Amiodarone-Induced Thrombocytopathy

A. Berrebi, M. Shtalrid, E.J. Vorst, Hematology Unit, Kaplan Hospital, 76100 Rehovot (Israel)

Amiodarone is a benzofurane-derived antiarrhythmic agent. The side effects of the drug include photosensitivity rash, peripheral neuropathy, and thyroid function disturbances [1]. Interaction with drugs has also been described, especially increased plasma digoxin concentration [2], potentiation of warfarin [3, 4], and adverse reaction with quinidine [5].

We would like to report a hitherto undescribed side effect of amiodarone. A 52-year-old male patient presented to our clinic with giant hematomas on his right arm which appeared a few days previously. He also complained of longstanding gingival bleeding and subcutaneous ecchymoses of his legs. On past medical history he had mild diabetes controlled by diet only and an old nonactive duodenal ulcer, non-treated. He suffered from a severe myocardial infarction 5 years earlier, and a coronary bypass operation was performed 4 years ago. At presentation he was on the following medication: Adalat (nifedipine), Isocardide (isosorbide dinitrate), Fusid (furosemide), Trasicor (oxyprenolol hydrochloride), slow K (potassium chloride), and Cordarone (amiodarone hydrochloride); Cordarone was taken for only 6 months. On physical examination, a giant ecchymose was seen on the right arm, and few other ecchymoses on his two legs. Further physical examination was normal.

The laboratory findings were as follows: hemoglobin 16.0g/dl, hematocrit 0.49, leukocytes $10^9\text{/L}$ with normal differential count, platelets $360\times10^9\text{/L}$. Alkaline phosphatase, SGOT, SGPT, LDH, serum proteins and electrophoresis, bilirubin, serum lipids were all within normal limits. The coagulation tests revealed: fragile clot with poor retraction, prothrombin activity 100%, activated partial thromboplastin time 47 s (normal 35–55 s), fibrinogen 3.4 g/l. The euglobulin lysis time was normal, the bleeding time (Duke) > 15 min.

Platelet aggregation tests showed a markedly decreased reaction with adenosine diphosphate, adrenalin, and ristocetin (fig. 1).

In order to look for a drug as a causal agent of the thrombocytopathy, we decided first to stop the drug, that he had taken for the shortest time, i.e., Cordarone. Within 2 months after withdrawal the gingival bleeding stopped, the ecchymoses disappeared, and on testing the platelet aggregation again we found a clear improvement (fig. 1).

To the best of our knowledge, no interaction between this drug and platelet function was described previously. Since amiodarone has been found to interact with other drugs, we cannot exclude such an interaction with one of the patient’s medications, resulting in the disturbance of platelet function.
As this drug is widely used in patients also receiving anticoagulants, this side effect had to be emphasized.

The yellow crystals were seen in about 20–30% of the neutrophils and the number varied from 2 to 10 per cell. They measured $3.5 \times 1.5 \mu m$ on an average.

Fig. 1a. Thin smear (Leishman) showing two crystals in a neutrophil. b Same field in polarized light: bright birefringent rhomboids. $\times 1,200$.

Fig. 1. Platelet aggregation with ADP(a), adrenalin (b), and ristocetin (c) using FragUigraph model D.

= Patient’s platelets at presentation;  
= patient’s platelets 2 months later;  
= control platelets resuspended in patient’s plasma.

References


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Bilirubin Crystals in Neutrophils of Jaundiced Neonates and Infants

A few investigations were carried out following the observation of yellow rhomboidal crystals within neutrophils in a severely jaundiced 2-month-old infant suffering from Pseudomonas septicemia. The results are briefly reported below.

Of 42 neonates and infants with very high serum unconjugated bilirubin (UCB 21.1. ± 5.08 mg/dl), 36 showed these crystals in the neutrophils. 14 children and adults with jaundice (UCB 3.29 ± 1.96 mg/dl) did not show such crystal formation. In all the cases blood samples collected in EDTA vials were used for preparing thin and buffy coat smears that were stained by using Leishman’s stain (fig. 1).

Direct smears of blood from the cases with high UCB and smears from different vials containing heparin, double oxalate, and citrate and from defibrinated blood did not show any crystals in neutrophils. These were only seen in blood samples with high UCB that were collected in EDTA vials and allowed to stand for over 30 min.