Scabies in a Patient with Rheumatoid Arthritis Treated with Adalimumab – A Case Report

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ABSTRACT Rheumatoid arthritis is a chronic systemic inflammatory disease characterized by synovitis, erosions, and destruction of affected joints. If untreated, it leads to severe disability and premature mortality. Tumor necrosis factor alpha (TNF-α) inhibitors are biological drugs used in treatment of rheumatoid arthritis. Possible side effects include skin allergic reactions, which, if generalized, are the reason for discontinuation of the drug. We report the case of a 46-year-old female patient with rheumatoid arthritis who presented with pruritus and erythematous papular exanthema after administration of the second dose of adalimumab. At first, we suspected a drug hypersensitivity reaction. As the signs and symptoms persisted for 2 months after discontinuation of adalimumab and despite continuous administration of antihistamines and glucocorticoids, further work-up was performed, and scabies was diagnosed. The patient was treated with topical 10% crotamiton. The symptoms were persistent and additional applications of the preparation were needed. After clinical remission of scabies, treatment of active rheumatoid arthritis with adalimumab was restarted without any complications.

KEY WORDS: rheumatoid arthritis; tumor necrosis factor alpha; adalimumab; hypersensitivity; scabies; crotamiton

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized by synovitis, erosions, and destruction of affected joints (1). If untreated, it leads to severe disability and premature mortality (2). The prevalence of RA in developed countries is estimated at between 0.5% and 1% (3). Over the last decade, the optimal use of conventional disease-modifying antirheumatic drugs (DMARDs) and the availability of new biologic drugs significantly contributed to the success of treatment and prognosis (1).

Proinflammatory cytokines, particularly tumor necrosis factor alpha (TNF-α), play a critical role in pathogenesis of RA (4). TNF-α inhibitors are biological drugs used in treatment of RA (5). Possible side effects

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include skin allergic reactions, which, if generalized, are the reason for discontinuation of the drug (6).

We report a 46-year-old female patient with RA who presented with pruritus and exanthema after administration of the second dose of adalimumab. At first we suspected a drug hypersensitivity reaction, but further work-up revealed scabies.

CASE REPORT

The patient with a 20-year history of RA was started on treatment with adalimumab due to high disease activity (DAS28CRP 7.05), despite treatment with 2 DMARDs (methotrexate and sulphasalazine) at maximum doses, and methylprednisolone at a dose of 12-16 mg daily. Adalimumab was administered subcutaneously at a 2-weekly dose of 40 mg. Five days after administration of the second dose, generalized itching and rash appeared.

The patient also had 10-year history of arterial hypertension, 3-year history of diabetes mellitus and osteopenia, and bilateral nephrolithiasis with loss of the excretory function of the left kidney. In addition to RA medications, she was taking daily urapidil at a dose of 120 mg, felodipine 10 mg, moxonidine 0.6 mg, ramipril 10 mg, spironolactone 25 mg, metformin 1000 mg and cholecalciferol 800 IU, and weekly folic acid at a dose of 10 mg.

The patient was examined by a rheumatologist on the ninth day after the appearance of symptoms. She reported generalized itching, which was more intensive at night, and a reddish rash. Skin examination revealed erythematous papules and numerous linear excoriations in the axillary regions, under the breasts, on the abdomen, lower back, and both legs (Figure 1, 2). Lymph nodes were not palpable. Adalimumab was discontinued because of a suspected hypersensitivity reaction. Over the next two months, the patient was successively treated with different oral antihistamines at maximum doses, the dose of methylprednisolone was increased up to 32 mg/day, and parenteral antihistamines and methylprednisolone were also intermittently administered. She was also examined by a dermatologist several times. Due to the persistence of symptoms, the patient was hospitalized at our Department for further work-up.

At admission, laboratory tests revealed mild eosinophilia – eosinophil count 0.60 $x10^9$/L (normal values up to 0.43 $x10^9$/L), normal leukocyte count, and slightly elevated serum concentration of C-reactive protein (CRP) – 10.8 mg/L (normal values up to 5 mg/L). Serum immunoglobulin E (IgE) levels were normal. Other routine laboratory tests were in the reference ranges. A dermatological examination was performed, including skin scraping of visible lesions and microscopy of potassium hydroxide preparation of the specimen. At first, microscopical examination revealed no *Sarcoptes* mites, eggs, or eggshell fragments. However, due to continued clinical suspicion, the skin scraping was repeated. That time, *Sarcoptes* mites were identified.

The patient was treated with topical scabicide – 10% crotamiton cream (two applications within a 24-hour interval). Household members were treated concurrently with the same preparation. Pruritus and exanthema initially withdrew, but reappeared 4 weeks later. At dermatological follow-up, skin scraping was repeated, but revealed no *Sarcoptes* mites, eggs, or eggshell fragments. Further specific treatment was not recommended at the time. At subsequent rheumatological follow-ups, the patient was continuously reporting pruritus, and gradual progression of the exanthema was observed. Six months after the initial treatment of scabies, skin scraping was repeated and *Sarcoptes* mites were identified again. The patient was re-treated with 10% crotamiton (two applications within 24-hour interval). Ten days later, because of the persistence of signs and symptoms, the same treatment regimen was repeated. At further rheumatological follow-ups, the patient reported no pruritus, and complete regression of exanthema was observed.

Adalimumab treatment was continued 4 months after the clinical remission of scabies. Over the next 5 months of follow-up, no signs or symptoms of scabies relapsed, and no other complications of the treatment were seen. Significant control of RA activity was achieved (DAS28CRP 2.9).

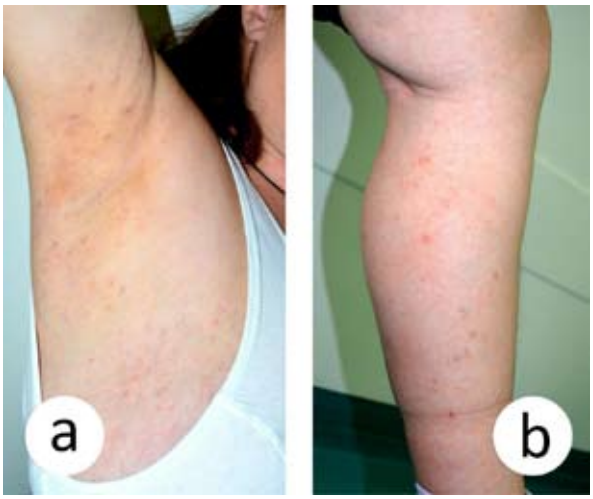

Figure 1. Scabies - erythematous papular exanthema (a) in the right armpit and (b) on the left lower leg

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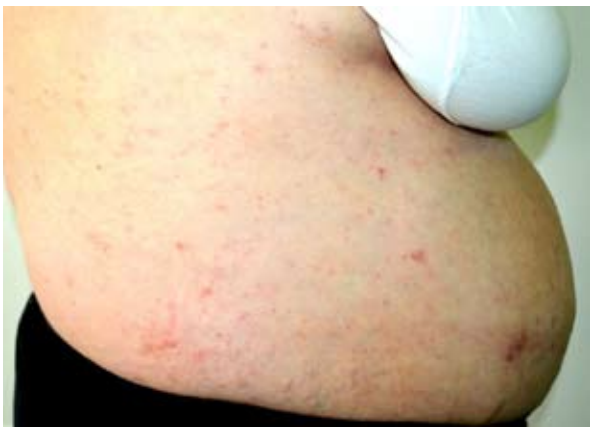

Figure 2. Scabies – erythematous papular exanthema and excoriations in the abdominal region.

DISCUSSION

Scabies is an ectoparasitic infestation caused by the mite *Sarcoptes scabiei var hominis*, an arthropod of the order *Acarina* (7). Signs and symptoms are caused by a delayed hypersensitivity reaction to the mite and its excrements, and typically include generalized pruritus predominantly at night, erythematous papules, and pathognomonic burrows. The latter is, however, often not visible at examination. Crusted (Norwegian) scabies, a special clinical form of the disease, usually develops in immunocompromised individuals and presents with hyperkeratotic plaques and mild or absent pruritus (8,9).

To our knowledge, six patients with scabies manifesting during the treatment with biological drugs have been reported in the literature. Crusted scabies occurred in three patients being treated for juvenile rheumatoid arthritis with infliximab (10), severe psoriasis with etanercept (11), and RA with tocilizumab (12). Scabies with atypical skin changes and generalized rash was described in two patients with ankylosing spondylitis treated with adalimumab and etanercept, respectively (13). In a patient with RA treated with adalimumab, scabies presented typically with pathognomonic burrows. Due to the persistency of symptoms, the treatment was difficult and prolonged (14).

In our patient, scabies presented after the second application of adalimumab, with generalized pruritus, erythematous papular exanthema, and secondary excoriations (Figure 1, 2). We initially suspected a possible hypersensitivity reaction to the recently introduced drug. Due to the persistence of signs and symptoms despite discontinuation of adalimumab and continuous treatment with antihistamines and glucocorticoids over the following two months, the patient was admitted to the hospital for additional work-up. Although the first microscopical examination of a skin scraping specimen was negative, on our request the test was repeated, and diagnosis of scabies was eventually established.

Treatment with crotamiton failed initially, and afterwards additional applications of the topical agent were required. A clinical study showed a significant elevation of serum TNF-α level in children with scabies compared to the control group (15), suggesting possible role of the cytokine in the immunological response of the host to the *Sarcoptes* mite. Initial failure and the need for prolonged treatment of scabies in our patient might be attributed to immunomodulatory properties of the TNF-α inhibitor, or, more likely, to the lack of efficacy of topical crotamiton (16).

Several months after the achievement of complete clinical remission of scabies, treatment of active RA with adalimumab was resumed without any complications over the next 5 months of follow-up. The impact of the biological drugs on RA control was significant.

CONCLUSION

The aim of our case report was to emphasize the importance of considering scabies in differential diagnosis of pruritic skin lesions in patients taking TNF-α inhibitors. Early diagnosis and treatment of the infestation is essential in preventing further transmission of the disease.

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