CLINICAL VIGNETTE

Live-Attenuated Vaccination for Rheumatic Patient

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Case Presentation

A 49-year-old women with diabetes, obstructive sleep apnea, and exercised induced asthma presented to rheumatology for bilateral, symmetrical, metacarpophalangeal joints pain, swelling, and morning stiffness. Symptoms were present for more than three years and serological testing was negative for antinuclear antibodies (ANA), rheumatoid factor (RF), and cyclic citrullinated peptide (CCP). Radiographic evaluation of hands and feet were negative for any erosive changes, but point of care point musculoskeletal ultrasound noted active synovitis at bilateral radiocarpal and midcarpal joints. She was diagnosed with seronegative rheumatoid arthritis and started on nonsteroidal anti-inflammatory drugs (NSAIDs) for pain control and methotrexate 20 mg weekly as the disease-modifying agent. After three months of therapy, her hand pain and swelling resolved. She achieved clinical remission per American College of Rheumatoid (ACR) clinical disease activity index (CDAI) and stopped all NSAIDs but remined on methotrexate 20 mg weekly.

One month after clinical remission was achieved, she visited her primary care physician for annual physical exam. She was found to have no antibody against varicella virus and denied any childhood history of chicken pox infection. Patient frequently travel internationally for work and was considered as high risk for infection. Her primary care physician recommended the live varicella virus vaccine (VARIVAR) during the visit and she was asked to hold her methotrexate for two weeks without consulting rheumatology.

Two weeks after receiving the live varicella vaccination, patient noticed itchy, fluid-filled blisters at the site of the vaccination. She denied any systematic symptoms including fever, chill, or malaise. She followed up with her primary care physician regarding the blisters concerning for injection site infection. Culture the blisters were positive for varicella zoster virus by polymerase chain reaction (PCR) and she was started on oral valacyclovir 1000 mg three times a day for total of ten days with closely monitor for systematic symptoms. The blister scabbed within a week without progression of other symptoms. Methotrexate was re-started two months after the vaccination.

Discussion

Rheumatic diseases and immunosuppressive medications make patients more susceptible to infections.[1] Vaccines to reduce illnesses from common pathogens, and standardized vaccine schedules for children and adults have been widely adapted for both healthy people and individuals with chronic illnesses.[2,3] American College of Rheumatology has recommended rheumatic patients to be vaccinated again preventable infections.[4] However, the safety of vaccines is different in patients with rheumatoid diseases which requires modification of the vaccination schedule.

Knowledge of the complete medications list is the key first step when vaccinating rheumatic patients. Not all rheumatological medications are considered immunosuppressive. Non-immunosuppressive medications do not impose safety concerns and patients do not require any modification in vaccination schedule. Examples of non-immunosuppressive medications are hydroxychloroquine, sulfasalazine, colchicine, apremilast, and denosumab.[4] Other rheumatological medications are considered immunosuppressive and require modification in vaccination schedule. Examples of immunosuppressive medications are high dose glucocorticoids (equivalent to prednisone $\geq$ 20mg daily), methotrexate, leflunomide, azathioprine, mycophenolate, calcineurin inhibitors, biological disease modifying antirheumatic drugs (bDMARDs), and any B cell-depleting agents (rituximab, ocrelizumab, obinutuzumab).[4]

The second step is knowing the type of vaccine and whether it is non-live attenuated versus live attenuated. Example of non-live attenuated vaccine are injectable seasonal influenza, pneumococcal, haemophilus influenzae, hepatitis A, hepatitis B, human papillomavirus, inactivated polio, meningococcus, tetanus toxoid, injectable typhoid, and zoster subunit.[4] Rheumatic patients receiving non-live attenuated vaccines do not need to delay vaccination or hold any immunosuppressive medication other than two exceptions. Exception #1: rheumatic patients on high dose glucocorticoids (prednisone $\geq$ 20mg daily or any equivalent dosing) should defer any non-live attenuated vaccination until the glucocorticoids are tapered to the equivalent of prednisone < 20mg daily. Exception #2: it is encouraged, but not an absolute necessity, to hold methotrexate for two weeks after influenza vaccination to improve the vaccine responses if disease activity allows.[4,5]

For live-attenuated vaccines, it is important to hold immunosuppressive medications before and after vaccination. Holding medications after vaccination is the same for all immunosuppressive medications which should be restarted four weeks after.[4,6] However, the length of time to hold immunosuppressive medication prior to vaccination varies. For high dose glucocorticoids (prednisone ≥ 20mg daily or any equivalent dosing), methotrexate, leflunomide, azathioprine, mycophenolate, and calcineurin inhibitors, immunosuppressive medications should be held for four weeks prior to the admirations of live-attenuated vaccine. For JAK inhibitor, it is important to hold one week prior to the admirations of live-attenuated vaccine. For biological DMARDs, it is important to hold one dosing cycle prior to the admirations of live-attenuated vaccine, depending on the dosing cycles of each biological DMARDs. Intravenous immunoglobulin (IVIG), should be held eight to eleven months prior to the admirations of live-attenuated vaccine, depending on the IVIG dosing.

Conclusion

Rheumatic diseases and immunosuppressive medications make rheumatic patients more susceptible to infections. Vaccines are important tools to reduce illness from common viral and bacterial infections. Some rheumatic medications are not considered immunosuppressive and therefore alternation of vaccination schedule is not needed. For patient who are on immunosuppressive medication, it is crucial hold immunosuppression prior and after the administration live-attenuated vaccine.

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