

REDUCTION IN THE INCIDENCE OF MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS IN FRANCE

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Summary

We retrospectively analysed the respective annual incidence of the various types of primary chronic glomerulonephritis observed at Necker Hospital from 1971 to 1983 (1231 as a whole), of which the diagnosis had been established on the basis of renal biopsy. A marked reduction in the annual number of membranoproliferative glomerulonephritis was observed after 1976. When comparing the 1971-76 period (651 patients) and the 1977-83 period (580 patients), a highly significant decrease appeared for the membranoproliferative glomerulonephritis group (from 17.5 to 6.6 patients/year, $p < 0.001$), whereas the mean annual incidence and the respective proportion of all other types of glomerulonephritis did not significantly vary. The decrease was only observed in type I (subendothelial deposits) membranoproliferative glomerulonephritis and in patients born and living in France, whereas the annual incidence of membranoproliferative glomerulonephritis was unchanged in patients referred from Maghreb or Antilles. Such data suggest a possible favourable influence of extensive prophylaxis of pharyngeal infections in industrialized countries as observed for rheumatic heart disease.

Introduction

The finding of an unexpectedly low incidence of membranoproliferative glomerulonephritis cases in French nephrology units during evaluation of baseline data for a multicentre therapeutic trial led us to record the annual number of cases referred to our institution throughout the decade 1971-1980. In an early preliminary report, we observed a significant reduction in the incidence of membranoproliferative glomerulonephritis from the periods 1971-74 and 1975-77 to the 1978-80 period [1]. As this tendency was apparently sustained during the following years, we re-analysed the whole series of patients with primary chronic glomerulonephritis referred to the Necker Hospital between 1971 and 1983,

in order to confirm this observation and to assess the variations in the incidence of membranoproliferative glomerulonephritis by comparison with other varieties of primary chronic glomerulonephritis.

Patients and methods

The study was entirely retrospective. We recorded the reports of all kidney biopsies performed from January, 1971 to December, 1983 in patients over 15 years of age when referred to our institution. Clinical charts were reviewed in order to assess the primary or secondary nature of the glomerulonephritis. We selected for study all cases classified as primary chronic glomerulonephritis. Excluded from the study were glomerulonephritis secondary to systemic diseases, primary acute glomerulonephritis and rapidly progressive glomerulonephritis. All specimens were reviewed by the same pathologists (DD and LHN) and analysed by both light microscopy and immunofluorescence, as well as by electron microscopy when required. Membranoproliferative glomerulonephritis was classified as type I (subendothelial deposits) or type II (dense intramembranous deposits) according to the criteria of Habib et al [2]. The geographical and ethnical origin of the patients was recorded.

Comparison of annual incidence between the various groups of glomerulonephritis was made using the χ^2 test.

Results

Among more than 2000 biopsies, 1231 were identified as primary chronic glomerulonephritis. They were classified into five groups: membranoproliferative glomerulonephritis (151 patients), membranous glomerulonephritis (241 patients), IgA nephropathy (396 patients), focal glomerulosclerosis or minimal change nephrosis (251 patients), and other and unclassified glomerulonephritis (192 patients).

The respective incidence of the five groups of glomerulonephritis, expressed as a percentage of the total number of glomerulonephritis annually observed throughout the 13-year study period, is shown in Figure 1. A marked reduction in the annual frequency of membranoproliferative glomerulonephritis is clearly manifest after 1976, whereas no modification was apparent at any time in the other types of glomerulonephritis.

As the inflection of the time-curve for membranoproliferative glomerulonephritis lay between 1976 and 1977, we compared the mean annual incidence of the various types of glomerulonephritis from 1971 to 1976 (period I, 651 patients) and from 1977 to 1983 (period II, 580 patients).

As shown in Table I, a highly significant difference between period I and period II appears for the membranoproliferative glomerulonephritis group (with a mean annual incidence decreasing from 17.5 to 6.6 patients/year, $p < 0.001$), whereas the mean annual incidence and respective proportion of all other types of glomerulonephritis did not vary significantly.

This reduced incidence was observed only in patients with type I membrano-

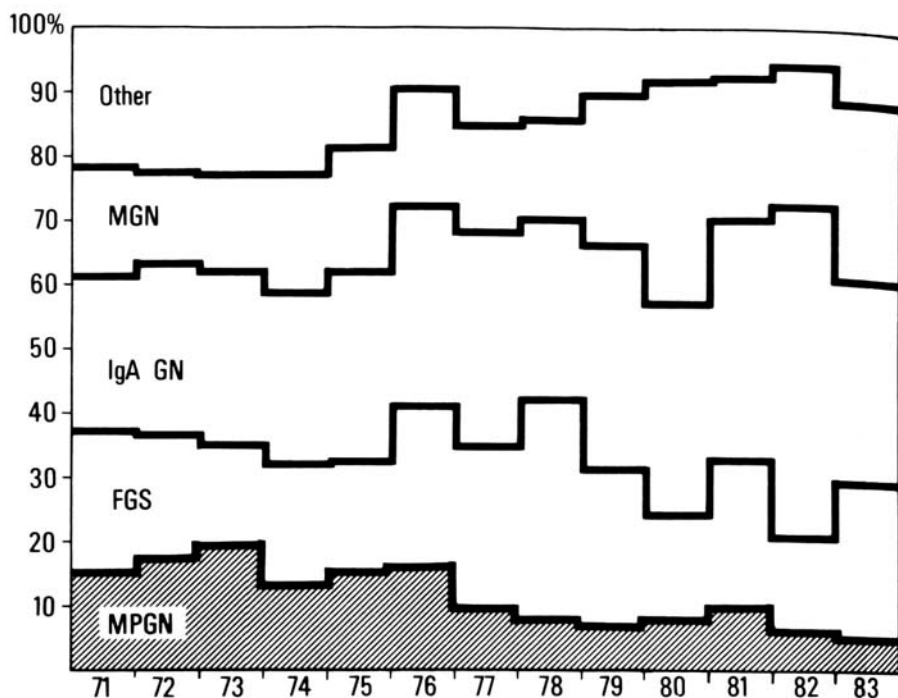


Figure 1. Annual incidence of membranoproliferative glomerulonephritis (MPGN) and other types of chronic primary glomerulonephritis (GN) throughout the 1971–1983 period (Necker Hospital)

TABLE I. Annual incidence of membranoproliferative glomerulonephritis (MPGN) and of other types of primary glomerulonephritis (GN) from 1971–1976 and 1977–83 (Necker Hospital)

Type of GN	Period I (1971–76)		Period II (1977–83)	
	Total No (%)	No/year	Total No (%)	No/year
MPGN	105 (16.1)*	17.5	46 (7.9)*	6.6
type I	99 (15.2)		42 (7.2)	
type II	6 (0.9)		4 (0.7)	
MGN	111 (16.9)	18.5	130 (22.4)	18.6
IgA GN	188 (29)	31.3	208 (36)	29.7
FGS and MCNS	115 (17.8)	19.2	136 (23.4)	19.4
Other and unclassified	132 (20.2)	22.0	60 (10.3)	8.6
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Total biopsies	651 (100%)	108.5	580 (100%)	82.9

* χ^2 test: $p < 0.001$

proliferative glomerulonephritis, whereas the mean annual incidence of type II membranoproliferative glomerulonephritis and its relative proportion to the total number of biopsied glomerulonephritis patients did not significantly vary between periods I and II (Table I).

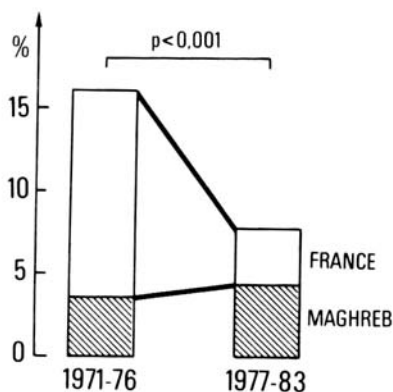


Figure 2. Comparative frequency of membranoproliferative glomerulonephritis in patients originating from France and from Maghreb, from 1971-76 and 1977-83 (Necker Hospital)

Moreover, the decrease in the incidence of membranoproliferative glomerulonephritis was only observed in patients born and living in France, with a mean annual incidence falling from 12 to three patients (11.1% to 3.6% of glomerulonephritis, $p < 0.001$), whereas in patients originating from the Maghreb, black Africa or the French Antilles neither the mean annual incidence (4.1 to 3.6 patients/year) nor the relative frequency (3.8% to 4.3%) varied significantly (Figure 2).

Discussion

The reduction in the incidence of membranoproliferative glomerulonephritis among all other varieties of chronic glomerulonephritis first noted three years ago in the French population is confirmed by the present study. This reduction in the annual number of new patients with membranoproliferative glomerulonephritis observed in our institution cannot be explained by the slight reduction in the annual number of renal biopsies performed for glomerulonephritis at the Necker Hospital. As a matter of fact, both relative and absolute frequency of all other varieties of chronic primary glomerulonephritis were unchanged during the same period. Such a selective reduction of membranoproliferative glomerulonephritis has recently been confirmed by an Italian study, where a significantly decreased frequency (from 21% to 6%) of membranoproliferative glomerulonephritis from the 1972-1975 to the 1980-1983 period was observed in the Milan area, whereas the annual incidence of the other types of primary glomerulonephritis did not vary significantly [3]. In both studies, the inflection of the

time-incidence curve for membranoproliferative glomerulonephritis occurred between 1976 and 1979, and was observed only for type I membranoproliferative glomerulonephritis. Moreover, in our study, the decrease in the incidence of membranoproliferative glomerulonephritis was only observed in patients born and living in France but not in patients originating (or referred) from the Maghreb, the French Antilles or tropical Africa. Thus, membranoproliferative glomerulonephritis appears to be disappearing in industrialized, but not in developing countries.

The reason(s) for such a reduction are only conjectural. However, there is close parallelism between the decline in membranoproliferative glomerulonephritis and the decline in rheumatic fever and, more recently, in rheumatic heart disease observed in industrialized countries during the past three decades [4], whereas both acute glomerulonephritis [5] and rheumatic fever are still frequent in non-industrialized countries such as Tunisia [6], or French Antilles [7]. The decrease in rheumatic fever in Europe and in the USA is usually attributed to better hygienic conditions and to the generalized early treatment of pharyngeal infections since the early sixties. Thus, one could expect that other post-streptococcal diseases, such as acute glomerulonephritis, and perhaps certain forms of chronic primary glomerulonephritis should also be favourably influenced by prophylaxis of streptococcal infections.

If this hypothesis is correct, one should expect a parallel decline in the annual incidence of acute glomerulonephritis and of rheumatic fever in countries where prophylactic treatment of pharyngitis is routine. As a matter of fact, a dramatic decrease in the annual incidence of acute glomerulonephritis (and of rheumatic fever) has been observed in the last four years in the French Antilles, where a pilot study directed towards eradication of rheumatic heart disease was started in 1980 under the sponsorship and co-ordination of the French Ministry of Health (JF Bach, personal communication).

Although there is no evidence that membranoproliferative glomerulonephritis is an evolutive form of acute glomerulonephritis, there is no definite argument against the hypothesis that membranoproliferative glomerulonephritis represents an expression of post-streptococcal disease, besides typical acute glomerulonephritis. Immune response to group A streptococci cell membranes (which show some cross-reactivity with glomerular basement membranes) was found in patients with chronic proliferative glomerulonephritis [8,9]. Glomerular damage following group A streptococcal infection is probably far more frequent than generally suspected because most patients with renal involvement are clinically asymptomatic [5].

Both rheumatic heart disease, which represents nearly 50 per cent of cardiac surgery for valvular diseases [4], and membranoproliferative glomerulonephritis which represents about 50 per cent of chronic primary glomerulonephritis leading to dialysis [10], are a heavy burden on public health budgets. Our observations suggest that extensive prophylaxis of pharyngeal infections should substantially decrease the subsequent incidence of rheumatic heart disease and, hopefully, of membranoproliferative glomerulonephritis in developing countries.

References

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