Session 1: Treatment dilemmas

01 SHOULD WE VACCINATE ALL SLE PATIENTS AGAINST PAPILLOMAVIRUS AND HERPES ZOSTER?

Sarfraz Hasni. *National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS) of the National Institutes of Health (NIH), Bethesda, Maryland, USA*

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The dysregulated host immune system and treatment with immunosuppressive medications predisposes patients with systemic lupus erythematosus (SLE) to increased risk of infections such as Human Papilloma Virus (HPV) and Herpes Zoster (HZ).

HPV causes genital warts and malignancy including cervical, penile, and anogenital cancers. In a recent meta-analysis, the prevalence of HPV in SLE was found to be significantly higher than controls, with an odds ratio (OR) = 2.87.¹

SLE is associated with the highest rate of HZ infection in all age strata below 70 years, with an age-adjusted incidence of 12.0/1000 person-years (hazard ratio 1.7).² The use of cyclophosphamide and mycophenolate mofetil with glucocorticoids in lupus is associated with a seven-fold increase in HZ reactivation. Similarly, the use of anifrolumab in SLE clinical trials was associated with OR = 4.089 of HZ infection.³

Immunization against common pathogens can potentially be very beneficial in preventing infections in SLE. However, safety and efficacy of vaccines for patients with SLE generate perennial controversy. Concerns are fueled by case reports of *de novo* development of autoimmune disease or flares of existing autoimmune disease after administration of vaccines. In addition, theoretical concerns about inadequate host immune responses to vaccines raise doubts about their effectiveness in protecting patients with SLE from infection.

Overall, HPV vaccines seem to be safe and immunogenic in patients with SLE. A study of 210 patients with SLE, HPV vaccine was found to be immunogenic in ~90% of patients with no serious side effects or increased lupus flare at one-year follow-up.⁴ The use of cyclophosphamide was associated with low rates of HPV seroconversion. The live-attenuated HZ vaccine was also found to be safe and immunogenic with no increase in incidence of herpes zoster in patients with SLE on milder immunosuppressants.^{5, 6} There is still no data regarding the efficacy of the subunit and inactivated HZ vaccines in SLE patients, but studies in other immunocompromised populations showed it to be safe and immunogenic. Vaccination against HPV and HZ in SLE patients resulted in significantly lower rates of infections.

Overall, HPV and HZ vaccines appear to be safe and effective in patients with stable lupus on low intensity immunosuppressants.

Learning Objectives

- Describe the high incidence of human papillomavirus and herpes zoster infections in patients with SLE
- Address concerns associated with vaccination administration in SLE
- Explain the safety, efficacy, and limitations of data from studies of HPV and HZ vaccines in SLE patients

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02 HYDROXYCHLOROQUINE MYOPATHY: CARDIAC AND SKELETAL MUSCLE TOXICITY

Murray Urowitz. *University of Toronto, Canada*

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Antimalarial myopathic toxicities may involve both skeletal and cardiac muscles. In skeletal muscle it is a deposition myopathy and in cardiac muscle there may be a direct chemical action toxicity or a deposition myopathy.

In skeletal muscle there are isolated case reports of clinical myopathy and two prospective studies, one of 119 cases and the other of 21 cases.^{1, 2} Both showed $\pm 19\%$ abnormal muscle enzymes. Clinical weakness was very uncommon but biopsies in 15 patients showed classic EM findings of antimalarial toxicity. All patients improved with cessation of antimalarials.

In chemical toxicity of cardiac muscle, antimalarials may cause QTc prolongation. This is based on isolated case reports. In one cross sectional case series of 90 patients there was no difference in QTc between those on antimalarials and those not.³ There are no reports of sudden death in lupus patients starting antimalarials. Perhaps the more significant findings are related to the deposition of antimalarials in cardiac muscle resulting in antimalarial induced cardiomyopathy (AMIC). Clinical, serologic, imaging and biopsy features of this complication will be described in 8 patients recently seen in the University of Toronto Lupus Clinic.⁴ A systematic review of 47 patients with biopsy proven AMIC will be presented.⁵ Features of AMIC include morphologic/structural changes (biventricular/septal hypertrophy, bi-atrial enlargement); functional defects (impaired systolic and diastolic function); conduction disorders (RBBB, LAFB, cAVB/SSS); elevated biomarkers (troponins [cTnI], BNP, CPK). In 151 lupus patients with no prior history of heart disease we found 16 (10.6%) had abnormal cTnI and/or BNP.⁶ Of these six were diagnosed with AMIC, five with other diagnoses and five do not yet have a definite diagnosis. Cardiac biomarkers should be ordered in patients who are older, have a decreased eGFR, have elevated CK without clinical myositis, and who have taken antimalarials for more than 5 years.