PLATELET SURVIVAL IN ACUTE PROLIFERATIVE GLOMERULONEPHRITIS

J. A. CARRUTHERS, I. RALFS, T. M. D. GIMLETTE AND R. FINN

Renal Unit, Sefton General Hospital, Liverpool, and
Department of Medicine, University of Liverpool

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SUMMARY

1. Platelet survival was measured in patients with acute proliferative glomerulonephritis or chronic renal failure and also in control subjects.

2. Platelet survival is markedly reduced in acute proliferative glomerulonephritis as compared with control subjects; it was slightly reduced in patients in chronic renal failure due to interstitial renal disease and maintained on dialysis.

Key words: platelets, proliferative glomerulonephritis, renal failure.

Thrombosis in the glomerular capillaries is thought to play an important part in the pathogenesis of proliferative glomerulonephritis (Vassalli & McCluskey, 1964). Attention has been mainly directed towards the part played by fibrin deposition, and the purpose of this paper is to demonstrate that platelet dynamics are also altered in this disease. We have therefore investigated platelet survival in patients with acute proliferative glomerulonephritis and the results are compared with findings in control subjects and in a group of patients with chronic renal failure receiving maintenance haemodialysis.

MATERIAL AND METHODS

Platelet survival studies

All subjects received an intravenous injection of 100 µCi of $^{75}$Se-selenomethionine (specific radioactivity 1–10 mCi/mg) and venous blood samples were obtained at intervals thereafter. The volume of blood taken on each occasion was 18 ml and was added to 2 ml of 0.13 mol/l sodium citrate. Peripheral platelet counts were performed on three or more occasions during each study. The blood was centrifuged at 1000 rev./min for 10 min, and the top 9 ml of supernatant drawn off and centrifuged at 1300 rev./min for a further 5 min. The top 7 ml of this second supernatant was drawn off and used for the preparation of the platelet button. Contamination by erythrocytes and leucocytes was consistently inside the limit set by Brodsky, Siegel, Kahn, Ross & Petkov (1970) of less than one cell per thousand platelets. The platelet
button was prepared by centrifuging at 3000 rev./min for 30 min and was then washed twice with platelet washing fluid (Solum & Lopaciuk, 1969). At the end of each survival study, all the samples were counted for radioactivity simultaneously.

The platelet survival curve was plotted with platelet radioactivity, expressed as a percentage of the highest platelet radioactivity, on the ordinate and time on the abscissa. The interval from the 50% point on the ascending to the 50% point on the descending curve was considered to represent the platelet survival (Cohen, Cooley & Gardner, 1965). The time from the injection of the $^{75}$Se to the peak of the curve was also measured.

**Subjects**

Survival studies were performed on six control subjects, four patients with acute proliferative glomerulonephritis and five patients (age 28–41 years) on regular haemodialysis, the study being repeated on one of the last group after an interval of 4 months. The patients with acute proliferative glomerulonephritis are described in Table I. The patients on dialysis were being dialysed with either Travenol Ultraflo 100 or Avon Minicoil dialysers 3 days a week and all had been on regular dialysis for at least a month at the time of the study. The six control subjects had normal renal function, two were convalescent orthopaedic patients, three had stable cardiovascular disease and one had a neurotic disorder. Their ages ranged from 40 to 70 years. All subjects gave their informed consent.

**RESULTS**

Fig. 1 shows a composite curve of platelet radioactivity in the control subjects; the mean survival time is 13 days, which is slightly longer than the values of 9–11 days previously reported.

### Table 1. Details of patients with acute proliferative glomerulonephritis

All subjects were males. J.S. had a urea of 24 mmol/l (144 mg/100 ml) at the time of the study but was not being dialysed. The remaining subjects had normal renal function.

<table>
<thead>
<tr>
<th>Patient and age (years)</th>
<th>Clinical details</th>
<th>Biopsy</th>
<th>Platelet counts (no./mm$^3$)</th>
<th>Platelet survival (days)</th>
<th>Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.S. (19)</td>
<td>Sore throat, anuria, fluid overload, malignant hypertension</td>
<td>Severe, proliferative glomerulonephritis</td>
<td>63000–83000</td>
<td>1.67</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>A.C. (21)</td>
<td>Sore throat, gross haematuria and mild albuminuria</td>
<td>Not done</td>
<td>61000–87000</td>
<td>2.7</td>
<td>Recovery</td>
</tr>
<tr>
<td>D.K. (19)</td>
<td>Painless haematuria and albuminuria with facial oedema. Ankylosing spondylitis</td>
<td>Enlarged glomeruli with Bowman's space obliterated</td>
<td>96000–128000</td>
<td>3.2</td>
<td>Recovery</td>
</tr>
<tr>
<td>R.M. (46)</td>
<td>Cough, orthopnoea and painless haematuria for 4 weeks. Plasma urea 24 mmol/l (144 mg/100 ml) at time of study</td>
<td>Resolving, mild acute proliferative glomerulonephritis</td>
<td>190000–220000</td>
<td>6.2</td>
<td>Recovery</td>
</tr>
</tbody>
</table>
Platelets in acute glomerulonephritis

**Fig. 1.** Composite platelet survival curve in control subjects.

**Fig. 2.** Platelet radioactivity curves in patients with acute proliferative glomerulonephritis. In this figure and in Figs. 3 and 4 the broken line represents the average normal curve (see Fig. 1).
with this method (Cohen et al., 1965; Brodsky et al., 1970) and other methods (Aas & Gardner, 1958; Heyssel, 1961).

Fig. 2 shows individual curves of our patients with acute proliferative glomerulonephritis whose clinical details are given in Table 1. It can be seen that the platelet survival times are

![Platelet Survival Curves](image)

**Fig. 3.** Complete curve of re-appearance of $[^{75}\text{Se}]$selenomethionine in platelets in subject D.K., with acute proliferative glomerulonephritis, showing two peaks.

much reduced in these patients, ranging from 1.67 days in the most seriously affected patient to 6.2 days in the patient recovering from a mild condition. In determining the survival of these patients with very short survival times an unusually shaped curve of platelet radioactivity was encountered. These curves showed an initial peak, followed by a trough, followed by a second larger peak (Fig. 3). This type of curve occurred in all three patients with acute proliferative glomerulonephritis and very short survival times and we have assumed that the initial peak represents the platelet survival curve.

The curves for the patients receiving haemodialysis are shown in Fig. 4. The survival time is reduced in all these patients, ranging from 3 to 7 days with a mean of 4.25 days. In Fig. 5 the time from the injection of labelled compound to the peak of the platelet button radioactivity curve is tabulated for our three groups, demonstrating clearly the different shapes of the curves in the three groups.
Platelets in acute glomerulonephritis

Fig. 4. Platelet radioactivity curves in patients on regular haemodialysis.

Fig. 5. Comparison in the control subjects and two groups of patients [haemodialysis (RDT) and acute proliferative glomerulonephritis (APG)] of the time from injection of $^{75}$Se to the peak of the survival curve.
The data indicate that platelet survival is markedly reduced in the patients with acute proliferative glomerulonephritis. Three of the four patients had normal renal function and hence the shortened platelet survival times cannot be ascribed to uraemia. The demonstration of this phenomenon in all four cases studied suggests that it is typical of acute proliferative glomerulonephritis. In contrast the patients in end-stage renal failure maintained by haemodialysis had only moderately shortened platelet survival times. This could be due to the uraemia, in which circulating amounts of fibrin degradation products are known to be elevated suggesting a state of chronic low-grade intravascular coagulation (McNichol, Prentice, Briggs & Pidgeon, 1970), and to haemodialysis since platelets are known to be deposited on the dialysing membrane (Lindsay, Prentice, Davidson, Burton & McNichol, 1972). The very short survival time in J.S. (with acute proliferative glomerulonephritis) may have been partly due to his accompanying renal failure. The mechanism of the secondary peak in the platelet radioactivity curve in acute proliferative glomerulonephritis is not clear, but it could be due to disordered protein metabolism in these hypercatabolic patients with rapid recirculation of the isotope.

There are several possible explanations for the shortened platelet survival in acute proliferative glomerulonephritis. It is possible that the short survival time is due to disseminated intravascular coagulation, but there was no other evidence to support this possibility; thus the patients were not uraemic (except J.S.), the blood films were normal and there was no generalized bleeding tendency. An alternative explanation would be a state of localized intravascular coagulation limited to the kidney. The evidence for intraglomerular coagulation in proliferative glomerulonephritis is based on three main findings: hyaline thrombi are visible on light-microscopy; deposition of fibrin has been demonstrated by immunofluorescence and electron microscopy; fibrin degradation products are found in the urine in quantities related to the level of activity of the disease (Clarkson, MacDonald, Petrie, Cash & Robson, 1971). However, Brown, Clarkson, Robson, Cameron, Thomson & Ogg (1973) found no platelets in glomerular electron micrographs, but this could be due to their rapid degranulation and degeneration after aggregation.

The finding that platelet turnover is greatly increased in acute proliferative glomerulonephritis thus raises the possibility that platelet aggregation plays a part in intraglomerular clotting. If this were established, it would provide a further link in the chain of evidence implicating intraglomerular coagulation as an important process in the pathogenesis of proliferative glomerulonephritis.

REFERENCES


