Immunol Case Rep 2019, Volume 3 | DOI: 10.4066/2591-7366-C2-006

EFFICACY AND SAFETY OF TOPICAL IMIQUIMOD USE IN HPV-INDUCED VULVAR LESIONS IN TRANSPLANT RECIPIENTS: A CASE SERIES

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Background: Chronic immunosuppression is recognized as one of the main risk factors for human papillomavirus (HPV) infection, persistence and consequently, development of HPV-induced genital lesions. The treatment of some vulvar lesions is challenging because they are extensive, multifocal and recurrent. Topical immunomodulators as imiquimod have shown efficacy in the management of multiple malignant, precancerous and viral conditions. The ability to locally induce an immune response, presumably against tumor and viral antigens, makes topical immunomodulators a promising therapeutic option in organ transplant recipients. There is limited information on safety of use in these patients. Also, most studies are on skin diseases not in HPV-induced vulvar lesions. Complete response rates in high grade vulvar intraepithelial lesions ranged from 5% to 88% in immunocompetents. There is no data among immunosuppressed patients. This is a descriptive study of the efficacy and safety of imiquimod in renal transplant patients with HPV-induced vulvar lesions in a tertiary Hospital in Rio de Janeiro, Brazil.

Method: Patients with HPV-induced vulvar lesions were retrospectively enrolled. A total of three patients applied one sachet of topical imiquimod 5% cream three times per week. Dosing continued for an average period of 56 weeks regardless of lesion clearance. Patients were assessed for safety variables that included adverse events, local skin reactions, laboratory results and indication of graft rejection.

Results: No graft rejections or trends for a deterioration of graft function were detected. No complete response was observed. Also, no progression of any lesion was observed.

Conclusion: Imiquimod appears to be a safe additional option for the treatment of HPV-induced vulvar lesions in patients with solid organ transplants. Other alternative treatments may be necessary for complete resolution of the lesions. No similar response rates were observed for use in skin diseases in immunosuppressed patients. Larger studies are required to confirm these results.

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IMMUNOLOGY AND CANCER THERAPY

Accepted Abstract

May 22-23, 2019 | Rome, Italy

Immunol Case Rep 2019, Volume 3 | DOI: 10.4066/2591-7366-C2-006

NOVELTIES IN ADDITIVE MANUFACTURING AND BIO-PRINTING

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Here, author describes a unique strategy designed to identify dominant tumor antigens associated with lung cancer cells. Vaccines that induced immunity to dominant tumor antigens can induce therapeutic immune responses in tumor bearing mice and patients. In a squamous carcinoma mouse model of non-small cell lung cancer, the antigen-discovery strategy, this is based on the finding that genes encoding dominant tumor-associated antigens (TAA) (immunity to dominant tumor antigens can lead to tumor regression) are expressed in a highly immunogenic form by a non-malignant, allogeneic fibroblast cell line transfected with a cDNA expression library from lung cancer cells. The transfected cells, which express the products of multiple genes specifying an array of antigenic determinants, including genes specifying dominant tumor antigens were selected for antigen discovery. However, as only a small proportion of the transfected cell population was expected to have incorporated gene-segments that specified TAA (the vast majority specified normal cellular constituents), a unique strategy was developed that resulted in the identification of Cyp2e1, a derivative of cytochrome p450, as an immune dominant tumor antigen in murine squamous carcinoma cells and growth factor receptor bound protein 10 GRB10 and Trop1 as immune dominant tumor antigens in murine breast cancer cells. The strategy consisted of dividing aliquots of the suspension of transfected cells into 10-15 small pools (initial inoculums 10E3, using a 96 well cell culture plate was used for this purpose, allowing the cells from each pool to increase in number (to approximately 10E7,) small starting inoculums increase the likelihood that some pools will contain greater numbers of cells that express dominant cancer antigens than others). Afterward the transfected cell-populations from each pool were divided into two portions. One portion was maintained frozen/viable for later recovery. The remaining portion was co-incubated with (mitomycin C-treated) squamous carcinoma cells. Two independent assays, (ELISPOT interferon gamma-release and 51-Cr release cytotoxicity) were used to identify pools that stimulated immunity to the squamous carcinoma cells to the greatest, (and for later use and as a control) to the least extent. Frozen cells from these pools were re-established in culture; the cell-numbers were expanded and subdivided for additional rounds of immune selection (They reasoned that if the starting inoculums were sufficiently small, then randomly, some pools would contain greater numbers of cells that induced the anti-tumor immune response than others). After further rounds of immune selection, microarray was used to identify the products of genes over-represented in the cell pool that stimulated the antitumor immune response to the greatest and (for use as a control) to the least extent.

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Immunol Case Rep 2019, Volume 3 | DOI: 10.4066/2591-7366-C2-006

EFFECTS OF FOOD BORNE MYCOTOXINS ON TOLL LIKE RECEPTOR

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Mycotoxins are structurally diverse toxic secondary metabolites produced by the organisms of the Fungus kingdom. Due to the widespread presence of fungi in the environment, mycotoxins are regarded as an unavoidable contaminant in food products. Mycotoxins can cause mycotoxic nephropathy, hepatotoxicity, cytotoxicity, genotoxicity and induce dysregulation of the immune response and are able to either enhance or suppress resistance to pathogens. Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. Once microbes have breached physical barriers such as the skin or intestinal tract mucosa, they are recognized by TLRs which activate immune cell responses. In the present study, the effects of food borne mycotoxins on TLRs have investigated in the female BALB/c mice. Mycotoxins (citrinin, deoxynivalenol and zearalenone) were orally administered to seven weeks old female BALB/c mice at different dose rate for 14 days, and several immunotoxicity tests were performed. Normalized fold expression of TLRs in immune organs were differentially expressed. After priming of RAW 264.7 macrophage cell line by different TLR ligands, it was observed that mycotoxins differentially modulated TLR signalling by increased or decreased production of IL-1β, IL-10 and TNF-α. These results indicate that mycotoxins have multiple immune modulatory effects on TLRS in mice that may alter normal functions of immune system.

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SPECIFIC FEATURES OF IMMUNE COMPLEXES IN PATIENTS WITH SARCOIDOSIS AND PULMONARY TUBERCULOSIS

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Background: Clinical and radiological features of tuberculosis and sarcoidosis are quite overlapping and therefore, a diagnostic dilemma often persists. There are no commonly accepted criteria for the diagnosis of sarcoidosis due to the lack of data on the etiology of the disease. The exclusion of tuberculosis in every patient with suspected sarcoidosis is a mandatory stage of diagnosis, especially in countries with a high burden of tuberculosis.

Materials & Methods: A prospective study was conducted with two groups of patients: Group I (n=50)-patients with pulmonary sarcoidosis established according to standard criteria; group II (n=28)-patients with pulmonary tuberculosis with bacterial excretion. The control group (n=24) was presented by healthy subjects. The examination complex included x-ray, bacteriological, immunological (Mantoux test with two TE and TB.SPOT test) and histological methods. All patients and healthy subjects were assessed for immune complexes with the use of the dynamic light scattering (DLS) method and adding of "healthy lung tissue extract" antigens and specific tuberculosis antigens ESAT-6 and SFP-10 *in vitro*.

Results: Significant differences were found in determining of specific immune complexes in patients with pulmonary sarcoidosis and pulmonary tuberculosis. Registration of specific immune complexes formation with "healthy lung tissue extract" in 100% cases may indicate the autoimmune nature of sarcoidosis. The absence of the immune complexes formation in response to ESAT-6/SFP-10 antigens can be used for the differential diagnosis of two diseases. The diagnostic significance of the DLS method was 100% for sarcoidosis and 92.2% for tuberculosis.

Conclusions: The data obtained in the study allows not only understanding the etiology of sarcoidosis but also obtaining new criteria for the differential diagnosis of tuberculosis and pulmonary sarcoidosis.

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Immunol Case Rep 2019, Volume 3 | DOI: 10.4066/2591-7366-C2-006

TREATMENT OF TNBC USED BY RSC001

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In several cases, traditional cancer treatment can cause many side effects both in short and long term problems that occur when affect healthy tissues and organs. Because of the traditional surgical treatment only, can remove the tumor that has been formed, it cannot completely prevent cancer metastasis or growth. Although chemotherapy can increase the survival rate of patients with surgical treatment, it still cannot completely inhibit tumor growth. Therefore, in order to completely suppress the development of cancer cells, the research and application of immunotherapy have attracted more and more people's attention, using T cell in autoimmune system to attack tumor cell also using small molecular in tumor cell cycle as a targeting. The classic pathway JAK-STAT induces chemokines expression, chemokines CXCL10 and CXCL11 will recruit CD8+ T cell for attacking tumor cell. STAT1 and STAT3 are different transcription factor in this pathway. We found a small molecule RSC001 should interact with this pathway and chemokines; it should be affecting the effect of immunotherapy or can be a new targeting point for cancer immunotherapy in future.

Note: