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Case Report

Koebner's phenomena observed in patient receiving adalimumab in psoriasis

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ABSTRACT

Koebner's phenomena, first described in 1877 as the appearance of psoriatic lesions in the uninvolved skin of psoriatic patients as a consequence of trauma. Koebner phenomena has been associated with the use of biological response modifiers. The development of the anti-TNF therapies is a milestone in the therapy of rheumatic diseases. As in all new treatment opportunities it is of concern whether all potential undesired side effects have been evaluated. We report a case involving a 31-year-old young male patient diagnosed with psoriasis and psoriatic arthritis (PsA) since a year, who received Adalimumab as part of his treatment and developed Koebner's phenomena.

Keywords: Koebner's phenomena, Psoriasis, PsA, Adalimumab

INTRODUCTION

Heinrich Koebner (1838-1904) described that appearance of new psoriatic lesions in the non-involved (healthy) skin region following an injury/trauma (mechanical, thermal, allergic irritant, treatment procedure) to the healthy skin areas of psoriatic patients.[1] Lesions seen in Koebner phenomenon adopt the same clinical and histological features as the patient's original skin disease.

PsA is a chronic inflammatory disease characterized by a symmetric polyarthritis. Since persistently active PsA often results in articular cartilage and bone destruction and functional disability, it is vital to diagnose and treat this disease early and aggressively before damage ensues.[4] Major role play for Treatment of PsA regimen constitutes NSAIDs, DMARDs, biological response modifiers.

Disease-modifying antirheumatic drugs (DMARDs) are so named because of their ability to slow or prevent structural progression of PsA. Methotrexate is the DMARD of choice for the treatment of PsA and is the anchor drug for most combination therapies, although it also exhibits several side-effects.

Newer compounds like, biological response modifiers have revolutionized the treatment of PsA over the past decade.[4] They are protein therapeutics designed mostly to target cytokines and cell-surface molecules. The tumour necrosis factor alpha (TNF-α) inhibitors were the first biologicals approved for the treatment of PsA. The TNF-α inhibitors **e**tanercept and adalimumab have shown good clinical result in the treatment of PsA and other autoimmune disorders. Adalimumab is fully humanised monoclonal antibody of the IgG1 isotype that binds with high affinity and specificity to human TNF.[6] These agents are associated commonly with immune mediated side effects like headache, nausea, infections, congestive heart failure lupus like syndrome, induction of auto-antibodies injection site reaction, agranulocytosis, rash, respiratory infection, lymphomas and other malignancies among them various cutaneous reactions have also been encountered.[7]

Presently, there are 5 existing TNF-α inhibitors approved by the food and drug administration (FDA): Etanercept, adalimumab, golimumab, infliximab and certolizumab

pegol.[2] Use of these biological response modifiers drugs is increased. They may be expensive but they have improved quality of life of patients. Since these drugs are relatively new their entire spectrum of side effects is not known.

Here we present a case of suspected Koebner's phenomena in a patient of PsA who received adalimumab.

CASE REPORT

A 31-year-old male patient presented to our hospital with oval shaped white silver coloured scaly patch, which was itchy, red to purplish in colour, pinpoint bleeding under the skin which occurred on lateral side of the right arm at the injection site (Figure 1). There was no involvement of any other area of the body.

On history taking, patient was a known case PsA and psoriasis diagnosed a year ago.

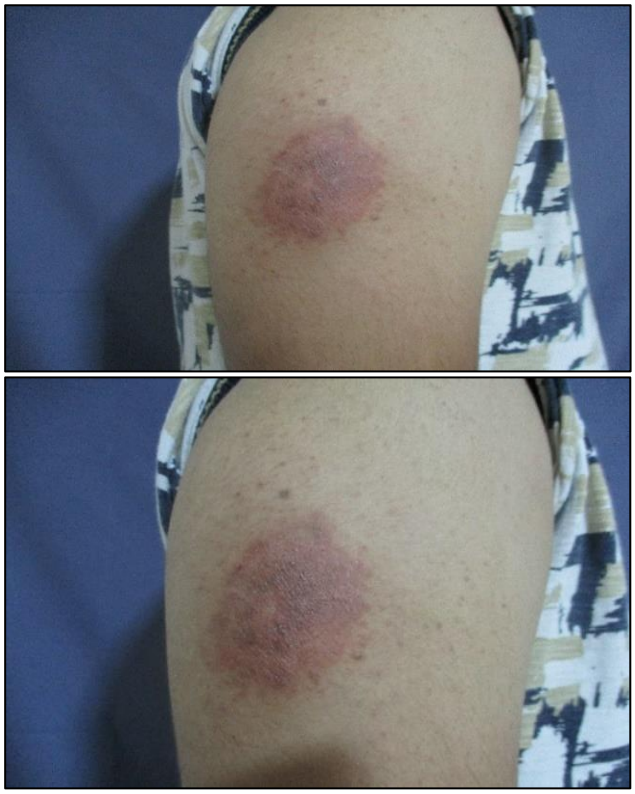

Figure 1: Reaction appearing after adalimumab injection.

He complained of progressive joint pain and psoriatic lesion for which he received Methotrexate with not much relief. Other concomitant medications included folic acid, methotrexate, naproxen. Patient was taking Methotrexate since last 9 months for psoriasis.

Patient clinical features of PsA included inflammatory backache and swelling and pain of the distal interphalangeal (DIP), wrist joint, proximal interphalangeal (PIP) joint ankle joint, metatarsophalangeal (MTP) joint, elbow joint and knee joint.

Patient was diagnosed with psoriasis one and half year ago. He started developing clinical feature like itching, silvery white scales, bulkeley membrane, pin-point bleeding over the extensor area of elbow, finger nails, scalp area, flexural area below the left chest area, he was prescribed itraconazole 200 mg, methotrexate 15 mg, hydroxyzine 10 mg orally and topical beclomethasone 0.025%w/v, clobetasol 1%w/v.

His investigations revealed: Hb 14.3 g/dl (13.7-17.5), WBC: 9330 cells/uL (4230-9070), platelets: 353000 cells/cumm (1,63,000-3,37,000), creatinine: 1.12 mg/dL (0.6-1.2), CRP: 83.18mg/L (0-6), ESR-1hr.: 28 (Below 50 years: Male: Up to 15 mm/hr, F: Up to 20 mm/hr, above 50 years: Male: Up to 20 mm/hr, F: Up to 30 mm/hr), anti-CCP IgG: 5.0/ml (0-25).

Patient was injected with 10 IU intradermal injection of tuberculin for Mantoux test and that was clinically negative soon after diagnosis.

The decision to begin adalimumab was considered in this patient as his symptoms were not relieved by steroids and methotrexate. On administration of first dose of adalimumab 40mg SC he developed suspected Koebner's phenomena at the injection site. The reaction did not seem to increase on subsequent 3 injection of adalimumab. The patient improved clinically with his laboratory reports showing trend of improvement (Table 1).

This adverse drug reaction (ADR) was notified to the nearest pharmacovigilance center and was uploaded on VigiFlow with unique id- IN-IPC-300639358. The causality assessment was evaluated as a "possible".

His investigations on the day of admission were as follows: Hb 15 g/dl (13-16), WBC: 5320 cells/uL (4000-6000), platelets: 269000 cells/cumm (1,63,000-3,37,000), creatinine: 0.8 mg/dL (0.4-1.5), CRP: 3.86mg/L (0-5), ESR-1hr.: 02 (Below 50 years: Male: Up to 15 mm/hr, F: Up to 20 mm/hr, above 50 years: Male: Up to 20 mm/hr, F: Up to 30 mm/hr), anti-CCP IgG: 5.0/ml (0-25). The symptoms of PsA relatively improving clinically but the suspected Koebner's phenomena remain the same.

Table 1: Trend of ESR and CRP value in blood during follow up.

Administration of adalimumab	ESR 1 hr. (mm/hr)	CRP (mg/L)
Before	28	83.18
After	02	3.86

DISCUSSION

The biological response modifiers are known to cause injection site reactions. The above case report describes a

patient who developed Koebner's phenomena to adalimumab.

Koebner phenomenon refers to the emergence of new psoriatic lesions in the healthy skin regions following an injury/trauma.[3] This phenomenon is also termed the isomorphic (from Greek, "equal shape") response, given the fact that the new lesions that appear are clinically and histologically identical to the patient's underlying cutaneous disease. Although pathophysiology is still not well understood, one proposed theory is that the changes in the local vasculature in addition to inflammatory infiltrate led to tissue ''memory'' of an inflammatory event at the site of past injury.[8]

Boyd and Nelder classified clinical entities with reported Koebernization into four categories: True Koebner phenomenon, pseudo-Koebner phenomenon, occasional traumatic localization of lesions, and poor or questionable trauma-induced processes (Table 2).[3]

Patient was a known case of psoriasis and PsA who received adalimumab and developed Koebner's phenomena at injection site on previously healthy skin following first dose. Appearance of skin lesion was same clinical histopathological features of his existing disease. This appears true Koebner's phenomena.

Table 2: Skin conditions linked to Koebner phenomenon as per Boyd and Nelder (1990) classification.

Classifications	Examples
True Koebner phenomenon	Psoriasis, Lichen planus, vitiligo
Pseudo Koebner phenomenon	Viral warts, molluscum contagiosum pyoderma gangrenosum
Occasional traumatic localization of lesions	Darier's disease, erythema multiforme Bechet's disease, Kaposi's sarcoma lichen sclerosis
Questionable trauma-induced processes	Pemphigus vulgaris, bullous pemphigoid eczema, lichen nitidus, dermatitis herpetiformis

There are wide variety of triggers/agents that may induce Koebernization such as irradiations, Mantoux test, surgical incision, needle puncture, prosthesis, secondary syphilis, cupping therapy, ECG, itching, and viral infections.[7] Mantoux test was observed to be positive in this patient also. There is a seasonal predominance towards winter, possibly because of the lack of the sun's protective factor for PsA and psoriasis.[3] This patient also had exaggeration of symptoms of psoriasis and PsA in winter season not responding to Methotrexate.

Adalimumab belongs to the class of tumour necrosis factor alpha (TNF-α) inhibitor and it is most frequently associated with injection site reaction. Adalimumab is a recombinant IgG1 monoclonal antibody (mAb) that binds and neutralizes TNF-α and approved for PsA, ankylosing spondylitis, Crohn's disease, juvenile idiopathic arthritis, plaque psoriasis, rheumatoid arthritis and ulcerative colitis.[6]

The patient received three doses of adalimumab subsequently but did not develop any injection site reaction or new Koebernization or worsening of existing one.

Management of Koebner phenomenon relies on prevention, although this may not always be possible. The best way to keep it at bay is to take some precautions you usually do with psoriasis. There are many options, including:

Prescription medicines

Light therapy: Your doctor may recommend a device that gives you exposure to UV light on a regular basis to slow down the growth of your psoriasis.

CONCLUSION

Anti-TNF such as Adalimumab has transformed the care of diseases such as PsA. The most common side effects (injection site reaction and upper respiratory infections) do not necessitate the termination of therapy and if the minor side effects occur a specialist should assess the patient. More serious side effects, in particular, infection with TB, deep fungal infections and other atypical pathogens must be kept in mind when treating patients. Koebner phenomenon is critical in inducing new (secondary) psoriatic lesions in the healthy body regions following an injury/trauma.

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