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## Case report

# Plaque psoriasis and psoriatic arthritis associated with uveitis and cystoid macular edema treated with adalimumab: A case report and literature review



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## ABSTRACT

**Introduction:** Psoriatic patients, especially with psoriatic arthritis (PsA), are more prone to metabolic disorders and involving the eyes.

**Aim:** The aim of this study was to present adalimumab efficacy of several aspects of psoriasis and its comorbidities.

**Case study:** We present a 48-year-old male patient with severe plaque psoriasis and psoriatic arthritis who developed uveitis with cystoid macular edema in the right eye. The patient was obese although bariatric surgery 8 years earlier produced some weight loss with remission of diabetes and hypertension.

**Results and discussion:** The patient had been previously treated with systemic treatment with no improvement in psoriatic arthritis symptoms and skin lesions but rapidly responded to adalimumab. At week 8, the patient achieved the PASI 75, with no joint pain and normal macular architecture. At week 16, there was an incident of atrial fibrillation followed by a transient ischemic attack (TIA). The TIA subsided after intravenous fluids and antithrombotic treatment although acute urticaria developed after the first dose of acetylsalicylic acid. Adalimumab treatment was not stopped and the patient's condition continued to improve.

**Conclusions:** After careful consideration of the patient's underlying and comorbid conditions and previous treatment failures, adalimumab was instituted and continued since (1) its efficacy in psoriasis and psoriatic arthritis is well-documented; (2) obesity is not thought to affect its effectiveness; (3) in uveitis adalimumab acts quickly and induces

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long-term remission; (4) a significant improvement of hemostasis and fibrinolytic balance has been observed in patients on TNF- $\alpha$  inhibitors and adalimumab could be continued after the TIA.

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## 1. Introduction

Patients with psoriasis, especially when it is associated with psoriatic arthritis, need special management to prevent cardiovascular disease and other comorbidities as their increased risk for developing cardiovascular disease and other health problems is well documented.<sup>1</sup> Psoriasis affects not only the skin and nails, but also the mucous membranes and eyes. Ocular manifestations occur in approximately 10% of psoriasis patients and are more common in men than in women.<sup>2</sup>

We present a case of an obese male patient with psoriasis, psoriatic arthritis and uveitis associated with cystoid macular edema whose management required a multi-specialty approach.

## 2. Aim

The aim of this study was to present adalimumab efficacy of several aspects of psoriasis and its comorbidities.

## 3. Case study

A 48-year-old man was admitted to the Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology, Municipal Hospital in Olsztyn with a 16-year history of severe plaque psoriasis associated with psoriatic arthritis for 3 years. Until the present admission the patient had been treated for 30 months with methotrexate 20 mg weekly with folic acid supplementation and leflunomide for 6 months with some improvement of the pain in his knee and elbow joints. In the past he had several other treatments for psoriasis (PUVA, cyclosporine) but failed to achieve complete remission of psoriatic skin lesions (Fig. 1).

On admission the patient complained of pain in the wrists and small joints of both hands. The physical examination revealed decreased active and normal passive range of motion in the wrist joints, swelling and bony enlargement of the distal interphalangeal joint in the middle finger of the right hand and mild tenderness of the Achilles tendon insertion in the right foot. Radiographic examination of the joints showed numerous geodes in the metacarpophalangeal joints, but no erosions, bone proliferation or changes in the foot and sacroiliac joints. Sonography showed mild effusion in the second metacarpophalangeal joint of the right hand with features of inflammatory swelling of the synovium (grade II). There was some calcification of the right Achilles tendon

insertion possibly due to inflammation in the past, but no features of active inflammation. The clinical picture was consistent with psoriatic arthritis involving the peripheral joints. The HLA-B27 test was negative.

Additionally, for about a year the patient had observed redness of the right eye with periodic exacerbations and gradual deterioration of vision (Fig. 2). An ophthalmological examination found the best corrected visual acuity (BCVA) in



Fig. 1 – Patient's psoriatic lesions.



**Fig. 2 – Redness of the right eye.**

the right eye of 0.2; low-grade vitreous haze and macular edema. Optical coherence tomography (OCT) revealed macular retinal thickness 546  $\mu\text{m}$  (Fig. 3). Uveitis with cystoid macular edema was diagnosed. Symptomatic treatment was initiated at the Eye Clinic – periocular injections of methylprednisolone acetate 20 mg every other week (a total of four injections) and remission was achieved (BCVA = 1.0; resolution of the vitreous haze); OCT – macular retinal thickness reduced to 292  $\mu\text{m}$  (Fig. 4).

The patient had been obese for approximately 20 years. In 1999, hypertension and diabetes mellitus type 2 were diagnosed. In December 2008 his body mass index (BMI) reached 50.9 (165 kg BW) and the patient was referred for bariatric surgery (sleeve gastrectomy). Two months after the surgery, antihypertensive and antidiabetic treatment was withdrawn and after 6 months the body weight was reduced by 60 kg (BMI = 29.2). At present, laboratory investigations do not indicate any abnormalities suggestive of metabolic disorders.

Since the patient suffered from a number of disorders associated with TNF- $\alpha$  overexpression, it was decided that treatment with adalimumab would be appropriate.

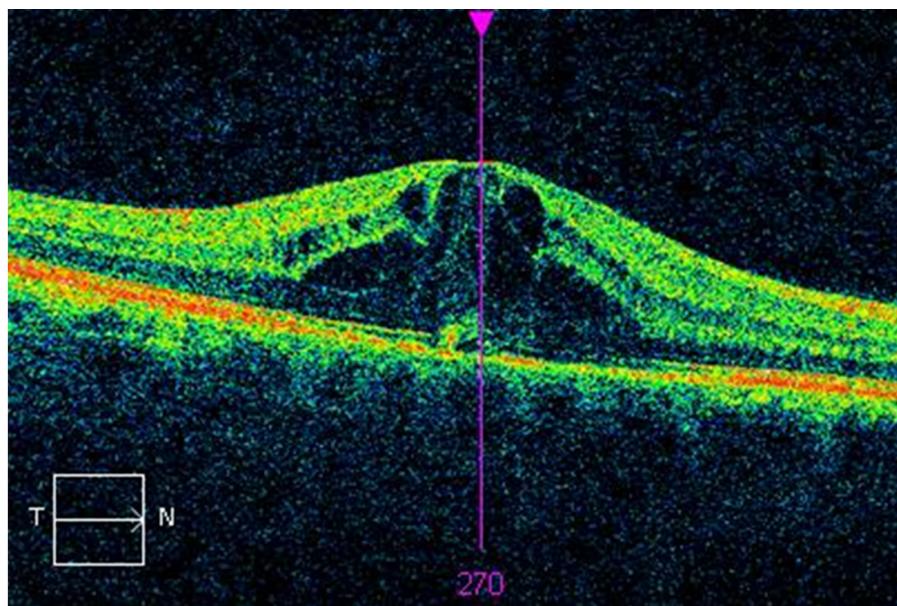
Methotrexate was discontinued. The patient was informed about beneficial effects of weight-loss diet on his disease and the effectiveness of treatment. The first adalimumab dose 80 mg was given in June 2015 followed by 40 mg every other week from 8 June 2015 until 11 March 2016. A complete remission of psoriasis was achieved. Psoriasis severity was assessed at baseline – Psoriasis Area Severity Index (PASI) – 19.7; Body Surface Area (BSA) 38%; Dermatology Quality of Life Index (DLQI) – 25 and the following measurements were performed: body weight – 108 kg; BMI = 33.33; waist circumference – 113 cm. At 8 weeks of adalimumab treatment the PASI, BSA and DLQI scores decreased by 75% and the joint pain was relieved. The body weight was reduced to 103 kg with the BMI of 32.4. On ophthalmological examination at 12 weeks of treatment the BCVA in the right eye was 1.0. OCT showed normal macular architecture and the central foveal thickness of 292  $\mu\text{m}$  (Fig. 5). To date, the patient has had no recurrence of uveitis.

In week 16 of the treatment the patient suffered an episode of atrial fibrillation complicated by transient ischemic attack (TIA) manifested as motor aphasia and hemiplegia which developed after a few hours of exposure to heat without adequate fluid intake.

The patient was admitted to a neurology ward and the symptoms subsided after intravenous fluids and antithrombotic treatment. However, a few hours after the first dose of acetylsalicylic acid the patient developed acute urticaria (itchy wheals on the upper trunk and facial edema). Treatment with intravenous dexamethasone 12 mg/day was given with complete resolution of urticaria. Adalimumab therapy was not stopped.

#### 4. Discussion

The association between psoriasis and other disorders has been well researched and the short literature review below



**Fig. 3 – First OCT examination of right eye – macular retinal thickness 546  $\mu\text{m}$  (9 April 2015).**

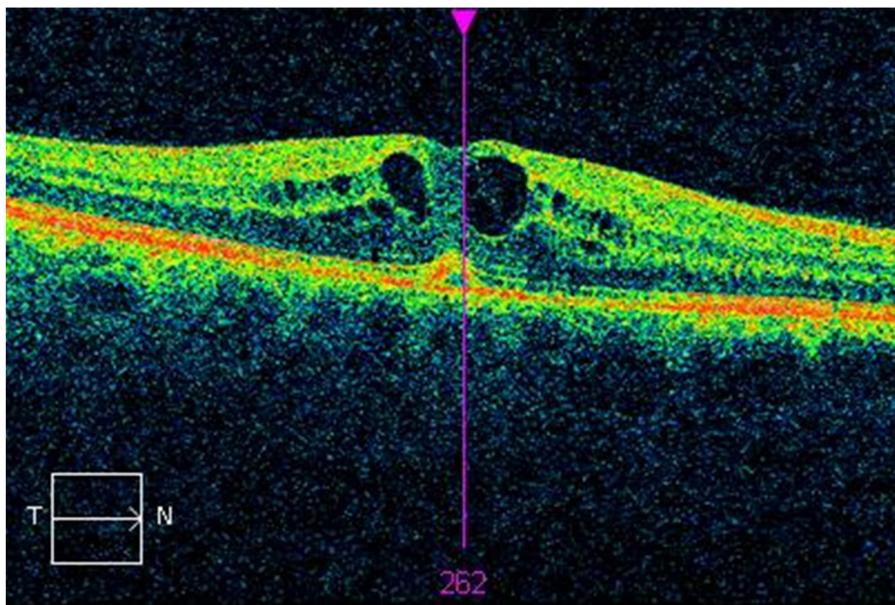


Fig. 4 – Improvement OCT result of right eye – macular retinal thickness reduced to 292  $\mu\text{m}$  (22 April 2015).

presents new studies concerned with this serious medical problem.

#### 4.1. Psoriasis and obesity

Numerous population-based studies confirm the association between obesity and psoriasis while some authors believe that obesity is an independent risk factor for psoriasis onset and a poorer long-term clinical outcome.<sup>3</sup> The BMI of 26–29 only slightly increased the risk for psoriasis onset but in obese subjects (BMI > 29) the increase was twofold.<sup>4</sup> It was calculated

that for each unit increment in BMI there was 9% higher risk for psoriasis onset and 7% higher risk for an increased PASI score.<sup>5</sup> A meta-analysis of 16 observational studies demonstrated that the odds ratio (OR) for obesity (BMI  $\geq$  30) among patients with psoriasis was 1.66 compared to subjects without psoriasis (1.46 among patients with mild psoriasis and 2.23 among patients with severe psoriasis).<sup>4</sup> This observation was confirmed by the study of Armstrong et al. who found that obesity increased the risk for psoriasis by over 50%.<sup>6</sup> On the other hand, one incidence study found that psoriasis patients have a hazard ratio of 1.18 (95% CI 1.14–1.23) for new-onset obesity.<sup>6,7</sup>

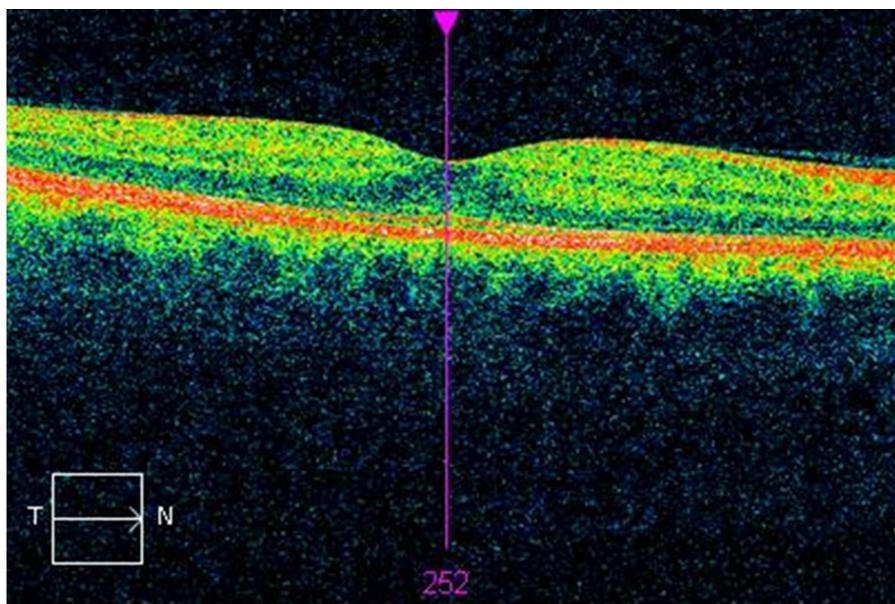


Fig. 5 – Normal result OCT of right eye (1 September 2015).

#### 4.2. Psoriatic arthritis and obesity

An increased risk for development of psoriatic arthritis with increasing BMI has been observed.<sup>8</sup> A Canadian study found a higher mean BMI in patients with psoriatic arthritis than in psoriasis patients without joint involvement and the general population<sup>9,10</sup> which was confirmed by a large prospective study from the United States.<sup>19</sup> Obesity is more frequently associated with psoriatic arthritis than rheumatoid arthritis which may result from the cytokine profile (TNF- $\alpha$ , IL-6) shared by obesity and psoriatic arthritis.<sup>11</sup>

#### 4.3. Psoriasis and bariatric surgery

A meta-analysis of the effects of bariatric surgery in obese patients with psoriasis proved the association between obesity and psoriasis as in nearly two-thirds of the patients a postoperative improvement in skin lesions was observed. The reduction of the systemic inflammation associated with obesity is likely to decrease TNF- $\alpha$  expression in adipose tissue.<sup>12</sup> Interestingly, improvement of psoriasis was observed immediately after surgery before any weight loss was likely to occur and another mechanism underlying weight loss was proposed. It is hypothesized that the glucose-lowering glucagon-like peptide 1 (GLP-1) secreted in the intestine is responsible for the effect. GLP-1 levels increase up to 20-fold after bariatric surgery. GLP-1 has an anti-inflammatory action, reduces appetite and gastrointestinal motility slowing gastric emptying which decreases food intake and leads to weight loss.<sup>13</sup>

#### 4.4. Psoriasis and weight-loss diet

It has been observed that patients with psoriasis, especially men, do not maintain good nutrition. A study from Brazil conducted in male patients with psoriasis and psoriatic arthritis, found in addition to obesity, dietary intake of fat, proteins and calories above the recommended levels.<sup>14</sup> An Italian study of Naldi et al. confirmed that weight loss achieved with diet and physical exercise reduced the severity of psoriatic skin lesions. Their study included 303 overweight or obese patients with moderate to severe psoriasis who did not achieve improvement after 4 weeks of systemic treatment. The patients were randomized to two study arms. In arm 1, patients received a 20-week programme of dietary intervention and physical exercise for weight reduction while in arm 2 they were simply informed about the ways to lose weight and its role in achieving clinical improvement of psoriasis. The PASI score reduction was by 48% in arm 1 and by 25.5% in the medication – only arm 2.<sup>15</sup>

#### 4.5. Psoriasis and psoriatic uveitis

Psoriatic uveitis is an autoimmune-mediated ocular inflammatory disease which may occur in patients with psoriasis. Usually the iris or ciliary body are affected (anterior uveitis) and less frequently the retina and choroid (posterior uveitis).<sup>2,16–18</sup> Anterior uveitis (iritis) is thought to occur more commonly in psoriatic arthritis and it is observed in 7–25% of the patients.<sup>16,17</sup> Usually it is unilateral and in most cases resolves spontaneously within 3 months of onset

although recurrences are frequent and the fellow eye may be affected.<sup>18,19</sup>

Some authors suggest that psoriatic uveitis is a distinct clinical entity.<sup>17</sup> In psoriasis patients, the predisposing factors include psoriatic arthritis, axial spondyloarthritis, pustular psoriasis, HLA-B27 positivity, late-onset psoriasis (type II) and male gender.<sup>2,18</sup>

#### 4.6. Psoriasis, cerebrovascular accident and atrial fibrillation

In a population-based study the risk for atrial fibrillation was 1.54-fold higher and the risk for TIA 2.74-fold higher in psoriasis patients compared to the general population.<sup>20</sup> In severe psoriasis associated with depression, the risk of atrial fibrillation and stroke increases 2.5-fold.<sup>21</sup> A Danish cohort study found that severe psoriasis is associated with a higher (up to 6-fold) risk of thromboembolic complications and these events occur in younger patients.<sup>22</sup> The study of Kimball et al. reported that in psoriasis patients (PASI score  $\geq 10$ ) the 10-year risk of stroke was 11.8% greater than in the general population which might be partly related to a higher prevalence and incidence of obesity among psoriasis patients.<sup>23</sup>

Atrial fibrillation is a major risk factor for the development of thromboembolic disease and is responsible for stroke in over 25% of cases.<sup>24</sup> The risk increases with age, BMI and raised level of inflammatory markers.<sup>6</sup> It is likely therefore that the incidence of atrial fibrillation is greater in psoriasis patients due to the presence of the above risk factors which have been also identified in the patient presented in this paper.

#### 4.7. Management rationale

In the presented case, when treatment with adalimumab was prescribed several aspects of the management of psoriasis and its comorbidities were taken into consideration.

1. In addition to its adverse effects on psoriasis activity, obesity with increased adipose tissue mass may alter the distribution volume of the administered medication and reduce its efficacy.<sup>25</sup> TNF- $\alpha$  inhibitor therapy itself has been observed to increase body weight by 2–3 kg after 6 months of treatment<sup>26,27</sup> which may possibly impact the effectiveness of biologicals given at fixed doses (etanercept, adalimumab). In the case of adalimumab there is no uniform opinion on the effects of obesity on treatment outcomes. Al-Mutairi et al. comparing treatment effectiveness demonstrated a decrease in the PASI score which was 15% greater in patients on low calorie diet leading to weight loss and concluded that body weight reduction in obese patients may increase the efficacy of the biologics.<sup>28</sup> Also, the study of Di Minno et al. confirmed that weight loss from baseline by at least 5% is associated with a higher rate of achieving Minimal Disease Activity (MDA) in obese patients with psoriatic arthritis starting treatment with TNF- $\alpha$  inhibitors.<sup>29</sup> On the other hand, according to Lauente-Urrez et al. obesity does not seem to have any impact on the effectiveness of adalimumab in decreasing the PASI score.<sup>30</sup>
2. TNF- $\alpha$  plays a major role in the development of uveitis. Injection of TNF- $\alpha$  into animal eyes caused uveitis. TNF- $\alpha$  is

elevated not only in the aqueous humor, but also in the serum of patients affected by uveitis while increases in its serum levels seem to be related to uveitis recurrences.<sup>31</sup> Numerous studies report adalimumab effectiveness in the treatment of uveitis, including associated cystoid macular edema. It is effective in patients who did not respond to previous conventional therapy and produces long-term remission.<sup>31–34</sup>

- Continuing adalimumab therapy in spite of a TIA seems a right choice. The studies of Di Minno et al. (CaRRDs Study Group) conducted in patients with psoriatic arthritis treated with TNF- $\alpha$  inhibitors demonstrated marked improvement in hemostatic and fibrinolytic balance compared to conventional DMARD as they affected plasminogen activator inhibitor-1 (PAI-1), tissue plasminogen activator (t-PA), D-dimer, coagulation factor VIII and von Willebrand factor.<sup>35</sup> TNF- $\alpha$  inhibitors reduce thrombotic tendency and platelet overactivity.<sup>29,35,36</sup>

## 5. Conclusions

Nowadays psoriasis is considered to be a metabolic disease frequently associated with other metabolic disorders such as obesity and diabetes, cardiovascular disease, inflammatory bowel disease, inflammatory ocular disease or depression. That is why the term psoriatic disease has been proposed which would better describe the complex nature of this disorder.<sup>33</sup>

In this context, not only does a dermatologist treat skin lesions but also should diagnose and monitor any comorbidities. Additionally, prompt and effective treatment for psoriasis may prevent the development of any associated disorders, above all the metabolic syndrome.<sup>1</sup>

## Conflict of interest

The authors have no conflict of interest.

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