Zoster Infections Increase the Risk of Flares in Patients with Systemic Lupus Erythematosus

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Background Microvesicles (MVs) expressing the type 1 interferon (IFN)-inducible protein galectin-3 binding protein (G3BP) may play a pathogenic role in systemic lupus erythematosus (SLE). Co-expression of DNA on such MVs may render them immunogenic and target for anti-dsDNA antibodies. Little is known about the mechanisms underlying generation of this MV population. In this study, we investigated how Toll-like receptors, interferon- (IFN-) and T cells are related hereto in healthy subjects.

Methods Peripheral blood mononuclear cells (PBMCs) isolated from 12 healthy donors were stimulated in-vitro for 24 hours with a series of TLR-agonists or the T-cell activating antibody OKT3 or were subjected to apoptosis by incubation with staurosporine. MVs in the supernatants were subsequently isolated by differential centrifugation and were quantified and characterized with respect to expression of G3BP and DNA by flow cytometry.

Results Stimulation of PBMCs with the TLR9-agonist and strong IFN- inducer ODN2395 significantly increased the release of MVs expressing G3BP. A large proportion of these MVs expressed augmented levels of DNA on their surface. The production of MVs with this phenotype was markedly enhanced by co-stimulation of T cells. Furthermore, dependency on IFN- in the generation of G3BP-expressing MVs was indicated by a marked reduction following addition of the IFN- inhibitor IFN alpha-IFNAR-IN-1 hydrochloride.

Conclusions The release of G3BP-expressing MVs from healthy donor PBMCs is induced by stimulation of TLR9 in an IFN-dependent manner. The co-expression of DNA accessible for anti-DNA antibodies on these MVs may render them relevant in lupus pathogenesis.

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Effect of IFN- inhibition on TLR9-induced release of MVs from mononuclear cells.

A Young Girl with Lupus, Recurrent Pericardial Effusion and Cardiac Tamponade

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Background Pleuritis and pericarditis, with or without effusion, are the commonest pulmonary and cardiovascular manifestations in children with systemic lupus erythematosus(SLE). However, SLE presenting as an isolated pericardial effusion with cardiac tamponade is distinctly unusual.

Methods We report one such case who went on to develop recurrent episodes of pericardial effusion and tamponade.

Results A-14-year-old girl presented with high grade fever, progressive dyspnea, pedal edema, periorbital puffiness for 7 days. She also had history of malar rash and photosensitivity. There was no history of oral ulcer and hair loss. Physical examination showed a prominent malar rash; heart rate 140/min; respiratory rate 40/min; muffled heart sounds;
hepatomegaly and ascites. She was initiated on decongestive measures with furosemide and digoxin. Chest X-ray showed cardiomegaly (cardiothoracic ratio 68%); 2D-echocardiography revealed cardiomegaly, pericardial effusion and features consistent with cardiac tamponade. She underwent emergency pericardiocentesis, 400 ml of serosanguineous fluid was drained followed by prompt clinical improvement. Investigations showed hemoglobin 90 g/L; total leukocyte count 1.3 × 10^6/L and lymphocyte count 0.18 × 10^6/L; platelets of 356 × 10^9/L. Urinalysis and renal function tests were unremarkable. Tuberculin skin test was non-reactive. Thyroid function tests were normal. In view of febrile illness, malar rash, photosensitivity, pericardial effusion, cardiac tamponade and lymphopenia, SLE was considered. Work-up showed positive antinuclear antibody (ANA)+ diffuse ANA positivity; positive anti-double stranded DNA (anti-dsDNA) – 60 (normal: 4.2 IU/ml); C3 51.8 mg% (normal 50–150 mg%), Skin biopsy revealed IgG and C3 deposits. Pericardial fluid analysis revealed low complement (C3 < 12 mg%); ANA positivity and positive LE cells. Bacterial culture of pericardial fluid and polymerase chain reaction to Mycobacterium tuberculosis were negative. Pericardial fluid showed no malignant cells on cytological examination. A diagnosis of SLE was offered based on positive clinical and immunologic findings. Pulse intravenous methylprednisolone was given (30 mg/kg/day for 5 days) followed by oral prednisolone (starting at 2 mg/kg/day and tapered thereof). 2D-ECHO showed a reduced volume of pericardial fluid with no additional reaccumulation and normal heart function. She remained well for the next 3 years without significant heart function. On follow-up evaluation, her heart function was normal. One hundred and eight (83.1%) patients had lung infection, while 23 (17.7%) patients had blood stream infection.

In the final multivariable logistic regression model, lymphocyte count < 800/ul, urea > 7.6 mmol/L, maximum prednisone dose in the past 60 mg/d, qSOFA score and age at admission were independent predictors for all-cause mortality. However, the history of hydroxychloroquine use was protective.

In a combined prediction model, the six predictors were weighted by OR values, making the LUPHAS score ranging from 1 to 10, indicating low-risk (score 1–3), medium-risk (score 4–6), and high-risk (score 7–10). The mortalities were 11.1% (4/36), 32.8% (22/67) and 100% (22/22) in low-risk, medium-risk and high-risk patients, respectively. ROC curve analysis indicated that LUPHAS score could effectively predict all-cause mortality in this population (AUC=0.895% CI=0.78–0.92). Furthermore, LUPHAS score performed better than the sole qSOFA score (AUC=0.6995% CI=0.59–0.80) in our cohort. The discriminatory performance of LUPHAS score was also superior than CURB-65 score (AUC=0.6995% CI=0.59–0.80) in the subgroup of patients with lung infection (n=108).

In this large emergency cohort of lupus patients complicating with invasive infection, an impressive high