The Autoantibodies of Neonatal Lupus Erythematosus

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The observation that Ro/SS-A (Ro) autoantibodies are frequently found in mothers and their infants with neonatal lupus erythematosus (NLE) suggested that these autoantibodies might play a role in the pathogenesis of the cardiac and skin injuries that occur in NLE. This hypothesis was strengthened by observations that the majority of patients with subacute cutaneous lupus erythematosus (SCLE) have Ro autoantibodies and that NLE and SCLE skin lesions are clinically and histopathologically similar. Furthermore, Lee and co-workers demonstrated that intravenously administered Ro autoantibodies were selectively deposited in and about the basal keratinocytes of human skin grafted on immunodeficient mice [1]. This immune deposition was augmented dramatically when the graft was pre-irradiated with ultraviolet B light, a known provocative agent of SCLE. Additionally the pattern of immune deposition closely mimicked the pattern found in NLE and SCLE skin lesions and paralleled the level of skin injury seen histopathologically in these two disorders.

Over the past several years it has been learned that there are several different proteins that react with Ro autoantibody-containing autoimmune sera. Three dissimilar human genes that encode Ro autoantibody-reactive proteins with molecular weights of 46, 52, and 60-kilodaltons (kD) have been characterized [2]. The 52- and 60-kD proteins, whose functions remain unknown, are reactive with the majority of sera that contain Ro autoantibodies by conventional immunodiffusion assays. The 46-kD Ro autoantigen is calreticulin, a calcium-binding protein that resides in the endoplasmic reticulum. Recombinant calreticulin has little reactivity with Ro autoantibody sera and its authenticity as a Ro autoantigen remains controversial.

To date there has been no evidence that a targeted Ro protein or Ro epitope is specific for a particular type of Ro autoantibody-associated autoimmune disorder (i.e., NLE versus SCLE versus Sjogren's syndrome). In this issue (p. 963) Lee et al determine the frequencies at which 52- and 60-kD Ro-reactive autoantibodies are present in NLE sera. Their data indicate that although 52-kD Ro-reactive autoantibodies are found frequently in NLE, 60-kD Ro-reactive autoantibodies were found in every one of their 20 NLE cases. Their data suggest that the 60-kD Ro autoantibodies may play a larger role in NLE, but does not rule out the possibility that the 52-kD Ro-reactive autoantibodies also contribute to the cardiac and skin injury in some cases of NLE. They found that the La/SS-B autoantibodies, which occur in parallel with Ro autoantibodies, occur less frequently in these patients. The U1 RNP autoantibodies, which have been reported previously in several cases of NLE in the absence of Ro autoantibodies [3], occurred in only one of 20 NLE cases in this study and were accompanied by Ro autoantibodies.

Earlier work that demonstrated greater sensitivity in Ro autoantibody detection using non-denatured native 60-kD Ro explains the higher frequency of 60-kD Ro-reactive antibodies found in this study compared to an earlier NLE study [4]. Lower titers of 60-kD Ro-reactive autoantibodies were found in NLE patients with skin disease when compared to NLE patients with cardiac disease. Lee and colleagues propose that this finding may be a consumptive phenomenon from autoantibody deposition in the skin.

These and previous data strongly suggest that the Ro autoantibodies play a role in the pathogenesis of NLE and SCLE. However, additional studies are needed to clarify this role and to explain why many infants that have acquired Ro autoantibodies transplacentally never develop NLE, and why some mothers that give birth to infants with NLE skin disease never develop SCLE lesions. Additional information is required to explain why, in several reported cases, mothers and their infants with NLE have not had detectable Ro autoantibodies, and why Sjogren's syndrome patients, who usually have Ro autoantibodies, rarely develop SCLE.

REFERENCES