HLA Study of ECD Patients

The ECD Global Alliance has been made aware of a study being done by Dr. Julien Haroche in Paris, France. He is currently looking for results of HLA I and II blood tests from ECD patients. ECD patients are encouraged to talk with their own treating doctors about the possibility of participating in this study. The blood test can be done locally with the results being sent to Dr. Haroche. A letter from Dr. Haroche to treating physicians outlining his study can be found below along with his contact information.

Because of the rarity of ECD, most feel it is unlikely there will be any clinical trials related to ECD in the near future. However, we are encouraged that the study being conducted by Dr. Haroche may help in the understanding of ECD. With better understanding we will be closer to having better treatments made available.

If you have any questions regarding this study you can contact support@erdheim-chester.org or have your physician contact Dr. Haroche directly.

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Dears Colleagues,

First described in 1930, Erdheim-Chester disease (ECD) is a rare, non-Langerhans form of histiocytosis characterized by tissue xanthomatous infiltration by foamy histiocytes. By September 2008, approximatively 350 cases of ECD were reported in the literature.

Very little is known regarding the pathogenesis of this disease. In summary, pathological studies have shown that typical cellular infiltrate of ECD is characterized by the presence of a xanthomatous infiltration of the involved tissues with CD68+ CD1a- histiocytes, Touton giant cells, and a contingent of lymphocytes displaying a Th1 profile. The Th1-polarized microenvironment contributes to the activation of the infiltrating histiocytes, as shown by expression of various chemokine receptors. The vessels comprised within the lesions and around them express various chemokine receptors suggesting that a complex biochemical network is orchestrating recruitment, accumulation and activation of histiocytes. Pro-inflammatory cytokines typical of Th1 response such as IL-1, TNFα, and IL-6 are strongly expressed in the lesions and in the blood, accounting for the systemic symptoms observed in ECD and inducing bone remodeling.

Many diseases are the result of an interplay between predisposing genes and triggering environmental factors, leading to loss of self-tolerance and an immune-mediated destruction of autologous cells and/or tissues. Genes of the HLA region on human chromosome 6p21 are among the strongest predisposing genetic factors and are a critical susceptibility locus for many human autoimmune diseases including rheumatoid arthritis, multiple sclerosis and type 1 diabetes. The HLA complex is a highly polymorphic region on the short arm of chromosome 6 and HLA molecules themselves control antigen presentation to T-cells, thereby regulating immune responses. A probable mechanism is preferential presentation by the disease-associated HLA molecules of pathogenic peptides to T cells.

In this study, we would like to investigate the class I and class II HLA phenotypes of ECD patients to determine whether specific haplotypes are associated with an increased susceptibility to the disease or segregate with specific tissue involvement of ECD, such as cardiovascular or neurological involvement. A positive association would underline the potential role of antigen presentation to T-cells in ECD and allow better understanding of the pathogenesis of the disease. We currently have a personal series of 37 ECD patients that are (or were) followed in our institution. By getting 15 or more samples we could get above 50 ECD patients which would constitute a unique collection in order to try making progress in understanding the pathophysiology of this disease.

By advance thank you for your collaboration,

Best regards,

Julien Haroche,  
MD, PhD