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Exclusion of Thrombocytopenia as a Contraindication for Invasive Radiofrequency Ablation in a Patient with Paroxysmal Atrial Fibrillation by Using Magnesium Anticoagulation Instead of EDTA: Another Case of Anticoagulant-Induced Pseudo-Thrombocytopenia

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ABSTRACT

Thrombocytopenia might be an exclusion criterion for invasive radiofrequency catheter ablation; therefore it is necessary to differentiate between pseudo-thrombocytopenia and a low platelet count due to other etiologies.

A 69-year-old female presented to the cardiology department with recurrent atrial fibrillation that was resistant to conventional drug treatment. The initial laboratory findings were within the normal ranges, except for low platelet counts that occurred without a specific bleeding history. The reason for thrombocytopenia was anticoagulant-induced in vitro aggregation of platelets in the presence of EDTA as well as in citrated blood samples. As recently communicated, magnesium anticoagulated blood samples prevent platelet aggregation in individuals with anticoagulant-associated pseudo-thrombocytopenia. Although its aggregation-inhibiting effect is known from previous clinical observations, magnesium sulphate has not been introduced as an anticoagulant in analytical medicine.

Based on our observations, blood anticoagulated with magnesium sulphate is recommended to verify low routine platelet counts before final clinical decisions are made.

INTRODUCTION

Thrombocytopenia might exclude patients from invasive procedures, such as radiofrequency (RF) ablation for atrial fibrillation or percutaneous vascular interventions (PCI), which necessitate anticoagulation [Gage 2006]. Therefore low platelet counts must be clarified before clinical decisions can be made regarding intervention. Patients with low platelet counts and a missing history of prolonged bleeding or spontaneous hematoma development are suspicious for pseudo-thrombocytopenia (PTCP), a time- and temperature-dependent phenomenon of in vitro platelet aggregation with consecutive low platelet counts [Schrezenmeier 1995].

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Patients suffering from recurrent arrhythmias with increasing frequency undergo invasive electro-physical catheter ablation. This elective procedure might be complicated either by thromboembolism or by bleeding complications at the site of arterial puncture or by cardiac tamponade due to catheter-induced perforation. Therefore, it is preferred to treat patients at risk for coagulopathy with conventional antiarrhythmic medication [Gage 2006; Cappato 2009].

In the following research, we describe a patient who was primarily selected for cardiac ablation therapy who presented with anticoagulant-associated pseudo-thrombocytopenia. The reported prevalence of this threatening pre-analytical error ranges from 0.1-2.1% among hospitalized patients [Cohen 2000; Erkurt 2014] and 15-17% in selected blood samples from patients with thrombocytopenia [Silvestri 1995]. The pathophysiology of EDTA-induced in vitro aggregation is not known in detail, but seems to be associated with conformational changes of the platelet GIIb/IIIa-receptor due to the calcium-chelating effect of EDTA, thus facilitating the binding of autoantibodies. This time-dependent phenomenon of PTCP was also reported from citrated and heparinized blood, but not from magnesium-salt anticoagulated blood samples [Schuff-Werner 2013].

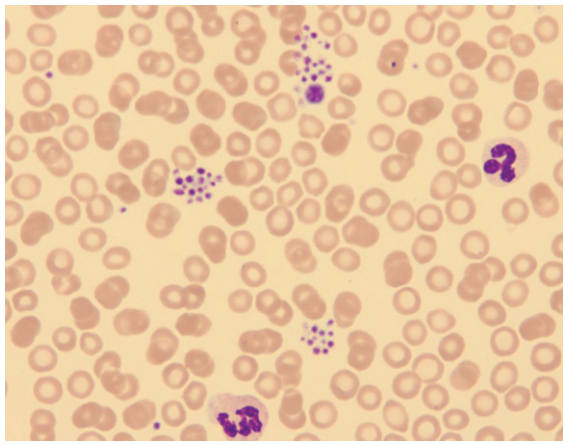

Figure 1. Patient's blood film showing EDTA-induced platelet aggregation. In smears of magnesium salt anticoagulated blood, no aggregates were found.

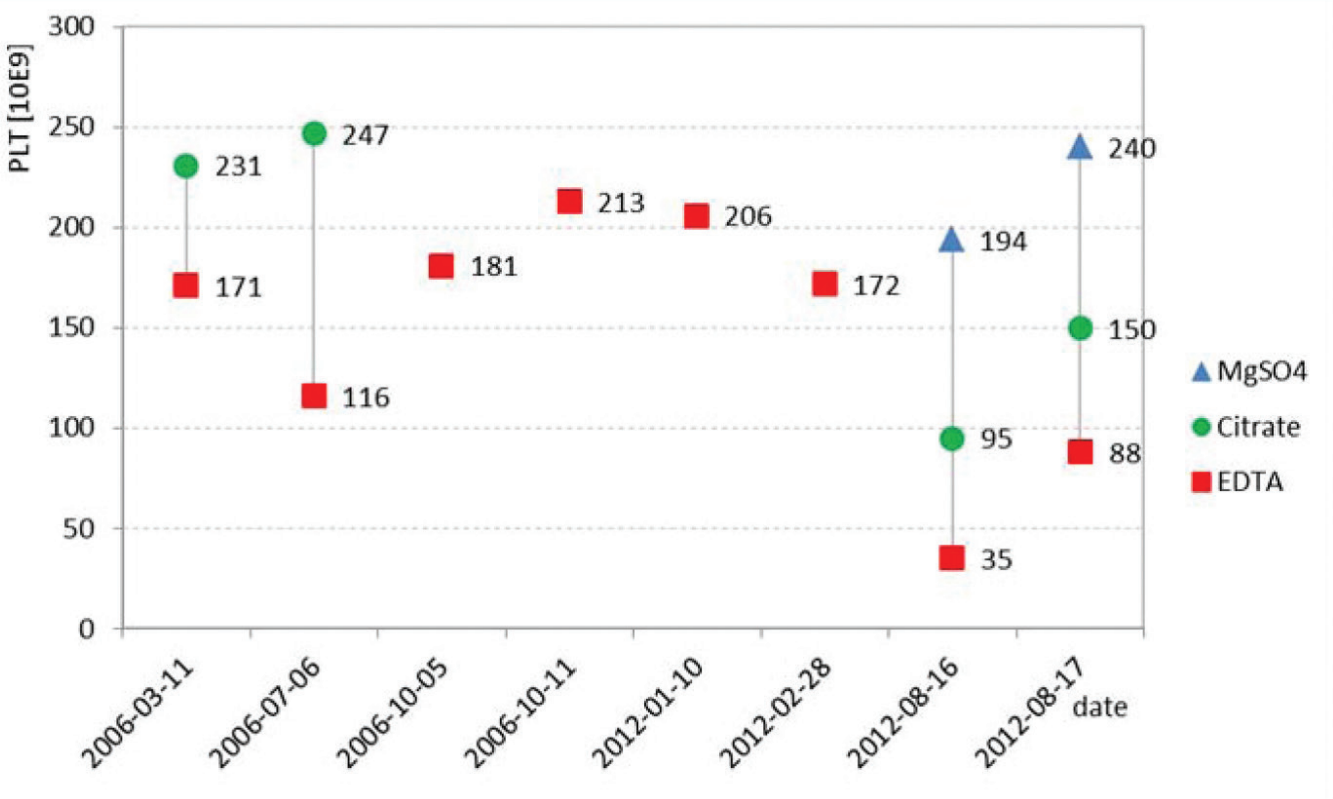

Figure 2. Patient's platelet counts, measured in whole blood samples anticoagulated with EDTA, citrate, or magnesium sulfate at admission to the hospital (on August 16-17, 2012). The phenomenon of PTCP had obviously been recognized six years earlier in an external hospital (June 7, 2006) when citrated blood was measured at the same time. Markedly fluctuating platelet counts measured in the meantime can be explained by time dependency of platelet aggregation after sample collection. Low platelet counts in EDTA blood were interpreted as a contraindication for cardiac intervention. Although there was no analyzer flag, a blood smear was examined. After verification of platelet aggregates, the new platelet count in citrate and magnesium anticoagulated blood showed normal values, allowing for catheter ablation.

CASE REPORT

A 69-year-old woman with symptomatic atrial fibrillation (AFIB) refractory to drug therapy was scheduled for pulmonary vein isolation (PVI). The number of AFIB episodes increased with class 1c antiarrhythmics and with amiodarone. Coronary artery disease was excluded three years prior. The patient denied any history of unexpected bleeding events or sudden hematomas while on oral anticoagulation with dabigatran-etexilate.

On admission, the ECG showed sinus rhythm and no signs of any disturbed excitation propagation. The laboratory findings, including coagulation parameters, were within the normal range except for relative lymphopenia (18.5%), hypokalemia (3.5 mmol/L), elevated LDL cholesterol (4.26 mmol/L) and thrombocytopenia of 35 × 10^9/L as measured in EDTA-blood. Examination of the corresponding blood smear gave evidence for the presence of platelet aggregates (Figure 1).

The platelets were counted again using citrate- and magnesium anticoagulated blood samples (S-Monovette Citrat 3 mL; S-Monovette ThromboExact 2.7 mL, Sarstedt, Nürmbrecht, Germany), respectively. The resulting platelet count was 95 × 10^9/L in citrated blood, but 253 × 10^9/L when magnesium salt was used as an anticoagulant. The suspected diagnosis of anticoagulant-associated pseudo-thrombocytopenia was confirmed and the patient was chosen to undergo intended treatment.

DISCUSSION

Based on current guidelines, patients with atrial fibrillation and consecutive risk of thromboembolic events are to be considered for continuous oral anticoagulation. Anticoagulation is also indicated after left atrial ablation procedures irrespective of the inherent risk, because ablation itself creates a thromboembolic milieu. During the ablation procedure, continuous heparin infusion is used with the aim of achieving an activated clotting time that ranges from 300-350 s. Today, anticoagulation with vitamin K antagonists is often maintained during the procedure itself, since the risk of both bleeding and thromboembolism is reduced [Wazni 2007]. Bridging with low molecular weight heparin is still mandatory with novel oral thrombin antagonists (NOAK). In the case of severe thrombocytopenia, systemic anticoagulation might be difficult to manage because of bleeding risks during

and after the procedure. Therefore, severe thrombocytopenia might be an exclusion criterion for any invasive intervention.

There are several reasons for unpredictable thrombocytopenia, e.g. drug-induced thrombocytopenia (DIT), heparin-induced thrombocytopenia (HIT), and anticoagulant-induced spontaneous in vitro aggregation of platelets (PTCP) [Stasi 2012]. Due to the pre- and post-procedural replacement of oral anticoagulation by heparin, HIT was reported in patients who were to undergo percutaneous vascular interventions [Baetz 2010].

Real thrombocytopenia is mostly accompanied by a history of bleeding events or by recently started heparin therapy. If patients do not report prolonged bleeding or sudden hematoma formation, if platelet counts show wide variations in the antecedent laboratory reports (Figure 2) due to time- and temperature-dependent in vitro aggregation in the presence of EDTA and quite well in citrate [Schuff-Werner 2013], and if hematological analyzers indicate platelet clumping, the diagnosis of anticoagulant-induced PTCP is likely [Lippi 2012]. A simultaneous platelet count using magnesium anticoagulated tubes can confirm the diagnosis [Schuff-Werner 2013].

Although a common but relatively rare in vitro phenomenon with a prevalence ranging from 0.1 to 2.1% [Cohen 2000; Erkurt 2014], anticoagulant-induced PTCP might result in unjustified clinical decisions, such as cancellation of elective invasive interventions. We therefore recommend verifying low routine platelet counts with magnesium anticoagulated blood before the final therapeutic decision is made.

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