have been made in SLE patients. Finally one should not forget that lupus is certainly a much more complicated situation. Recent advances in this field could not be all covered in this short review and we would like to mention only a recent finding in BXSB mice (another lupus-prone strain of mice). These mice have another genetic defect. They express the Yaa molecule, which could be an abnormal adhesion molecule favouring T cell activation [10]. Other genetic defects should be found in the future since it is clear for a long time that numerous genes are involved in this disease.

In spite of the fact that much remains to be done, new therapeutic possibilities emerge from the recent findings such as the use of anti-cytokine antibodies.

References


The nephrotic syndrome: does renal biopsy affect management?

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Introduction

Fifty years after percutaneous renal biopsy was introduced into clinical medicine by Alwall [1] and Iverson and Brun [2], it is reasonable to assess whether histological diagnosis is essential for the effective management of patients with a nephrotic syndrome. One viewpoint is that blind treatment of the nephrotic syndrome with steroids is as effective as treatment based on renal histology. To address this viewpoint three questions need to be answered. Firstly what are the causes of the nephrotic syndrome. Secondly what is the histological pattern underlying the nephrotic syndrome. Thirdly does the response of each of the histological causes of the nephrotic syndrome to treatment differ sufficiently to justify renal biopsy. The present review is of the nephrotic syndrome in patients in temperate climates. The aetiology and patterns of glomerulonephritis in tropical countries and its responsiveness to treatment differ considerably and have been reviewed elsewhere [3].

Aetiology

In a patient with a nephrotic syndrome a careful history and simple laboratory investigations will usually identify possible aetiological factors such as systemic lupus erythematosus, malignancies, diabetes mellitus, infections, e.g. hepatitis B, and drugs such as gold and penicillamine or non-steroidal anti-inflammatory drugs. No one would disagree with the usefulness of a diagnosis in these circumstances as this provides a good guide to the outcome either untreated or with treatment.

Pathology

Clinicopathological studies in the 1960s and 1970s established the histological patterns of glomerulonephritis in patients with a nephrotic syndrome (Table 1). In children an idiopathic glomerulonephritis accounts for 90% of all cases of the nephrotic syndrome [4] and in adults for approximately 80% of patients.
The nephrotic syndrome in children

In the original studies of the International Study of Kidney Diseases in Children (ISKDC) the diagnosis of minimal-change nephropathy was based on renal biopsies [6]. From these and other studies it was established that in a child aged 1–6 years with a nephrotic syndrome and highly selective proteinuria and who did not have microscopic haematuria, hypertension, or renal impairment the likely diagnosis was minimal-change nephropathy. Such children had a greater than 90% chance of going into remission with steroids within 4 weeks. Based on these observations, children aged between 1 and 6 years with a nephrotic syndrome and the features summarized above are no longer subjected to renal biopsy and are instead treated with a trial of steroids. This leads to the term steroid-responsive nephrotic syndrome of childhood and most but not all of such children will have minimal-change nephropathy. In children characterized in this way, if there is no response of the proteinuria to steroids at a 4–8 weeks, then a renal biopsy should be considered to establish the diagnosis especially if the child is aged over 6 years. This is likely to be a focal segmental glomerulosclerosis, mesangioproliferative glomerulonephritis or a membranous nephropathy. In neonates and in children aged less than 1 year there is a high probability of the congenital nephrotic syndrome or diffuse mesangial sclerosis and therefore renal biopsy should be considered as neither of these lesions respond to steroids.

The main area of dispute is whether knowledge of renal pathology in adults with an apparently idiopathic nephrotic syndrome confers any advantage over treatment of all patients with this condition with steroids. Only 25% of adults with a nephrotic syndrome have minimal-change nephropathy and are likely to respond to steroids [5]. More adults than children with minimal-change nephropathy are hypertensive (30%), have microscopic haematuria (28%), renal impairment at diagnosis (60%), and poorly selective proteinuria (50%) [7]. For these reasons it is difficult to determine on clinical grounds the likelihood that an individual has minimal-change nephropathy.

The usefulness of renal biopsy in adults with a nephrotic syndrome has been strongly challenged [8]. Kassirer [9] on the basis of decision analysis questioned the value of renal biopsy in the management of idiopathic nephrotic syndrome in adults. A very strong argument was put forward that as the prognosis for remission of the nephrotic syndrome and for renal function was determined solely by the responsiveness to steroids and not by the histological lesion, blind treatment with 2 months of alternate-day high-dose steroids was at least as good as biopsy-based treatment. These analyses were based on several assumptions. Firstly from the observations of the collaborative study in the USA that in patients with membranous nephropathy, alternate-day prednisolone for 8 weeks was effective in slowing down the progression of renal impairment as compared with placebo [10]. A striking feature of that particular study was that 50% of all patients with a nephrotic syndrome had membranous nephropathy. If one assumes that a further 25% had minimal-change nephropathy then the case for blind treatment with steroids is persuasive. However, in most other studies membranous nephropathy accounts for only 20% of all cases of the nephrotic syndrome in adults [5]. Further, two other controlled studies showed no benefit of steroids in membranous nephropathy [11,12] and the balance of evidence is that steroids are ineffective in this disorder. A further point that is often overlooked is that the nephrotic syndrome in adults with minimal-change nephropathy responds to steroids slightly less often than in children and also more slowly. Only 60% of adults with minimal-change nephropathy are in remission at 8 weeks and this rises to 76% at 16 weeks [7]. There is thus good reason to conclude that in these patients, 8 weeks of alternate-day steroids may not lead to remission of the nephrotic syndrome. Finally if one accepts that more intensive immunosuppression with alternate months of prednisolone and chlorambucil is of benefit in inducing a remission and slowing down the rate of progression of renal impairment in patients with membranous nephropathy [13], then it is unlikely that such potentially toxic treatment could be considered without a secure diagnosis.

A further argument against the usefulness of renal
biopsy is that we lack adequate therapy for each type of renal disease and that the 'informational content' of renal biopsies is judged by the physician's opinion on treatment and prognosis and often not on the basis of randomized controlled studies. An important example of this point is the management of adults with a nephrotic syndrome due to a focal segmental glomerulosclerosis. We have reported that the nephrotic syndrome in patients with the glomerular tip variant of FSGS and also what we have called early classical focal glomerulosclerosis does respond to steroids and immunosuppressants and that with this treatment progression to renal failure is reduced [14]. It is argued that even though in these patients a renal biopsy changed management, in the absence of randomized controlled studies of sufficient power to indicate the effectiveness of the proposed treatment, then the biopsy would in itself have been useless.

Conclusions

The ISKDC guidelines for the initial treatment of children with a nephrotic syndrome with steroids as outlined above remain valid. We would argue that in adults with an idiopathic nephrotic syndrome, blind treatment with steroids means unnecessary treatment of a large proportion of patients (approaching 70%) with a potentially toxic drug. It also means that no assessment would be available of the type of glomerulonephritis or an estimate of the likelihood of a response to treatment and of the prognosis for long term renal function. This differs substantially depending on the histology. In skilled hands the dangers of renal biopsy are small and outweighed by those of unnecessary steroid treatment. Nevertheless the arguments for blind treatment of the nephrotic syndrome with steroids emphasize the paucity of effective treatment for the nephrotic syndrome in adults and the need for controlled studies in these disorders.

References


Does the modality of haemodialysis treatment affect lipoprotein composition?

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Why is lipoprotein clearance decreased in chronic renal failure?

Many haemodialysis patients suffer from cardiovascular morbidity and mortality. Usually, several recognized risk factors are present, i.e. hypertension, left ventricular hypertrophy and dyslipidaemia. The characteristic lipid abnormalities consist of a moderate hypertriglyceridaemia, increased lipoprotein (a), relatively normal total cholesterol, but decreased HDL cholesterol. Changes can be detected before the patient has reached end-stage renal failure, and they become more pronounced when renal failure progresses and