Case Report

Valproic Acid Associated Platelet Dysfunction: Case Report

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SUMMARY

Valproic acid is commonly used as an anticonvulsant. It has been shown to inhibit the secondary phase of platelet aggregation. This can be reflected in increased bleeding times and haemorrhage. We describe a case of a 56-year-old male with a history of bleeding during a previous operation. He had valproic acid associated platelet dysfunction.

Keywords: Valproic acid; Platelet aggregation; Platelet function tests; Preoperative care; Haemorrhage.

INTRODUCTION

Preoperative evaluation of bleeding disorders relies heavily on history taking. The first step is to establish if the patient has had a history of major surgery and/or trauma and whether there was any significant bleeding associated with these events. If previous major surgery and/or trauma had not been associated with significant bleeding then surgery can proceed. When the patient has had no history of major surgery or trauma, history still remains important to establish the likelihood that the patient has an acquired bleeding disorder or the likelihood of an inherited bleeding disorder in the patient and/or in close relatives. Drug history must be considered when one is evaluating for an acquired bleeding disorder.

CASE REPORT

A 56-year-old male with recurrent meningioma was preoperatively screened for a bleeding tendency after he gave a history of bleeding during a previous operation for the meningioma. He was on valproic acid for seizure prophylaxis. The full blood count was normal: white cell count (WCC) 9.0, haemoglobin (Hb) 14 and platelet count (Plt) 213; as were prothrombin time (PT) and activated partial thromboplastin time (aPTT). A prolonged PFA-100 bleeding time of 15 minutes led to further investigations. Von Willebrand screening tests; von Willebrand factor antigen (VWF:Antigen), von Willebrand factor-collagen binding activity (VWF:CBA) & von Willebrand factor ristocetin cofactor (VWF:RCo) assay, factor VIII (FVIII) level, and the multimer pattern were all normal. Platelet aggregometry on platelet-rich plasma showed lack of aggregation with arachidonic acid (AA) but there was aggregation with adenosine diphosphate (ADP), epinephrine (EPI), Collagen (Col), and ristocetin (Figure 1). These findings were suggestive of a drug induced platelet dysfunction. Since valproic acid was the only drug which the patient was taking, it was stopped for two weeks under close monitoring for seizures. The bleeding time and platelet function tests were then repeated. The bleeding time normalised and the platelet function tests were all normal. The patient proceeded with the operation which was uneventful.

DISCUSSION AND CONCLUSION

There are no standard guidelines on the testing and interpretation of platelet function tests [1] but lack of aggregation with only AA acid is found in the

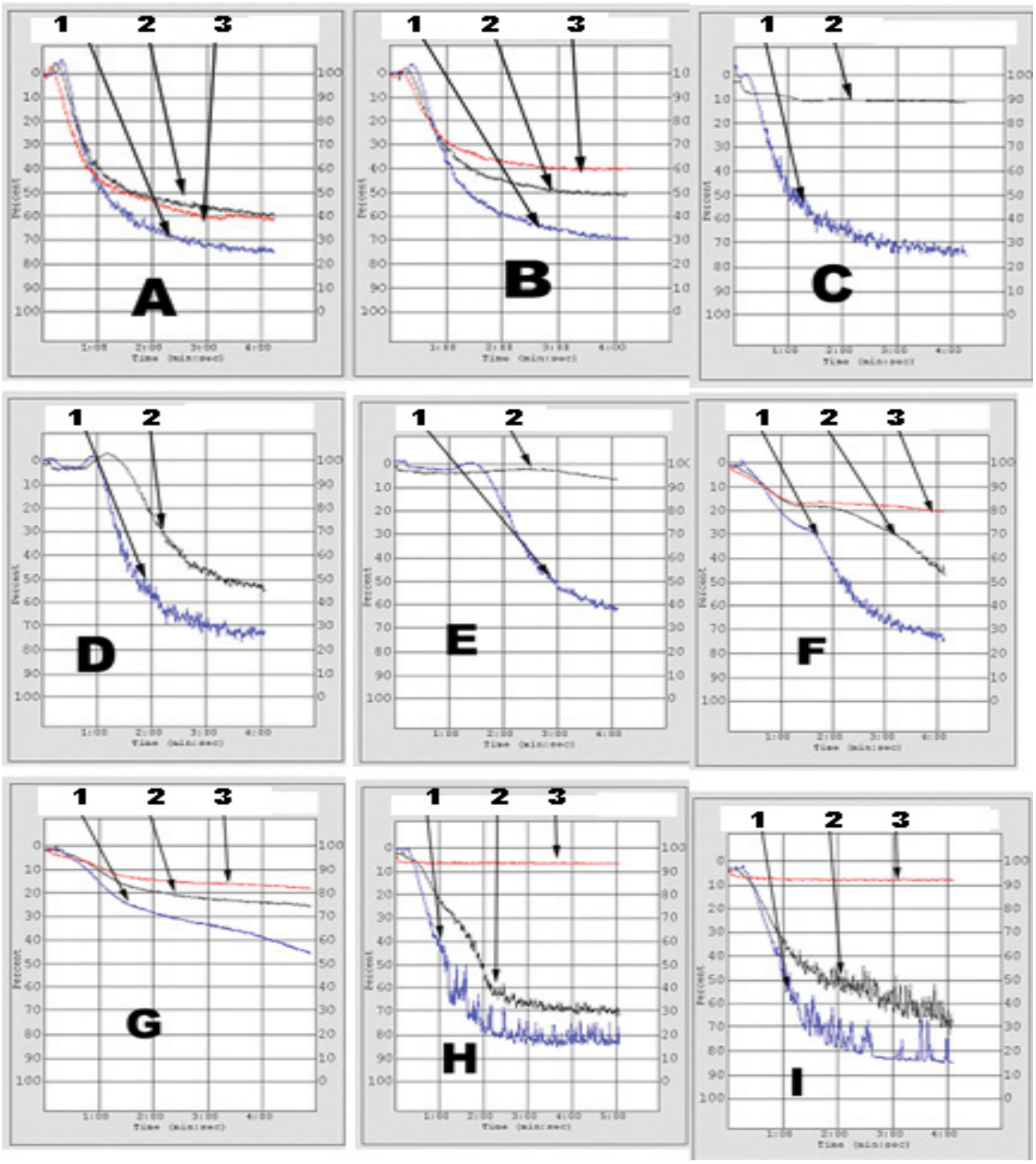

Figure 1. Aggregometry results. (A and B) adenosine diphosphate (ADP); (A) is control and (B) is patient's sample. Traces 1, 2 and 3 represent high, medium and low concentrations of ADP respectively. Graph (B) shows aggregation with ADP. (C) Arachidonic acid (AA); Trace 1 is control and Trace 2 is patient's sample. There was no aggregation with AA. (D and E) Collagen (Col); (D) is control and (E) is patient's sample. Traces 1 and 2 represent high and low concentrations of Col. (E) shows aggregation with Col. (F and G) epinephrine (EPI); (F) is control and (G) is the patient's sample. Traces 1, 2 and 3 represent high, medium and low concentration of EPI. (G) shows aggregation with EPI. (H and I) ristocetin; (H) is control and (I) is patient's sample. Traces 1, 2 and 3 represent high, medium and low concentrations of ristocetin respectively. (I) shows aggregation with ristocetin.

so called "aspirin-like defect" [1] of platelets which is seen in patients taking aspirin and other drugs. The lack of aggregation with AA implies inability by the platelets to produce thromboxane A2 which is required for the AA agonist to induce platelet aggregation. Platelet aggregation testing with AA has been suggested as the ideal test to perform before all other aggregation tests to screen for induced platelet dysfunction. [2] It should of course be noted that the impedance-based whole blood platelet aggregation test may give different aggregometry patterns to the ones obtainable by the method we used (optical-based platelet-rich plasma test). [3]

An association between valproic acid and excessive bleeding during surgery has been well described. [4-5] Valproic acid may affect both platelet count and function (thereby prolonging bleeding time) and coagulation factors such as fibrinogen and factor VIII. [6-7]

This case emphasises the role of a proper medication history in the workup of a patient with a bleeding diathesis.

FOOTNOTES

Conflicts of interest: The authors declare no competing conflicts of interest

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