Positive imaging of an inflammatory process at an arteriovenous access site with $^{111}$In-Indium-labeled platelets

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INTRODUCTION

Vascular access thrombosis remains a major cause of morbidity in hemodialysis patients. It has been demonstrated that $^{111}$In-labeled platelets accumulate at sites of thrombosis as well as on endothelial injury. Since this technique permits a simple and accurate evaluation of platelet kinetics and sites of abnormal deposition, we are routinely examining early thrombogenicity of vascular accesses using radiolabeled platelets.

Case history

We are reporting on a 70-year-old woman requiring already two months hemodialysis for end stage renal disease of unknown primary disease. There was no history of diabetes or hyperlipidemia. Blood coagulation except of elevated fibrinogen (6.2 g/l; normal < 4.5 g/l) was normal. Anemia was corrected by recombinant human erythropoietin to a hemoglobin of 11.0 g/dl. No antiplatelet drug or anticoagulant was prescribed.

Three weeks after surgery for AVF she underwent her first platelet scintigraphy. At this time hemodialysis was regularly performed by temporary Quinton catheter. To avoid platelet deposition on dialyzers, the investigation was performed in the hemodialysis interval immediately after the last therapeutic session.
There was no clinical evidence of bacterial infection or edema, the scar was slightly red. Blood analysis for inflammation included a normal white blood cell count (7.6 g/l), a slightly elevated CRP of 6.8 g/l (normal < 5 g/l) and a blood sedimentation rate of 38/62. Platelet count was 333 G/l. Doppler sonography showed a normal morphology of the shunt, but a reduced flow of 230 ml/min, which was due to the small caliber of the fistula.

**MATERIALS AND METHODS**

Platelets were labeled as previously described. Briefly, blood (16 ml) was drawn from the non-occluded contralateral cubital vein of the shunt arm into Monovette vials (Sarstedt, Dreieich, Germany) using 2 ml acid citrate dextrose (ACD) as an anticoagulant for 8 ml blood per Monovette. After closing the vials with the sterile plug, 10 minutes were allowed for sedimentation of the red blood cells at 22°C. The vials were then centrifuged at 150 g for 5 minutes. The supernatant platelet rich plasma (PRP) was then transferred into another sterile Monovette vial and centrifuged at 500 g for 10 minutes to obtain a pellet. The supernatant platelet poor plasma (PPP) was withdrawn and preserved. The pellet was gently resuspended in 1 ml Tyrode buffer (pH 6.2) and 100 µCi $^{111}$In-oxine were added in 100 µl (total incubation volume 0.9 ml). After 5 minutes incubation at 37°C and removal of free $^{111}$In-oxine by a further centrifugation step, the sterile PPP was added and the radiolabeled platelets were reinjected. As the labeling efficiency was 93%, 93 µCi $^{111}$In-oxine finally were administered.

Four hours and 24 hours after reinjection of autologous $^{111}$In-labeled platelets gamma camera imaging (Toshiba, GCA 901A, Osaka, Japan) using a matrix of 256 × 256 was performed for both arms in a 20 minutes static study. After 24 hours in anterior-posterior view regions of interest (ROI) were inserted over the spleen and liver and the spleen/liver ratio was estimated using the counts per pixel for the spleen divided by the ones derived for the liver after background subtraction. Labelling efficiency and recovery were in the normal range as reported earlier. Antibody scintigraphy was performed using BW 250/183 (CIS Medipro SA, Geneve, Switzerland) radiolabeled with $^{99m}$Tc as described by the manufacturer. Imaging was performed after 4 and 24 hours.

Fig. 1.—*Images of the AVF obtained 4 hours (A) and 24 hours (B) after reinjection of $^{111}$In-labeled autologous platelets.*
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**RESULTS**

In this patient early scintigraphy imaging four hours after reinjection showed a significant focal platelet accumulation in projection of the AVF which almost completely disappeared after 24 hours (Fig. 1). Spleen/liver ratio amounted 1.2 (normal range 0.8-1.5). Subsequently, antigranulocyte antibody scintigraphy was performed which revealed a positive focal uptake in projection of the identical region at both imaging intervals.

In absence of any clinical features of infection the patient had not received any antibiotic treatment. Three months later, both early and late imaging of $^{111}$In platelet scintigraphy were completely negative. Spleen/liver ratio amounted to 0.9 and the platelets showed a normal recovery. Clinically, for the whole observation period of 20 months there was never a suspicion of bacterial infection. Although sufficient for adequate hemodialysis, Doppler flow parameters were low between 230-300 ml/min due to the small vessel.

**DISCUSIÓN**

It is known that the higher the thrombogenicity, the earlier is the increased radioactivity detected and the more platelets are accumulated. Depending on the activity of a process, platelet accumulation is plateauing somewhere between 8 and 72 hours. Early activity alone, however, suggests increased perfusion reflecting inflammation. Furthermore, radiolabeled platelets are usually contaminated by < 5% with white blood cells. This may additionally contribute to the presence of radioactivity at the site of an inflammatory process.

Since antigranulocyte antibody scintigraphy detects inflammation—including bacterial infection—the diagnosis was confirmed by anti-granulocyte antibody scan and the site was considered infection free based upon the patient’s clinical course.

The follow-up platelet scintigraphy three months later was negative in the persistingly aseptic patient. This was in accordance with the Doppler ultrasonography, which showed no morphological change compared to the preliminary examination and a flow rate of 300 ml/min.

We conclude that early positive platelet imaging reflected an inflammatory process as it was confirmed by the presence of granulocytes. Since infection was excluded, mechanical irritation might have been the cause of sterile inflammation. This observation suggests that platelet scintigraphy for monitoring of thrombogenicity may serve as an additional marker for imaging non-specific inflammation.

**BIBLIOGRAFÍA**