Risk Factors for Infectious Complication in Patients with Systemic Lupus Erythematosus

The prognosis for patients with systemic lupus erythematosus (SLE) has improved over the past several decades (1). In some studies, 10-year survival estimates of >90% have been reported. This improvement has likely been the result of more judicious use of immunosuppressive medications including corticosteroids and immunosuppressants and the availability of better treatment for the organ damage that can result from chronic inflammation, particularly end-stage renal disease.

Despite the linear improvement in survival rates, mortality in SLE is still appreciable. In the 1970s, renal disease was the most common cause of death. In 1981, a multicenter study of outcome in SLE (2) reported that lupus-related organ system involvement (mainly active nephritis) and infection were the most frequent primary causes of death (31% and 33%, respectively). In 1985, a multicenter study conducted by the Research Committee for Autoimmune Diseases supported by the Japanese Ministry of Health and Welfare (3) revealed that infection is the most frequent cause of death (35%), followed by cerebral vascular accident (10%), renal failure (9%) and central nervous system disease (9%).

Accordingly, it is important to identify contributing factors for infection in SLE in the management of this disease. In this issue, Yuhara et al (4) have attempted to identify risk factors for infection in hospitalized SLE patients with active disease. Using a sophisticated statistical procedure (i.e.: stepwise logistic regression analysis), variables such as a decrease in serum albumin level, an increase in serum creatinine level and prednisolone pulse therapy were found to be independent multivariate predictors for infection.

Previous studies reported several attributing factors for the increased infection rate in SLE: a) the underlying disease itself (5), b) immunosuppressive therapy, including corticosteroids and immunosuppressants (6), c) increased disease activity (7–9). Duffy et al (9) reported that infection is significantly associated with disease activity (SLE Disease Activity Index, SLEDAI), but not with disease duration or prednisone dosage.

The identification of the serum albumin levels by Yuhara et al (4) as an independent risk factor for infection in patients with SLE is highly suggestive. Hypoalbuminemia was shown to be closely relevant to the disease activity of patients with SLE and was selected as a variable of disease activity criteria proposed by the Research Committee for Autoimmune Diseases supported by the Japanese Ministry of Health and Welfare (10). The serum albumin level is only the complex end result of synthesis, degradation and distribution. Several mechanisms such as a loss from nephritic kidney or a decreased production in the liver are thought to contribute to the induction of hypoalbuminemia in patients with active SLE. It remains to be clarified whether a similar reduced production in the liver of patients with active SLE, of proteins which is important in the defense against infection may contribute to increased susceptibility to infection.

The role of cytotoxic agents such as azathioprine and cyclophosphamide in the susceptibility to infection was not elucidated, because of the small number of patients taking these agents. Since mortality rates and cause of death reflect the nature of each center’s patient population, a prospective multicenter study on a large number of patients should be carried out in the future.

In conclusion, the identification of risk factors for fatal infection may give rationale for the administration of the prophylactic anti-microbial agents and the institution of high-risk patients under a more aseptic condition.

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