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CASE OF SEVERE JUVENILE-ONSET ANKYLOSING SPONDYLITIS IN A PATIENT WITH RECURRENT UVEITIS

Abstract

The objective of the study: To describe a clinical case of severe juvenile-onset ankylosing spondylitis in a patient with persistently recurrent uveitis. **Materials and methods.** Patient I., 43 years old, was constantly monitored since the age of 26 at the Department of Rheumatology of the Saratov Regional Clinical Hospital with ankylosing spondylitis, an early onset of extra-skeletal manifestations in the form of frequently recurring uveitis, and a number of complications. **Results.** Some complications, which caused complete loss of vision in both eyes, occurred during the observation period due to poor treatment adherence. **Conclusion.** The clinical observation presents some features of the disease course, treatment and the development of complications in the patient with ankylosing spondylitis and recurrent uveitis.

Key words: *ankylosing spondylitis, uveitis, extra-skeletal manifestations, complications*

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AS — ankylosing spondylitis, DMARD — disease modifying antirheumatic drugs, GEBD — genetically engineered biological drugs, GC — glucocorticoids, NSAIDs — nonsteroidal anti-inflammatory drugs, SpA — spondyloarthritis, HJ — hip joint, TEP — total endoprosthesis

Introduction

Spondylarthritis (SpA), due to the variety of its extra-skeletal manifestations, constantly requires differential diagnosis with other rheumatic diseases, in particular, with various inflammatory arthritis. Often, patients with SpA need advice from related specialists, most often ophthalmologists, cardiologists. The extra-skeletal manifestations themselves may be additional risk factors for a severe course of the underlying disease, more rapid progression of complications. The joint work of doctors of several specialties can help in the early diagnosis of non-skeletal manifestations, preventing the future development of severe complications, disability of patients, maintaining the quality of life in such patients.

One of the most common non-skeletal manifestations of SpA are uveitis, which accounts for 20 to 40 % of cases [1, 2]. In numerous eye diseases, the proportion of uveitis in patients with rheumatic diseases accounts for 5–12%. At the same time, uveitis is the cause of blindness in 25 % of cases [3]. Uveit onset, according to the literature, takes place at the age of 32–45 years [4-7].

The most common disease characterized by uveitis is ankylosing spondylitis (AS), although this

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extra-skeletal manifestation occurs in all forms of SpA [8]. With respect to the difference in the incidence of uveitis depending on sex, the data are contradictory. There is evidence of the prevalence of uveitis in males (men:women — 1.1:2.5) [9–11], but according to other studies, the incidence of uveitis in women is 40 %, and in men — 15.8 % [12]. An important component in the diagnosis of AS and associated uveitis is the coordinated work of doctors of two specialties — rheumatologists and ophthalmologists [8]. The severe course of AS itself may portend a severe course of uveitis, and uveitis, in turn, may be an independent factor in the severity of the course of the main rheumatic disease, reflecting the variety of complications [8, 13, 14]. At the same time, there are different views on the severity of some non-skeletal manifestations of AS, including the course of uveitis, the prognosis of which is sometimes considered as favorable: attacks, as a rule, are short-term, manageable by local treatment, including instillations and sub-conjunctival injections of corticosteroids [13].

The article presents a clinical case of severe juvenile-onset ankylosing spondylitis in a patient with recurrent uveitis.

Case report

Female patient E., aged 43 years, is monitored at the Regional Clinical Hospital (Saratov) since 2000 (from the age of 26 years).

From history it is known that at the age of twelve (1986) for the first time arthritis of the ankle and wrist joints developed. For juvenile arthritis, glucocorticoids (GC) were prescribed, which were taken occasionally, briefly, without significant effect. Later, the patient periodically experienced pain of inflammatory nature in the joints, and she used non-steroidal anti-inflammatory drugs (NSAIDs) on here own occasionally with a positive effect to manage it.

At the age of 21 (1995) after the childbirth she noted the increase in the severity of peripheral joints arthritis (hands, feet, elbows, knees, ankles) and the appearance of back pain of an inflammatory nature. She was not examined, was not treated regularly and she periodically took NSAIDs.

At the age of 24 years (1998), acute bilateral anterior uveitis was diagnosed for the first time, the characteristic features of which were the acute onset of the disease, pain in the eyes, lacrimation, photophobia, and decreased vision. Laboratory analysis revealed the presence of HLA-B27. In biomicroscopy, moderate or severe pericorneal injection of the eyeball, edema of the cornea endothelium with the deposition of small and medium-sized precipitates of light gray color, and hyperemia of the iris were determined. A feature of the anterior uveitis was the rapid formation of broad persistent posterior synechiae along the pupillary edge, leading to deformation of the pupil (Fig. 1).

The main characteristic feature of HLA-B27 associated uveitis was its recurrent course with frequent exacerbations. Aggravating factors were general overcooling, stress, and an increase in the activity of arthritis. Clinically, the course of uveitis relapse normally did not differ from the first attack of fibrinous plastic iridocyclitis, but acquired a more severe course with the generalization of inflammation in the posterior parts of the eye and the development of complications, which led to a decrease in visual acuity of less than 0.1 (with correction) of the right eye and further complete loss of vision of the left eye, due to the presence of such complications as secondary glaucoma, retinal detachment, and then subatrophy of the eyeball.

Given recurrent uveitis, the presence of peripheral arthritis, increased erythrocyte sedimentation rate, high CRP level and positive HLA-B27, ankylosing spondylitis was suggested for the first time. From that time, for 5 years, the patient was constantly taking NSAIDs, periodically prednisolone 5 mg

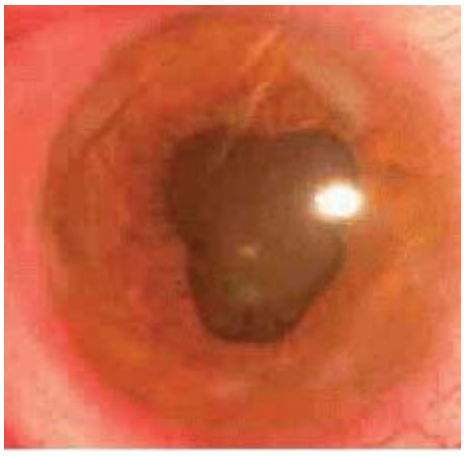

Figure 1. *Pupil deformity. Multiple posterior synechiae*

per day with a slight positive effect in the form of reduced activity of peripheral arthritis. Due to the severity of the disease and frequent relapses of uveitis, the patient was observed and periodically received treatment in the in-patient clinic of eye diseases of Saratov State Medical University n.a. V.I. Razumovsky.

At the age of 26 years (2000) due to the high activity of arthritis of peripheral joints, increased pain in the lumbar spine, increased number of uveitis relapses (up to 4 exacerbations in each eye over the past year), the patient was for the first time hospitalized in the Department of Rheumatology of the Regional Clinical Hospital (Saratov). Examination during hospitalization revealed bilateral sacroiliitis of the stage IV, arthritis of peripheral joints of the stage IV, arthritis of the knee joints of the stage III, ESR 50 mm/h, CRP+++, HLA-B27 positive, BASDAI (the Bath Ankylosing Spondylitis Disease Activity Index) — 7, ASDAS (AS Disease Activity Index) according to CRP — 3.6, and excluded inflammatory bowel disease and psoriasis.

In the hospital, juvenile-onset ankylosing spondylitis of high activity; polyarthritis of the Rg stage IV; bilateral sacroiliitis of the Rg stage IV with systemic manifestations: bilateral recurrent iridocyclitis, acute stage, corneal dystrophy, complicated cataract, vitreous fibrosis, chorioretinal dystrophy, exudative and tractional retinal detachment of both eyes, secondary glaucoma, and subatrophy of the left eye; and secondary bilateral osteoarthritis (gonarthritis) of the Rg stage III were newly diagnosed. Visual functions were light perception with the wrong projection of the light in the right eye and complete blindness of the left eye. NSAIDs with oral and topical GCs (instillations and parabulbar injections in iridocyclitis exacerbation) were prescribed. For secondary glaucoma — locally a combination of ß-blockers and carbonic anhydrase inhibitors. In relation to the development of peripheral arthritis — methotrexate 10 mg per week.

However, after discharge from the hospital, the patient refrained from the recommended therapy, constantly taking only high doses of NSAIDs orally. She did not visit a doctor for a long time. As a result of the lack of adequate therapy, the patient experienced joint deformities: flexural contractures of the wrist joints (Fig. 2), knee, ankle joints, ankylosing and lack of movement in all parts of the spine with BASMI (the Bath Ankylosing Spondylitis Metrology Index) of 0.4 (maximum — 2).

Up to the age of 37 years (2010), the patient was treated on an outpatient basis; attempts were made to prescribe sulfasalazine 500 mg per day. However, on therapy with sulfasalazine, the development of dyspepsia and epigastrial pain were noted, and therefore the drug was withdrawn.

During hospitalization in 2010 at the age of 37 years at the Regional Clinical Hospital, high activity of the disease was detected in the patient (clinically and in the laboratory — ESR 42 mm/h, CRP 61 mg/l). Upon X-ray imaging of the joints, arthritis of the knee joints of the stage IV, aseptic necrosis of the head of the left femur, arthritis of the left hip joint (HJ) of the stage IV and of the right HJ of the stage II were found, and upon X-ray imaging of the spine and pelvis — complete ankylosis, sacroiliitis of the stage IV.

Based on the patient's complaints of low vision in the right eye, no vision in the left eye, the data of medical history (the uveitis in remission), examination data (diffuse cataract, tractional retinal detachment), she was diagnosed with chronic uveitis in remission, dystrophy of cornea, complicated cataract, tractional retinal detachment, chorioretinal dystrophy of the retina of both eyes. Secondary glaucoma, subatrophy of the left eye. Microinvasive vitrectomy with tamponade by perfluoroorganic compounds with replacement with silicone oil, as well as cataract phacoemulsification with implantation of the right eye intraocular lens were performed. In postoperative period: visus OD = counting fingers against the face.

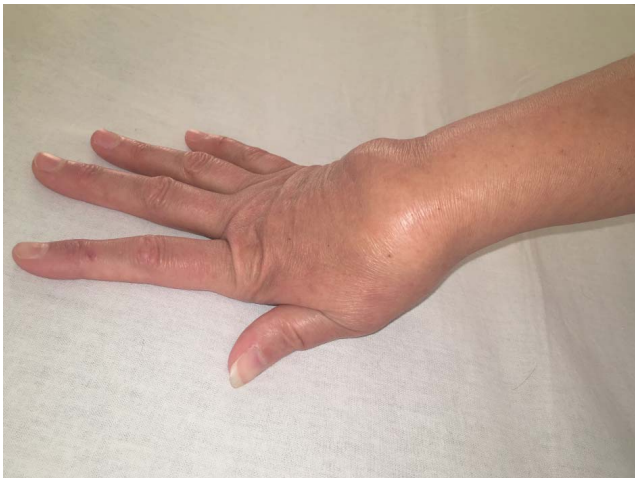

Figure 2. *Deformity of wrist and hand joints*

In the hospital, high doses of GC in the form of pulse therapy with prednisolone 510 mg No. 3 with the clinical effect of reducing the disease activity were administered, and methotrexate therapy at the dose of 15 mg per week was recommended at the outpatient stage. However, the patient again did not take methotrexate, continued taking prednisolone 15–20 mg per week, NSAIDs as required. An orthopedist recommended total endoprosthesis (TEP) of the left hip and knee joints.

Since 2011, due to the increase in AS activity, the patient independently began taking methotrexate 15 mg per week, GC 15 mg per day, NSAIDs daily. TEP of left HJ (Figure 3) was performed in March, 2011, TEP of the left knee joint — in September, 2011, TEP of the right knee joint — in March, 2012 (Fig. 4).

Due to the failure of the basic treatment, the persistence of disease activity (BASDAI of more than 4, ASDAS according to CRP of more than 3.5) and systemic manifestations — frequent relapses iridocyclitis, presence of significant complications, a combination of cytotoxic drugs with genetically engineered biological drugs (GEBD) was recommended. Since 2012, the patient started therapy with GEBD (infliximab) in combination with disease modifying antirheumatic drugs (DMARD). From 2012 to 2015, therapy with Remicade 400 mg was performed once every 8 weeks. Tolerance is good, there was a decrease in clinical and laboratory indicators of disease activity (BASDAI less than 4, ASDAS for CRP — 1.5), in relapses of uveitis up to 1 time per year, the need for NSAIDs increased only 2–3 days before the subsequent injection of Remicade. In 2013, X-ray imaging of the joints revealed osteoarthritis of the left shoulder joint of the stage IV, TEP for this reason (Fig. 5).

Figure 3. *Scar after prosthesis of the left hip joint*

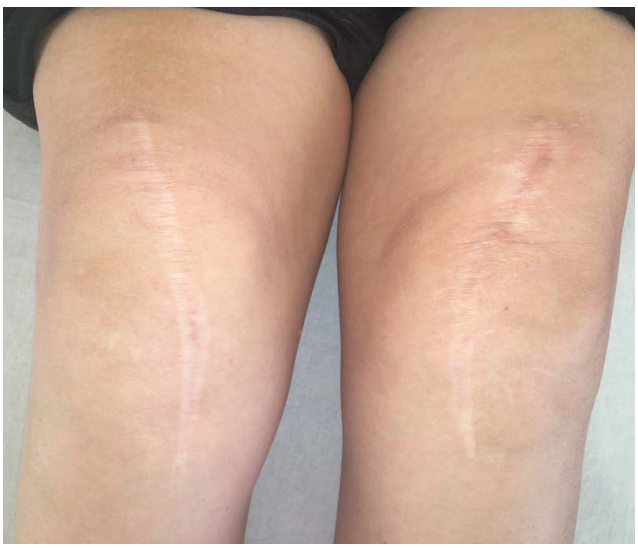

Figure 4. *Scars after prosthesis of the knee joints*

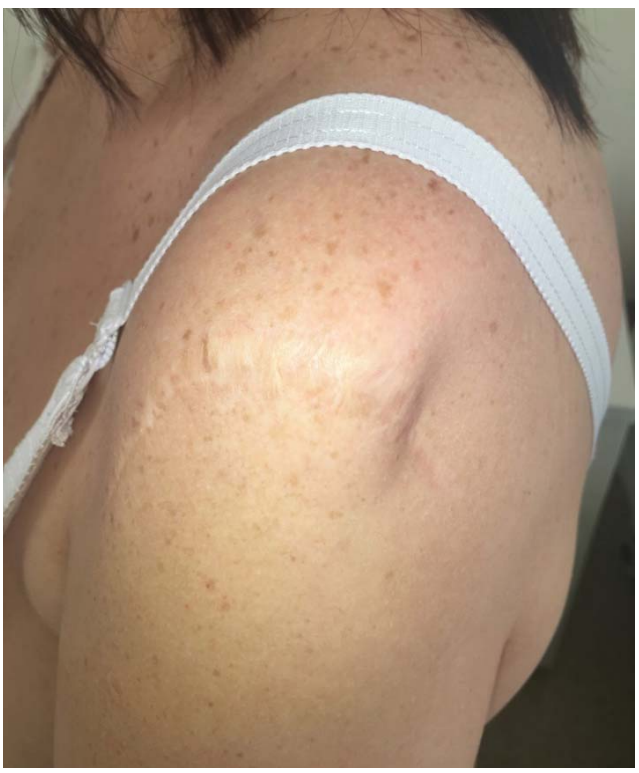

Figure 5. *Scar after prosthesis of the left shoulder joint*

From 2015 to 2017, due to the lack of Remicade, therapy with etanercept 25 mg per week was carried out. The effect was incomplete — clinically there was no need for NSAIDs, in the laboratory there was increase in activity indicators (ESR — up to 40 mm/h), exacerbation of uveitis — up to 4 times a year. With an increase in the dose of etanercept to 50 mg per week, a decrease in the activity of the process according to laboratory parameters to a low degree of activity was noted, but uveitis relapses still occurred up to 2 times a year.

From 2017 to the present time, the patient receives constant therapy with Remicade 400 mg injected once time every 8 weeks with a positive effect (BASDAI less than 4, ASDAS according to CRP — 1.3).

Discussion

This clinical case demonstrates some features of the course of uveitis in AS. First, attention is drawn to the onset of uveitis as a non-skeletal manifestation of the disease at a young age, secondary to inadequately treated arthritis, non-diagnosed spondylitis. For several years, no attempts to treat uveitis, to stop its progression were effective enough. Since the underlying disease was not verified, there was no appropriate therapy.

According to literature, uveitis is one of the most common non-skeletal manifestations of AS [13]. Despite the fact that the predominant form of uveitis in AS is iridocyclitis (anterior uveitis) and rarely involves the posterior parts of the eye with an immediate threat to vision, some patients may develop complications that lead to a significant decrease in visual functions. It is known that the frequency of complications correlates with the frequency of uveitis exacerbations: more than two attacks of uveitis per year, even without taking into account their duration and severity of inflammation, may be sufficient for the development of complications [13]. Thus, the main factor of the unfavorable prognosis of uveitis in patients with AS is a recurrent course.

An indicator of uveitis severity in AS is the need for GEBD administration: in accordance with the domestic recommendations for the treatment of AS, as well as the recommendations of the International Association of Ophthalmologists for the treatment of uveitis in SpA, recurrent uveitis is an indication for the administration of GEBD, and in most cases they have a positive effect on the frequency of uveitis exacerbations.

With the development and progression of the disease in the patient, who had not received adequate therapy for a long time, the most pronounced left-sided damage to the joints and eyes, namely, early complications in the form of severe uveitis of the left eye, which resulted in complete blindness, and severe secondary arthritis with the outcome in prosthesis of the left HJ, left knee joint, left shoulder joint were diagnosed.

Due to the late diagnosis of the underlying disease, there was also a late start of adequate therapy of both the AS and non-skeletal manifestations of the disease. In addition, the patient was characterized by low adherence to therapy, which significantly aggravated the progression of ankylosing spondylitis, and the severity of uveitis. To a certain extent, the turning point came after the beginning of therapy with GEBD: since that time, there has been a decrease in the activity of the disease, a decrease in the number of uveitis relapses.

This clinical case confirms the peculiarity of uveitis in patients with AS — in the absence of adequate therapy, including GEBD, uveitis is characterized by frequent relapses, occurring in one or both eyes, with the aggravation of the disease and the development of complications, significantly reducing vision in patients up to complete blindness.

Conclusion

In the diagnosis of AS and dynamic follow-up for patients, a thorough examination is necessary for the timely diagnosis of non-skeletal manifestations of the disease, including such common ones as uveitis. In turn, with the development and persistent recurrent course of uveitis, a thorough examination of the patient is necessary to identify rheumatic disease, including AS.

During both the onset of uveitis, and the onset of AS, there is need for diagnosis and examination by at least two medical specialists — a rheumatologist and an ophthalmologist, so that timely and correct diagnosis, as well as the high compliance of the patient promote early treatment of the

underlying disease and extra-skeletal ophthalmic manifestations, preventing the frequent recurrence of uveitis, reducing the risk of severe complications, which significantly reduce patients' quality of life.

Conflict of interests

The authors declare no conflict of interests.

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