

¹¹¹INDIUM-OXINE LABELLED PLATELETS IN THE DIAGNOSIS OF RENAL ALLOGRAFT REJECTION DURING CYCLOSPORIN A THERAPY

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Summary

The value of ¹¹¹Indium-oxine labelled autologous platelets in the diagnosis of renal allograft rejection was studied in 27 recipients receiving Cyclosporin A. The method used is based on imaging of the graft area secondary to renal platelet uptake. Graft platelet trapping was seen in 16 rejection episodes but not in acute tubular necrosis, functioning allografts or acute Cyclosporin A nephrotoxicity. These preliminary results suggest that this method may be useful in the management of kidney allograft recipients being treated with Cyclosporin A.

Introduction

¹¹¹Indium-oxine labelled autologous platelets have been of value in the diagnosis of kidney graft rejection in patients receiving conventional immunosuppression [1,2]. The use of Cyclosporin A raises the question of differentiation between rejection and nephrotoxicity, particularly in post-operative renal failure. We studied the value of this method in the diagnosis of rejection, based on imaging the graft area secondary to the trapping of autologous ¹¹¹Indium-oxine labelled platelets in renal allograft recipients treated with Cyclosporin A.

Material and methods

Since April 1984, 27 kidney allograft recipients receiving Cyclosporin A have been studied during the first post-transplant month. On the second post-operative day, autologous platelets were labelled with indium-oxine (Radiochemical Centre, Amersham, United Kingdom) by the method described by Thakur et al [3] and reinjected intravenously. The patients were scanned daily for a maximum of six days. The trapping of labelled platelets by the graft was calculated on the basis of graft activity versus contralateral iliac fossa ratio

[1,2]. The trapping in Cyclosporin A treated patients was compared to that documented for allograft recipients treated with azathioprine [4].

If no rejection appeared, the labelling was repeated twice more, until a maximum of three weeks. When rejection occurred, anti-rejection treatment was started. The diagnosis of rejection was based on clinical, biochemical and echographic data; in 16 patients graft biopsy specimens were obtained.

Immunosuppression was with low dose steroids and Cyclosporin A, starting at 15mg/kg/day and subsequent doses adjusted to achieve trough whole blood levels of 300–800ng/ml (RIA Kit, Sandoz). Rejection was treated with three intravenous 500mg methylprednisolone boluses.

Results (Table I)

Graft platelet trapping was seen in 12 patients with 16 acute rejection episodes (Figure 1). Eight episodes appeared in functioning grafts and five renal biopsies

TABLE I. Platelet trapping index in kidney allograft recipients

Group	Azathioprine (4)		Cyclosporin A		
	N	$\bar{x} \pm SD$	N	$\bar{x} \pm SD$	
Acute rejection	113 (bt)	1.9±0.5	19 (bt)	2.0±0.4	} p<0.001 } p<0.001 } NS
Post-operative renal failure	32	1.0±0.2	74	1.1±0.2	
Functioning graft	34	1.1±0.2	43	1.1±0.2	

N=number of scans; bt=before anti-rejection treatment; NS=not significant

disclosed four acute interstitial rejections and one acute vascular rejection. The remaining eight episodes appeared in post-operative renal failure and three renal biopsies revealed acute tubular necrosis plus acute interstitial rejection. The mean trapping index for these 16 rejection episodes was 2±0.4.

Fifteen patients did not suffer rejection and there was no graft platelet uptake. In six patients with functioning allografts without rejection the trapping index was 1.1±0.2. In seven patients with post-operative renal failure without rejection the mean index was 1.1±0.2; seven renal biopsies disclosed acute tubular necrosis. In two patients with functioning allografts and suspected acute Cyclosporin A nephrotoxicity no platelet uptake was found; two renal biopsies revealed signs of Cyclosporin A nephrotoxicity corresponding to the criteria described by Sibley et al [5].

There were statistical differences between the mean trapping index for cases of acute rejection and that for post-operative renal failure and functioning grafts without rejection during Cyclosporin A therapy; however, there were no significant differences in the trapping index for the last two groups receiving Cyclosporin A.

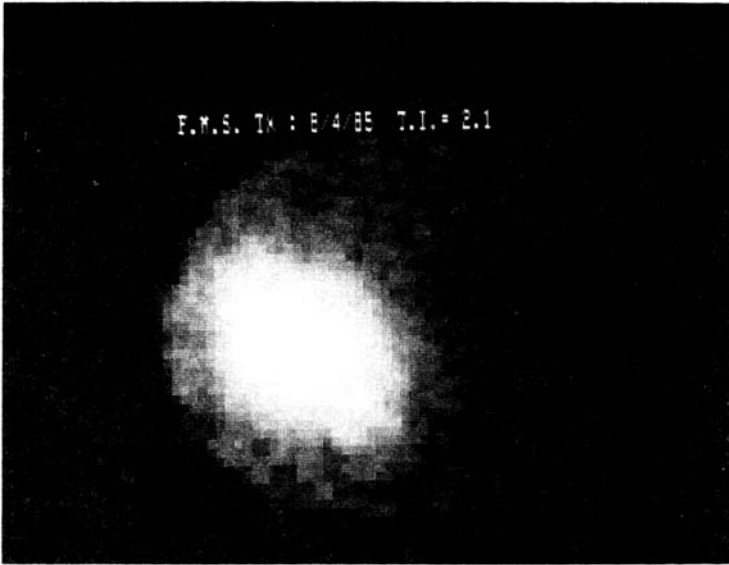


Figure 1. Graft platelet uptake in acute interstitial rejection. Trapping Index = 2.1

The azathioprine groups showed the same significant differences. When the same groups (acute rejection, post-operative renal failure, functioning allografts) were compared according to treatment, there were no statistically significant differences between patients treated with azathioprine [4] or Cyclosporin A.

Mean Cyclosporin A trough whole blood levels were 381 ± 286 ng/ml in patients with rejection and 628 ± 286 ng/ml in patients without rejection ($p < 0.0001$).

At the last follow-up, 25 grafts were functioning. One graft failed due to acute vascular rejection and the second one because of renal artery thrombosis.

Discussion

Our findings show 111 Indium-oxine labelled autologous platelets to be a useful diagnostic tool for detecting renal allograft rejection in Cyclosporin A treated recipients as well as in azathioprine treated ones [1,2,4]. In common with the findings reported by Jurewicz et al [6] in Cyclosporin A treated patients, we observed graft platelet uptake only in cases of acute rejection but not in functioning grafts or cases of acute tubular necrosis without rejection. The same results were reported for patients treated with azathioprine [4]. There was no difference between the trapping index for the various azathioprine or Cyclosporin A groups, suggesting that Cyclosporin A does not increase graft platelet uptake. Because acute tubular necrosis did not increase platelet trapping, this method may be particularly useful in the diagnosis of rejection in post-operative renal failure.

Moreover, acute Cyclosporin A nephrotoxicity did not appear to induce platelet uptake, which suggests the method to be of value in differentiating between rejection and Cyclosporin A nephrotoxicity, although further studies are needed to confirm this.

References

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