Renal Biopsy and the Prognosis of Lupus Nephritis

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At one time the prognosis of lupus nephritis was reported to be dire, with a 2-year survival of under 10 per cent [1]. This outlook was transformed by the advent of renal replacement therapy and effective immunosuppressive treatment for systemic lupus erythematosus. As a result, concern has focussed on whether patients who are at greatest risk of developing progressive renal failure may be identifiable early in their course, enabling the administration of potentially toxic therapeutic regimens to be limited to those with greatest need. Early histological studies reported an association between the presence of diffuse proliferative nephritis and poor renal outcome [2], in contrast to a relatively good outlook if histological appearances of focal proliferative nephritis or membranous nephritis were present. An association between diffuse proliferative disease and a poor prognosis was confirmed in some [3], although not all subsequent series [4].

Nevertheless, the prognostic value of renal biopsy was questioned by Freis and colleagues [5], who analysed their own and previous experience and claimed that renal histological appearances provided no additional prognostic information over that given by severity of proteinuria and elevation of blood urea. Some degree of renal histological abnormality is present in virtually all patients with SLE, even those without any clinical evidence of nephritis. If the relationship between renal histology and clinical outcome is unpredictable, and if clinical and laboratory variables offer an equally accurate prognosis, should renal biopsy be performed at all in these patients?

Studies in the past decade have attempted to answer this question in two ways. Histopathological analyses have tried to define more clearly markers which may be related to prognosis. Those emerging include presence of marked subendothelial deposits on electron microscopy [6], derivation of composite scores of the activity and chronicity of nephritis [7], and presence of tubular atrophy [8], all of which have been associated with poorer outcome.

Other studies have examined whether addition of specific histological information may increase the accuracy of predictive models based on clinical variables such as patient age, degree of renal impairment, and proteinuria. In this way, Whiting-O’Keeffe et al. [9] employing step-wise linear regression analysis, found that percentage of sclerotic glomeruli and presence of subendothelial deposits added to their clinical predictive model, whereas histological classification did not. In 1989 Esdaile and colleagues analysed the long-term outcome in 87 patients with various forms of lupus nephritis [10], using Cox’s proportional hazards model. They emphasized the value of poorly-appreciated clinical markers, such as duration of renal disease, and overall severity of SLE, in determining outcome, and they
confirmed the importance of serum creatinine and degree of proteinuria at presentation in long-term prognosis, whether renal impairment, end-stage renal failure, or death due to renal or non-renal SLE. Although indices of activity and chronicity and presence of tubulo-interstitial disease on biopsy were accurate predictors in their own right, they added little prognostic accuracy to that given by models based on the clinical information alone.

In this issue, Esdaile et al. have now in a similar fashion analysed predictors of short-term renal outcome (reciprocal serum creatinine after 12 months) in the same 87 patients [11], identifying increasing age and proteinuria, abnormal serum creatinine and lower platelet count as important. In contrast to long-term outcome, prediction of one-year outcome for all patients taken together was enhanced by addition of any of three biopsy variables to the clinical model; presence of diffuse proliferative lupus nephritis, marked subendothelial deposits, or a higher activity index. However, when their clinical model was again tested for its ability to predict outcome for an individual patient—the question of concern to physicians—its prognostic accuracy was not improved when biopsy variables were added.

Serum creatinine remained normal after 12 months in the great majority of patients (75 of 87) in this study, which may limit the generality of its conclusions. In addition, it is a retrospective analysis, in common with most other studies of prognosis in lupus nephritis. A further confounding issue is that virtually all patients were actively treated. Eighty-five received high-dose prednisolone and 68 an additional agent, usually azathioprine. This complicates predictions based on histological appearances because changes in histological classification are well-documented in the course of lupus nephritis, e.g. from focal to diffuse proliferative nephritis as the disease progresses, and from the latter to membranous nephritis in response to therapy [3]. Specific markers of activity, such as subendothelial deposits, may also disappear with therapy [12].

These reservations aside, the study and its earlier counterpart give a valuable perspective on the merits of renal biopsy in SLE, as prospective studies of the evolution of different forms of lupus nephritis in untreated patients are no longer ethically justifiable. Controlled trials from the NIH have demonstrated that 6-year renal survival in lupus nephritis is 65 per cent with prednisolone therapy alone, in dramatic contrast to earlier experience [1], and there is a further major improvement with addition of azathioprine or cyclophosphamide [13]. When, for example, a dual pathology is suspected, renal biopsy will remain an essential part of diagnosis and management in patients with SLE. However, it is not without its risks; is it, after all, necessary in SLE patients with clear clinical evidence of renal involvement? Perhaps the conclusions of Esdaile et al. are most appropriate. Renal biopsy undoubtedly may be useful in supporting a clinical estimate of short-term renal prognosis. Information derived from it may add to the predictive accuracy of clinically-based statistical models which are applicable to a population of patients. However, there is little clear evidence that it enhances the ability to foretell outcome in an individual case.

REFERENCES


