Abstract: This case report presents anaphylactic shock in which hyperfibrinolysis was diagnosed with Thromboelastography (TEG). A 45 year old female patient was scheduled for vacuum-assisted wound closure. At induction, she developed an anaphylactic shock that stabilized after standard treatment. TEG analysis revealed hyperfibrinolysis. Surgery was delayed and there were no signs of spontaneous bleeding. A repeat TEG analysis performed 30 minutes later showed a completely normalized coagulation pattern. Few reports have documented the association between anaphylactic shock and hyperfibrinolysis. This case illustrates the transient and short-lived nature of the phenomenon. The mechanisms and potential consequences are discussed.

Key words: Anaphylaxis ; fibrinolysis ; thromboelastography ; tranexamic acid ; mast cell.

Introduction

Anaphylactic shock is a rare but possibly lethal complication of anesthesia (1, 2). Insight into the pathophysiology is growing and clear guidelines exist for effective management of this possibly devastating condition. However, clinical awareness about the association of anaphylactic shock with hyperfibrinolysis is less well established.

Case Description

A 45 year old female patient presented for vacuum-assisted wound closure therapy. She had undergone multiple operations including gastric sleeve resection, abdominoplasty and a bilateral femoral hernia repair complicated by the development of a fistula for which a fistulectomy was performed. There were never any anesthetic problems during these interventions. However, because of poor surgical result, the patient was now scheduled for wound debridement and installation of vacuum-assisted closure therapy.

After preoxygenation with 100% oxygen and administration of 5 mg dexamethasone, induction of anesthesia was performed with propofol 200 mg, sufentanil 20 μg and cisatracurium 12 mg. Blood pressure and heart rhythm remained normal during mask ventilation. Suddenly, the monitor failed to measure saturation and blood pressure. Clinically a weak carotid artery pulse was palpated. Her extremities were cyanotic and mask ventilation became extremely difficult with wheezing at auscultation. The diagnosis of anaphylactic shock was made and therapy was started. After intubation, the patient was ventilated with 100% oxygen. The first measured end-tidal CO2 was 12 mmHg. Two liters of extra intravenous fluids with ringer lactate were infused and epinephrine was initially administered in aliquots of 100 μg. A total dose of 2.5 mg was given. A continuous infusion of epinephrine was not necessary.

After 20 minutes, hemodynamic stability was achieved with complete disappearance of the wheezing. Clemastine, hydrocortisone and ranitidine were administered. Surgery was cancelled and the patient was admitted to the intensive care unit for further sedation and ventilation. Before transfer to the ICU, a blood sample was taken for the determination of mast cell tryptase (MCT) and at the same time a thromboelastography (TEG) analysis was performed.

This TEG analysis revealed hyperfibrinolysis (Fig. 1). Because no surgery had taken place and there were no clinical signs of coagulopathy, no antifibrinolytic therapy was started. Repeat TEG analyses were planned every 30 minutes until normalization of the coagulation was seen. The next TEG analysis had already normalized (Fig. 2).
The patient could be weaned without problems and was discharged from the ICU in good clinical condition.

The MCT measured about one hour after the start of the anaphylactic shock was 270 μg/L (normal value: < 10 μg/L).

A written permission to report this case was given and an appointment with allergy clinic was scheduled for further investigation. Unfortunately the patient didn’t show up, leaving us with an incomplete biologic and allergological work-up:

(a) A baseline MCT to compare to and to differentiate from mastocytosis could not be determined.

(b) Without skin tests, the culprit agent, the pathophysiological mechanism and possible safe alternatives were not identified (1). The general practitioner was contacted to hasten the patient to complete this work-up, emphasizing the importance of a...
complete allergologic diagnosis to determine a safe anesthetic plan for future surgery.

**DISCUSSION**

Because Anaphylaxis is a possible life-threatening condition, attention is focused primarily on fast diagnosis and treatment. Up-to-date guidelines uniformly aim at gaining rapid control over the circulatory shock and bronchospasm (1, 2).

Few reports have commented on the effect of anaphylaxis on the coagulation. In 1994 MAZZI et al. reported a case of hyperfibrinolysis in a patient with anaphylactic shock after a sting bite (3). Although a paucity of case-reports have been publicized on this phenomenon (4, 5, 6), there are several lines of laboratory research that investigated the link between mast cells, the molecules they produce, and the coagulation system.

Fibrinolysis in vivo is a complex process (7). Plasminogen is activated to plasmin, when it binds with fibrin. The trypsin-like serine proteinase tryptase is able to activate uPA (8) and SILLABER et al. isolated the uPA receptor on the cell surface of mast cells (9). These authors also showed that mast cells produce and release tPA without the production of PAi’s and generate plasmin to induce clot lysis in vitro (10). These properties make the mast cell a very potent "profibrinolytic and antithrombotic cell" as compared to endothelial cells and macrophages, which produce tPA along with its inhibitors (11).

These in vitro observations along with the few case reports, including ours, suggest that anaphylaxis is almost invariably accompanied by a certain degree of fibrinolysis. This may be of particular concern in surgical patients, at risk of severe hemorrhage. In our patient, this risk was deferred because surgery was postponed. However, anaphylaxis can also occur after the start of the surgical procedure. In such scenarios rapid diagnosis and treatment may be of vital importance. De SOUZA et al. treated anaphylaxis-induced fibrinolysis during surgery successfully with tranexamic acid (4). Interestingly, tranexamic acid has been suggested as an additive treatment of anaphylaxis, due to its C1 esterase inhibitor activity and inhibition of plasmin and kallikrein system (12).

### Table 1

Overview of the characteristics of the publicized cases of anaphylaxis associated with fibrinolysis

<table>
<thead>
<tr>
<th>Author, year (number of cases)</th>
<th>Diagnosed allergy</th>
<th>Diagnosis of fibrinolysis</th>
<th>Clinical bleeding</th>
<th>Treatment of coagulopathy</th>
<th>Time course of fibrinolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAZZI et al. (5) 1994 (1)</td>
<td>Insect bite</td>
<td>aPTT, PT, fibrinogen, D-dimers, ATIII, antiplasmin activity</td>
<td>None</td>
<td>None</td>
<td>Normalisation 40 hours after admission</td>
</tr>
<tr>
<td>De SOUZA et al. (4) 2004 (4)</td>
<td>unknown</td>
<td>Gelfusin (TEG)</td>
<td>Not mentioned</td>
<td>200 mg TA, 2 FFP 1 g TA</td>
<td>Normal repeat TEG (40 min after TA) Normal repeat TEG (68 min after TA)</td>
</tr>
<tr>
<td>Case 2 : Gelfusin ( TEHG)</td>
<td>unknown</td>
<td>Gelfusin (TEG)</td>
<td>Not mentioned</td>
<td>500 mg TA 1 g TA</td>
<td>No repeat TEG performed Normal repeat TEG (55 min after TA)</td>
</tr>
<tr>
<td>Case 3 : Gelfusin (TEG)</td>
<td>unknown</td>
<td>Gelfusin (TEG)</td>
<td>Not mentioned</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 4 : Gelfusin (TEG)</td>
<td>unknown</td>
<td>Gelfusin (TEG)</td>
<td>Not mentioned</td>
<td></td>
<td></td>
</tr>
<tr>
<td>De SOUZA et al. (5) 2005 (1)</td>
<td>Unknown</td>
<td>TEG</td>
<td>No clinical sign</td>
<td>200 mg TA, 2 FFP 1 g TA</td>
<td>Normal repeat TEG (1 h 55 min after the event)</td>
</tr>
<tr>
<td>IQBAL et al. (6) 2010 (1)</td>
<td>Amoxicillin</td>
<td>TEG</td>
<td>No clinical Sign</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(TA : Tranexamic Acid).

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Our report and others show that the fibrinolysis is probably short lived. Iqbal et al. diagnosed anaphylaxis induced fibrinolysis using TEG before cardiopulmonary bypass. Reanalysis four hours later showed that the fibrinolysis had resolved without antifibrinolytic treatment and without haemostatic problems (6).

De Souza published one case of anaphylactic shock with spontaneous resolved fibrinolysis. The second TEG in this report was done about 2 hours after the first (5). Our second TEG had already normalized within 30 minutes.

Although we didn’t need to use tranexamic acid in our treatment strategy, tranexamic acid should be considered when anaphylaxis occurs during major surgery or in refractory anaphylactic shock (4, 12).

In conclusion, this case report reactivates the anesthesiologist’s clinical awareness of hyperfibrinolysis associated with anaphylactic shock. The phenomenon is probably short lived, but may cause severe hemorrhage during surgery. For that reason, prospective monitoring of the coagulation status and rapid treatment with tranexamic acid should be considered.

References


