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Allergic Contact Dermatitis and Autoimmune Diseases - Epidemiological and Experimental studies

Summary

Allergic contact dermatitis is a frequent disease, and up to twenty percent of the adult population is sensitized to one or more contact allergens. There does not appear to be genetic predispositions, which could explain this high quantity of sensitized individuals, and allergic contact dermatitis is therefore in essence an environmental acquired disease, where development of disease is due to exposure patterns. Allergic contact dermatitis is a cellular mediated disease, which involves both the innate and the adaptive immune system, and is the prototype of a delayed-type hypersensitivity reaction. Allergic contact dermatitis is diagnosed by patch testing, an internationally standardized in vivo test. Due to the involvement of various different immune cells, it is possible that allergic contact dermatitis could influence the occurrence of other diseases involving the immune system.

The aim of this PhD study was to investigate associations between allergic contact dermatitis and autoimmune disease.

The PhD work was done as two separate projects: an epidemiological study (**Part 1**) and an experimental murine study (**Part 2**).

For **Part 1**, the register from the Dermatological Department at Gentofte Hospital, which contains results of patch tests, was linked with the Danish National Patient Register, which contains discharge diagnoses. The relationship between a positive patch test and type 1 diabetes or inflammatory bowel disease (IBD) was studied. A significant inverse association to type 1 diabetes (OR: 0.63) and IBD (OR: 0.71) was found. In the IBD study, Crohns disease appeared to be the driving factor for the association. Type 1 diabetes and Crohns disease are two autoimmune diseases where genetic predispositions play a large role, and it is therefore interesting that an environmental disease is associated inversely with these diseases.

For **Part 2**, the Non-Obese Diabetic (NOD) mouse was used to investigate whether an experimental allergic contact dermatitis influenced the development of diabetes. NOD mice were first treated according to the Local Lymph Node Assay (LLNA) with the potent allergens p-phenylenediamine (PPD) and 2,4-dinitrochlorobenzene (DNCB) to establish that they could respond to allergens. Subsequently, an incidence study was initiated to evaluate the effect of allergic contact dermatitis on diabetes development, and it was found that repeated treatment with PPD reduced the diabetes development ($P= 0.048$), while this was not the case for DNCB. For further study of the effect of allergens on the innate immune system, C57BL/6 mice were treated with PPD and DNCB, and it was established that both allergens stimulated Natural Killer T cells (NK-T) in the liver, while seemingly only PPD resulted in an increase of NK-T cells in the draining lymph node.

In conclusion, allergic contact dermatitis appeared to be inversely correlated with autoimmune diseases, such as type 1 diabetes and Crohns disease. This could be due to environmental and/or genetic factors. Support for the role of an environmental factor was found in animal experiments, and additionally we found that the allergens increased the quantity of NK-T cells in the liver.