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Rheumatology: Current Research

Short Commentary

Remember Your Ps: Some Considerations for Initial Testing and Ongoing Monitoring for Patients on DMARDs

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ABSTRACT

The care of patients with rheumatic diseases including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis has been revolutionized with the introduction of biologic medications including tumor necrosis factor-α inhibitors (TNFi); interleukin-6 (IL-6) antagonists; interleukin-17 (IL-17) antagonists; B cell antagonists; T cell antagonists; and Janus kinase inhibitors (JAKI).

Keywords: Rheumatic diseases; DMARDs; Immunization; Psoriatic arthritis

STUDY ANALYSIS

The initial mainstay of treatment is with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) including methotrexate. Over the years, as newer treatment options have been developed, the treatment paradigm is gradually shifting to using biologic disease modifying anti-rheumatic drugs (bDMARDs) or targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) earlier in the course of the disease.

Treating physicians are often challenged with balancing the potential adverse events with the efficacy of these agents. The adverse events of special interest include infections, serious infections, tuberculosis, herpes zoster, or fungal infections [1].

Here we propose a mnemonic of a series of Ps to aid in the recall of what the initial workup and ongoing monitoring could be for patients with a rheumatic disease:

Purified protein derivative/interferon gamma release assay (IGRA) /T spot assay

It has been known for some time that many of the DMARDs may lead to a re-activation of a tuberculosis infection. The package insert for most DMARDs recommends screening at baseline and then periodically [2]. We recommend annual screening just as most hospitals require for its employees. The preferred method is an IGRA. If this is in-determinant, our infectious disease department recommends repeating it in a month and considers obtaining a T spot assay.

Posterior anterior and lateral chest x-ray

A standard posterior-anterior chest x-ray should be done before starting all DMARDs. This will not only detect any active lung diseases but will also demonstrate previous granulomatous disease; hilaradenopathy; and other chronic stable disorders. Consider repeating a chest x-ray if a patient develops respiratory complaints while on a DMARD [3].

Panel for hepatitis B

Most of the bDMARDs carrier a risk for an exacerbation or re-activation of hepatitis B. It is recommended that all adult patients over the age of 19 be immunized if they do not demonstrate signs of active immunity. This is routinely performed at baseline only.

Pneumococcal vaccine

Until recently, the recommendation by the Advisory Committee on Immunization Practices (ACIP) was a two-step immunization first with the 13-valent pneumococcal conjugate vaccine (PCV13) followed by the 23-valent polysaccharide vaccine (PPSV23) for all adults aged ≥65 years. The current recommendation is a single immunization with the PPSV23 for all adults aged ≥65 years. It is also recommended that all adults

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19-64 receive 1 dose of PCV13 and 1 or 2 doses of PPSV23 with considerations given for those patients that may have increased risk factors [4]. This would include actively treated rheumatology patients.This is routinely performed at baseline only.

Pox (varicella) titer

According to the Center for Disease Control, there are several ways to assess whether a patient is immune to varicella infection. These include documentation of age-appropriate vaccination withvaricella vaccine; laboratory evidence of immunity or laboratoryconfirmation of disease; birth in the US before 1980; diagnosis or verification of history of varicella disease bya health-care provider; diagnosis or verification of history of herpes zoster by ahealth-care provider [5]. If a patient is non-immune and is over the age of 50, the killed recombinant adjuvant vaccine is preferred. For patients under the age of 50, the live zoster vaccine may be given 2-4 weeks before starting a DMARD. The varicella titer is routinely checked at baseline.

Panel for lipids

It has been shown that anti-inflammatory agents may cause a transient increase in cholesterol levels. These include the IL-6 antagonists and JAKI. It is appropriate to have a baseline level before starting these DMARDs and a repeat level at least 12 weeks after initiation of these therapies. Recent guidelines state that a non-fasting lipid level is appropriate for most patients. We suggest screening at baseline and then every 4-6 months while on therapy [6].

Pregnancy test

This should be done at baseline before starting DMARDs including methotrexate and leflunomide. In patients under the age of 50 and those who themselves nor their partner has had surgical sterilization, we routinely check a serum β HCG every 3-4 months [7].

Procalcitonin (PCT) level

Many of the DMARDs are associated with a risk of infection with respiratory being some of the more frequent ones reported. At times, it may be difficult to discern which patient may need antibiotics or not. PCT levels may help guide antibiotic use. Patients with advanced chronic kidney disease or medical/surgical trauma may have elevated baseline PCT (>0.5 ng/ml) in the absence of bacterial infection. If bacterial infection is suspected, consider repeat PCT in 2 to 4 days to guide de-escalation or discontinuation of antibiotic therapy [8]. We find that the use of this test may help prevent to over use of antibiotics.

Phungal (fungal) test/ β -D-glucan test

The Fungitell assay (Associates of Cape Cod, Inc.) is a chromogenic kinetic test that is approved by the Food and Drug Administration for the presumptive diagnosis of invasive fungal infections. It is used to detect Candida, Aspergillus and Pneumocystis species. Its major use has been in patients with hematologic malignancies who are increased risk for such infections [9].

Table 1: Different tests, their interpretation and suggested frequency of testing.

Test name	Interpretation	Suggested frequency of testing
PPD; Interferon gamma release assay; T spot	Varies depending on the test	Baseline and then once a year
PA and lateral chest x-ray	Varies	Baseline and then as needed for respiratory complaints
Panel for hepatitis B	Varies	Baseline only; immunize if non-immune per ACIP guidelines
Pneumococcal vaccine	Immune or non-immune	Baseline; immunize if needed per ACIP guidelines
Pox (varicella) titer	IgG<0.8 ISR: non-immune IgG 0.9-1.0 ISR: indeterminant IgG> 1.1 ISR: protective immunity	Baseline; consider checking if recurrent VZV infections occur; immunize if non-immune per ACIP guidelines
Panel for lipids, non-fasting	Varies	Baseline; repeat every 4-6 months
Pregnancy test (serum β HCG)	Positive or negative	Baseline; repeat every 3-4 months

Pro-calcitonin level	<0.1 ng/ml bacterial infection highly unlikely 0.1-0.25 ng/ml bacterial infection unlikely 0.26-0.5 ng/ml bacterial infection likely > 0.5 ng/ml bacterial infection highly likely	As needed for respiratory complaints; may also be used if sepsis is suspected
Phungal (fungal) test; β-D-glucan test	<60 pg/ml: negative/presumptive absence of fungal infection >80 pg/ml: positive/presumptive presence of fungal infection	Consider in patients on IL-17 therapy

Rheumatology patients treated with IL-17 antagonists have been known to develop fungal infection most of which are non-invasive and are limited mainly to mucocutaneous candidiasis. In patients where there may be a suspect fungal infection, we use this test (Table 1).

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