolution compared to the X-ray archive from January 2014. An increase in the number of erosions has proven. The doctors canceled Etanercept due to its insufficient effectiveness. Since September 2016, the patients Adalimumab therapy was started. A noticeable improvement has noted after the 2nd week of treatment in the form of pain reduction (VAS score was 2-3 points) in the joints of the hands, elbow, shoulder, knee joints, in the lumbosacral spine, reduced morning stiffness in the joints up to 20 minutes. The number of psoriatic plaques on the trunk and extremities decreased significantly (the PASI score was 5.3 points). Laboratory parameters showed a reduction of the ESR to 10 mm/h, CRP - up to 6.1 mg/l. In 8 weeks from the start of the therapy, a complete regression of pathological skin rashes was noted (the PASI score was 0 points). Subsequently, the rheumatologist continued to monitor the patient. The patient received a genetically engineered biological drug (GEBP) – Adalimumab once every 2 weeks in the rheumatology department of BI "Republican Clinical Hospital", the drug tolerability was satisfactory. In addition, the patient continued the administration of Methotrexate 25 mg subcutaneously (s/c) once a week under the control of complete blood count

and urine tests, also transaminases (ALT, AST) once a month. The patient received folic acid intake in the dose of 5 mg a day after taking Methotrexate. The doctors recommended the administration of nonsteroidal anti-inflammatory drugs (NSAIDs) against the background of taking anti-secretory drugs. From 2016 to the present, the patient has registered to be in persistent PsA remission, which indicated the effectiveness of the therapy (Fig. 1). There were no clinical and laboratory indicators of PsA activity and skin lesions. The patient's quality of life improved significantly, he continued to work at school, began to travel, and spent more time with his family. In May 2021, when examining the patient, his condition was satisfactory. The skin was of physiological color. There were no psoriatic skin rashes (the PASI score was 0). The hemodynamics was stable: the heart rate - 70 beats/min, blood pressure - 120/80 mmHg. Straightening of lumbar lordosis. Kushelevsky's symptoms 1, 2, the patient's distal

interphalangeal joints of the hands were moderately disfigured, the hand tightly clenched into a fist. The syndrome of transverse compression of the hands and feet was negative. According to the results of magnetic resonance imaging (MRI) of the sacroiliac joint performed in May 2021, stage III bilateral sacroiliitis remained without signs of activity. Taking into account PsA remission, the scheme of Adalimumab administration has changed to 40 mg s/c once every 4 weeks. The CBC findings showed leukocytes $4.4 \times 10^9/l$, hemoglobin 149 g/l, lymphocytes $1.6 \times 10^9/l$, rod-shaped neutrophils 4%, segmented neutrophils 48%, eosinophils 1%, lymphocytes 35%, monocytes 12%, the ESR was 6.00 mm/h. Biochemical analyses: C-reactive protein was 0.5 mg/l, calcium was 2.44 mmol/l, total protein was 73.0 g/l, gamma globulin was 13.9%. The rheumatologist continues to monitor the patient. He pursues his profession, the mood background is good, and his commitment to treatment is high.

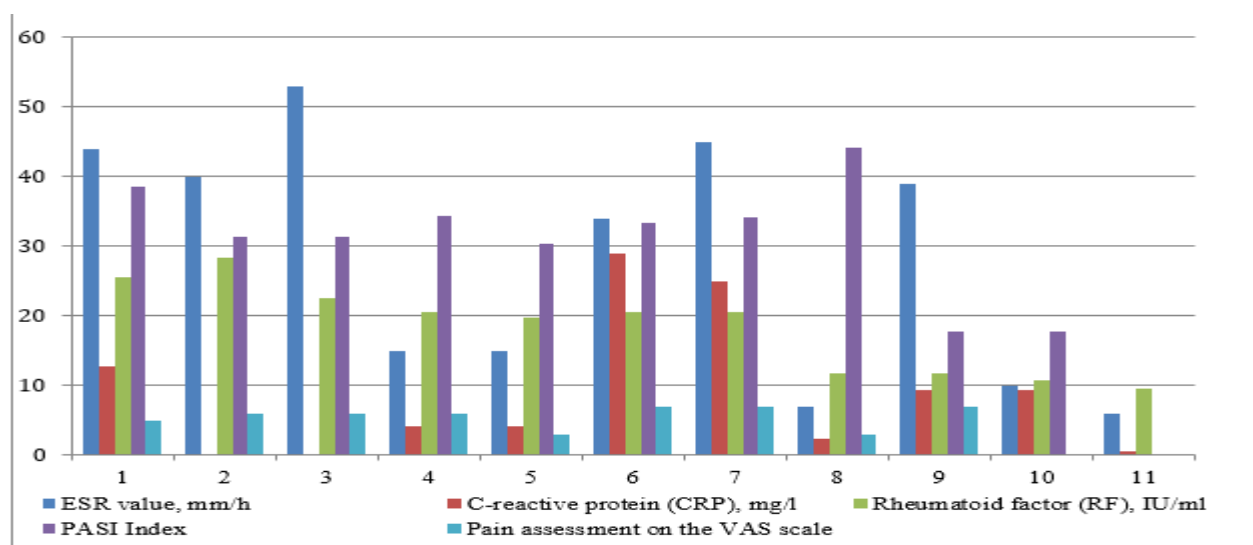


Fig 1: Clinical and laboratory indicators of patient P., in the dynamics of pharmacotherapy

Comment: 1 – 2002, 2 – 2009, 3 – 2010, 4 – 2012 (before Infliximab therapy), 5 – 2012 (Infliximab therapy), 6 – 2013 (Infliximab resistance formation), 7 – 2014 (Infliximab resistance formation), 8 – 2015 (Etanercept therapy), 9 – 2016 (before Adalimumab therapy), 10 – 2016 (Adalimumab therapy), 11 – 2021 (continuation of Adalimumab therapy)

DISCUSSION.

In our patient's PsA case, we could observe the prolonged development course. The patient received the therapy with intravenous infusions of sodium thiosulfate, local treatment with salicylic and steroid ointments, PUVA therapy, and physiotherapy. The treatment gave impermanent and ineffective result. Some scientists in their researches showed the same data and conclusions. Due to the circumstances, the scientists had found the new diagnostics & treatment methods. To improve the detection of PsA, dermatologists developed screening questionnaires, their sensitivity is 82%, and specificity is 73%. There are several questionnaires for screening patients with PsA in various conditions. Screening helps to identify a significant number of patients with undiagnosed PsA. Radiological signs of peripheral PsA has: asymmetric spread, damage to the distal interphalangeal joint, periostitis, decreased bone density and deformity of the "pencil in a glass" type in advanced cases of the disease. The most characteristic radiological sign of PsA is bone proliferation. Ultrasound examination is a reliable method for detecting signs of subclinical Achilles tendon enthesopathy and confirming the diagnosis in patients with symptoms of

damage⁹, which makes it possible to differentiate it from rheumatoid arthritis.¹⁰ Over the past decade, the opportunities for treating PsA have expanded due to a greater number of new therapeutic agents. However, therapeutic solutions for the use of these drugs are not always simple. It is necessary to adapt the choice of drug treatment to a specific patient, taking into account the type of his disease and concomitant diseases. The recommendations for the treatment of PsA developed by the EULAR, ACR suggest "Treat to target" approach to achieve remission or low disease activity in the patient. This approach uses therapy sequentially, starting with simple treatment methods such as nonsteroidal anti-inflammatory drugs (NSAIDs) for pain relief or topical treatment of psoriasis, followed by disease modifying drugs (DMARDs). If patients do not respond to previous treatment, the doctors have to use the possibility of treatment with biological drugs (bDMARDs). Most patients take nonsteroidal anti-inflammatory drugs as symptomatic therapy, while it is necessary to take into account their side effects. In the initial stages, corticosteroids are often been used in the form of intra-articular or intramuscular injections. The doctors can use intra-articular steroid injections for persistent mono- or

oligoarthritis.¹¹ The specialists do not recommend oral steroid medications. Methotrexate remains the most common first-line therapy; in addition, Sulfasalazine, Leflunomide, Cyclosporine has used in the treatment. These drugs are able to prevent structural damage to the tissues. Recently, the use of molecular targeted therapy with biological drugs has spread to various rheumatic diseases. A typical example of this is psoriatic arthritis.¹² These agents target certain components of the immune system that are necessary to create and maintain the pathogenetic process. They have significantly changed the approach to PsA treatment. Up to 50% of patients with PsA need biological therapy.¹³ Tumor necrosis factor- α (TNF- α) inhibitors, IL-12/23 inhibitors, IL-23 inhibitors, IL-17 inhibitors, JAK inhibitors, phosphodiesterase-4 inhibitor are used for the treatment. Our case was so difficult & complicated. Despite the use of glucocorticosteroids, no complete regression of psoriasis has observed, the PASI score was 35.3-36.3 points. At the age of 30, the patient developed lower back pains, enthesites, and the PASI score of 37.1 points. The specialists add nonsteroidal anti-inflammatory drugs to the treatment. Even the MRI showed us that the treatment was ineffective. The foreign countries rheumatologists came to the same conclusions.^{12, 13} The genetically engineered biological drugs treatment gave the permanent effective result.¹² Drugs that are registered in Russia for PsA treatment are TNF- α inhibitors (Infliximab, Adalimumab, Etanercept, Golimumab, Certolizumab) and monoclonal antibodies to IL-12/IL-23 (Ustekinumab). TNF- α inhibitors (TNF- α) were the first biological drugs for PsA (Adalimumab, Certolizumab, Etanercept, Golimumab and Infliximab), they are still used today in cases where there is no effect from two standard basic anti-inflammatory drugs (BAID) based on a longer experience of their use and the greatest amount of available data on long-term efficacy and safety. According to the EULAR, ARC published recommendations for PsA treatment, after ineffectiveness of one or more TNF- α inhibitors, administration of anti-IL17 and anti-IL12/IL23 biological drugs as the second-line biological therapy has indicated. Ustekinumab, an inhibitor of IL-12/23, is effective in PsA, enthesitis and dactylitis.¹⁵ After the prolonged current treatment at the age of 48 in 2016, Adalimumab therapy has started according to the scheme in combination with Methotrexate, as a result it was possible to achieve psoriatic arthritis remission and the skin rashes' regression – 0 PASI score. Our conclusions & results match with the foreign experts' observations.^{10, 12} Our case shows us that PsA diagnostics & treatment is a long-termed procedure. We have to use the modern methods including MRI & other instrumental treatment. C-reactive protein changes. It is so important to view the indicators of C-reactive protein erythrocyte sedimentation rate (ESR), RF in dynamic therapy. Taking into account the fundamental scientific evidence emphasizing the importance of Th17 pathway in PsA, a number of new therapies targeting this pathway has currently developed. Secukinumab (monoclonal antibody to IL-17A) is effective in psoriasis.¹⁶ A new drug for PsA treatment (Apremilast) is an inhibitor of phosphodiesterase-4¹⁶; its favorable safety profile in the absence of the need for regular blood monitoring and hepatotoxicity may be an advantage in practice. Prior to administering genetically engineered biological preparations (GEBP), it is necessary to perform the examination for tuberculosis, X-ray of the thoracic cavity, every 6 months it is necessary to assess the dynamics of these indicators. The index of the lesion area and the effectiveness

of treatment for psoriatic skin lesions evaluated in points according to severity and prevalence - the PASI index (Psoriasis Area and Severity Index): from 0-10 points - mild form; from 20-30 points - moderate severity; severe course of the disease corresponds to 30-72 points. Research continues in the field of rational pharmacotherapy for psoriatic lesions using topical drugs.¹⁷⁻²² New treatment methods have given clinicians the opportunity to choose the optimal therapy based on the effectiveness of drugs and their side effects. Psoriatic arthritis (PsA) is a chronic systemic disease of the musculoskeletal system associated with psoriasis.²³⁻²⁶ The presented clinical case demonstrates that in the treatment of PsA, correction of treatment regimens with the use of genetically engineered biological drugs against the background of basic therapy is necessary to achieve remission or low activity of the disease. TNF- α inhibitors have demonstrated efficacy in the treatment of the patient with active PsA. The doctors recommend TNF- α inhibitors to the patients with the risk factors for an unfavorable prognosis. The risk factors are arthritis, joint erosion, and prior administration of glucocorticoids with severe cutaneous psoriasis. Because of the therapy, the patient achieved a long-term stable remission of the disease. There were no adverse manifestations during the long period of therapy with Adalimumab, which confirms such characteristics of the drug as safety, high efficacy and absence of side effects. When describing this clinical case, we wanted to focus the attention of therapists and dermatologists on the need of individually analyze all the cases of cutaneous psoriasis, taking into account all the data about the patient and timely referring him to a rheumatologist.

CONCLUSION.

We have used clinical, laboratory and instrumental methods for the diagnostics by calculating the Psoriasis Area and Severity Index (PASI), the CASPAR diagnostic criteria. For the effective results we have used the biochemical analyses methods including C-reactive protein, erythrocyte sedimentation rate (ESR), in dynamic therapy. Simultaneously we had used the modern methods including MRI & other instrumental treatment. The psoriatic arthritis modern therapy with the use of Adalimumab - TNF- α - inhibitor contributed to the disease's long-term stable remission and completed the psoriatic skin rashes regression.

AUTHORS' CONTRIBUTIONS STATEMENT

Dr. Zhuravleva Nadezhda Vladimirovna and Dr. Sharapova Olga Viktorovna conceptualized and designed the study, Dr. Gerasimova Ludmila Ivanovna and Dr. Diomidova Valentina Nikolaevna gathered the data and prepared the original draft. Dr. Smirnova Tatyana Lvovna and Dr. Ukhterova Nadezhda Dmitrievna discussed the methodology and analysed the data. Dr. Karzakova Luiza Michailovna and Dr. Arkhipova Anastasia Vladimirovna provided valuable inputs in designing the manuscript. All authors read and approved the final version of the manuscript.

CONFLICT OF INTEREST

Conflict of interest declared none.

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