CASE REPORT

Anti-TNF therapy-induced lupus erythematosus-like syndrome in a patient treated with adalimumab for cutaneous psoriasis

Julie E. Stein, Jeffrey Patterson-Fortin, Benjamin E. Bodnar

Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Correspondence to
Dr Julie E. Stein,
jstein17@jhmi.edu

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SUMMARY

A 44-year-old woman with cutaneous psoriasis and no history of joint involvement recently treated with adalimumab was admitted to the inpatient Internal Medicine service for uncontrolled, severe joint pain so debilitating that it limited her activities of daily living and prevented her from working as a medical technologist. She had stopped taking adalimumab 3 weeks prior to presentation after receiving approximately 2.5 months of therapy for cutaneous psoriasis unresponsive to trials of topical steroids and methotrexate. Antinuclear antibody and anti-double-stranded DNA antibodies were positive at high titres. She received a course of oral corticosteroids with improvement in her symptoms.

BACKGROUND

Tumour necrosis factor antagonists (anti-TNF) have dramatically changed the treatment landscape for various autoimmune conditions since their introduction to market. Adalimumab, a monoclonal antibody against TNF, was first approved by the US Food and Drug Administration in 2002 after demonstrating improved patient-reported outcomes in patients with moderate to severe rheumatoid arthritis (RA) who had failed methotrexate, a traditional disease-modifying anti-rheumatic drug.¹ In 2008, adalimumab was approved for the treatment of moderate to severe plaque psoriasis after demonstration of improved patient-reported outcomes in patients with moderate to severe psoriasis.² However, anti-TNF agents are not without adverse reactions. Several case reports and a few retrospective reviews have been published documenting a lupus erythematosus (LE)-like syndrome after treatment with TNF antagonists.³ There are no unifying diagnostic criteria for this syndrome, but it has sometimes been defined as a clinical syndrome temporally associated with anti-TNF therapy, at least one serologic manifestation of systemic lupus erythematosus (SLE) (eg, anti-double-stranded DNA positivity) and at least one non-serologic manifestation of SLE (eg, arthritis).⁴ Anti-TNF therapy-induced LE-like syndrome is rare with an estimated prevalence of 0.5% to 1% of treated patients.³ Most of the cases reported in the literature involve patients with ankylosing spondylitis, Crohn's disease, juvenile idiopathic arthritis, psoriatic arthritis and RA.⁵ The clinical presentation of LE-like syndrome is varied, but previously

described symptoms of LE-like syndrome range from cutaneous-only manifestations to systemic involvement and include cutaneous lesions, such as malar rash, discoid rash or photosensitivity, arthritis and haematological abnormalities, such as leucopenia, myositis and serositis.^{4,5} No case studies to our knowledge have been reported of patients developing LE-like syndrome after being treated for cutaneous psoriasis with anti-TNF therapy.

CASE PRESENTATION

A 44-year-old Caucasian woman with a history of scalp-limited psoriasis presented to the emergency department with severe, uncontrolled joint pain. She reported that she was diagnosed with biopsy-proven psoriasis approximately 10 years previously. Her symptoms were limited to her scalp only (figure 1) and she denied any history of joint pain. She reported having had negative testing for antinuclear antibody (ANA) and anti-double-stranded DNA antibodies (anti-dsDNA Ab) 10 years prior as part of her initial work-up. She reported feeling bothered by both the symptoms and appearance of her psoriasis. She had failed treatment in the past with topical corticosteroids and in January of 2017 she tried 1 month of methotrexate without relief. She was then initiated on adalimumab therapy in February of 2017 which she continued for 2.5 months (40 mg subcutaneously every 14 days). She noted some improvement in her scalp lesions, but she stopped therapy in May 2017 when she developed severe joint pain in her ankles and knees, which progressed to include her shoulders (right worse than left) and her hands to the point where she could not make a fist. She described the pain as 'sharp' and 'throbbing'. The pain was so debilitating that it prevented her from accomplishing her activities of daily living, notably it would take her more than an hour to dress herself in the morning. She had no other relevant medical history. Her family history was significant for a sister with psoriasis and mother with lupus, but the patient did not have any details regarding the latter's diagnosis. She had no history of smoking. On physical examination, she presented with diffuse erythematous plaques of the scalp with overlying scale consistent with her known psoriasis. She had tenderness to palpation of her hands, including the metacarpophalangeal joints (MCPs), distal interphalangeal joints and proximal interphalangeal joints. There was slight

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Figure 1 Psoriatic involvement of the scalp.

swelling of the bilateral wrists as well as the MCPs of the second and third left digits. She also had mild bilateral knee effusions without overlying erythema or tenderness. Motor strength was impaired secondary to pain. No lymphadenopathy. There were no other significant examination findings.

INVESTIGATIONS

Laboratory studies revealed white blood cell count 7.03 K/mm^3 (reference range $4.50\text{--}11.00 \text{ K/mm}^3$), haemoglobin 12.3 g/dL (reference range $12.0\text{--}15.0 \text{ g/dL}$), platelet count 272 K/mm^3 (reference range $150\text{--}350 \text{ K/mm}^3$) and serum creatinine 0.6 mg/dL (reference range $0.5\text{--}1.2 \text{ mg/dL}$). Liver testing including total bilirubin, alkaline phosphatase and aminotransferases were normal. Urinalysis was negative for protein and without inflammatory changes. Anti-dsDNA Ab testing (IgG) was positive (1:320) and ANA testing was positive (1:320). Erythrocyte sedimentation rate was 30 mm/h (reference range $4\text{--}25 \text{ mm/h}$) and C reactive protein was 0.4 mg/dL (reference range $<0.5 \text{ mg/dL}$). Rheumatoid factor, cyclic citrullinated peptide antibody, HLA-B27 antigen and anti-RNP (ribonucleoprotein)/Smith antibody testing were negative. Complement levels (C3 and C4) were within normal limits. Serologies for anti-Ro Sjögren's-syndrome-related antigen A (SSA), anti-La Sjögren's-syndrome-related antigen B (SSB) and anti-histone were not tested.

A plain radiograph of the right shoulder was obtained, which showed minimal glenohumeral osteophytosis, but without any arthritic joint changes in the glenohumeral or acromioclavicular joint spaces.

DIFFERENTIAL DIAGNOSIS

Psoriatic arthritis.

Lupus erythematosus.

Anti-TNF therapy-induced LE-like syndrome.

The treatment of these conditions would be vastly different. Psoriatic arthritis would be considered a progression of psoriatic disease and would require trials of other biologics as treatment.

In contrast, anti-TNF therapy-induced LE-like syndrome would involve cessation of the offending drug agent and treatment with corticosteroids.

TREATMENT

She was initiated on oral prednisone 40 mg for 2 days with significant improvement in symptoms prior to discharge. She was discharged on oral prednisone 10 mg daily for 30 days with a plan for further taper to be monitored in the outpatient setting. She was also treated symptomatically with gabapentin, meloxicam, duloxetine, acetaminophen and oxycodone for breakthrough pain.

OUTCOME AND FOLLOW-UP

The patient's pain improved significantly after initiation of prednisone, and she was discharged with a plan for outpatient follow-up with her primary care doctor, rheumatology and dermatology services for further management. In addition to prednisone, she was discharged on acetaminophen and oxycodone for breakthrough pain.

The patient was contacted by phone following her steroid taper and endorsed complete resolution of her symptoms but had yet to restart any therapy for her cutaneous psoriasis.

The patient was unfortunately lost to follow-up. She was referred for outpatient follow-up by Rheumatology and Dermatology; however, she has not attended any of her appointments.

DISCUSSION

We describe the case of a patient developing severe, debilitating polyarthritis after recent initiation of anti-TNF therapy with adalimumab for treatment of cutaneous psoriasis.

Aetiologies of polyarthritis include systemic infections (viral or bacterial), haemoglobinopathies, hypermobility syndromes, gout, pseudogout or systemic inflammatory disorders. The patient denied any recent infectious symptoms and the clinical presentation made bacterial joint infection unlikely. Acute rheumatic fever can cause polyarthritis as well; however, the patient did not meet modified Jones criteria for diagnosis.⁶ Other possible viral aetiologies include parvovirus B19, hepatitis B, hepatitis C, enterovirus, rubella, mumps and HIV. Our patient denied any exposure history or compatible symptoms, and her complete blood count (CBC) and comprehensive metabolic panel, including liver function tests, as described above were within normal limits, ruling against any viral infection. Our patient denied any history of sickle cell disease or trait or thalassemias, and this was supported by an unremarkable CBC. There was no personal or family history of hypermobility syndromes such as Ehlers-Danlos, Marfan or benign hypermobility. The clinical presentation as well as available radiographic findings were not concerning for either gout or pseudogout.

Systemic inflammatory causes of polyarthritis can be divided into two groups: acute, secondary to a flare, versus chronic. Our patient had a history of cutaneous psoriasis notable for no history of joint involvement. Otherwise, she did not have any history of other systemic inflammatory disorders. A review of the literature was notable for several case reports and a few retrospective reviews documenting a LE-like syndrome after treatment with TNF antagonists.³ This LE-like syndrome is generally diagnosed clinically based on a patient meeting the following criteria: (1) temporally associated with anti-TNF therapy, (2) at least one serologic manifestation of SLE (eg, anti-dsDNA positivity) and (3) at least one non-serologic manifestation of SLE (eg, arthritis).⁴

Previous cases of LE-like syndrome associated with anti-TNF agent use in the treatment of psoriasis have been described in patients with pre-existing psoriatic arthritis. In a retrospective review of 233 cases, Ramos-Casals *et al* reported that autoimmune diseases secondary to anti-TNF therapy occurred in 187 patients with RA, 17 patients with Crohn's disease, 7 with ankylosing spondylitis, 6 with psoriatic arthritis and 3 with juvenile RA.⁷ In a small case series from Mayo Clinic, 14/121 patients treated with TNF antagonists over an 8-year period developed a LE-like syndrome. Of these 14, 4/14 carried a diagnosis of RA and the remaining 7 carried a diagnosis of Crohn's disease.¹

In summary, this case is unique in that it describes a case of LE-like syndrome with primary arthritic symptoms in a patient treated with TNF blockade for cutaneous psoriasis. Our patient met criteria for diagnosis based on the following: (1) recent treatment with adalimumab (anti-TNF therapeutic agent); (2) anti-DNA Ab, double-stranded positivity (1:320) and ANA positivity (1:320); and (3) polyarthritis (that was not part of the clinical syndrome for which she was receiving anti-TNF therapy). This case emphasises the importance of widespread awareness by providers and patients regarding the risks for and manifestations of LE-like syndromes following anti-TNF treatment. It is

possible that joint pain in a patient with psoriasis treated with anti-TNF agents may be seen as a manifestation of possible psoriatic arthritis, but it is important for clinicians to evaluate such patients for anti-TNF therapy-induced LE-like disease. Because of the frequent use of anti-TNF agents in rheumatological diseases that can have considerable symptomatic overlap, a high index of suspicion is needed in the appropriate clinical context.

Contributors JES examined the patient, analysed the patient data and was the primary author of the case report. JP-F examined the patient, analysed the patient data and contributed to the writing of the case report. BB examined the patient and analysed the patient data. All authors approved the final version of the case report manuscript.

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Learning points

- ▶ Tumour necrosis factor (TNF) antagonist-induced lupus erythematosus (LE)-like syndrome is a rare reaction to anti-TNF agents, but given the wide use of these agents in treating autoimmune disease, it is important for providers to be aware of the various presentations of this syndrome.
- ▶ This syndrome can be seen in a variety of conditions, including cutaneous psoriasis.
- ▶ This syndrome can be seen in patients who have no cutaneous findings of lupus.
- ▶ Typical treatment of anti-TNF-induced LE-like disease is withdrawal of the offending agent and sometimes corticosteroid therapy.

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