BRIEF COMMUNICATIONS

DOES ACQUIRED ANGIOEDEMA INCREASE THE RISK OF SURGERY WITH CARDIOPULMONARY BYPASS?

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Acquired angioedema is a rare condition characterized by the deficiency of C1 inhibitor (C1-INH). This results in continuous activation of the classical pathway, leading to consumption of its components (C1, C2, and C4), and impairs the regulation of the complement and contact systems, coagulation, and fibrinolysis. Potentially lethal complications may ensue in such patients, including laryngeal edema, acute abdominal syndromes mimicking surgical emergencies, and hemorrhagic diathesis.¹⁻³ Cardiopulmonary bypass (CPB) determines complement activation because of contact of blood with artificial surfaces and may result in increased vascular permeability, acute pulmonary failure resembling adult respiratory distress syndrome, multiorgan failure, and bleeding disorders.² Anecdotal reports regarding favorable² or unfavorable³ outcomes after cardiac surgery are reported in the literature in patients with acquired angioedema, but the stratification of surgical risk is difficult to assess because of the paucity of data.

Clinical summary. A 62-year-old patient with a 7-year history of acquired angioedema of autoimmune origin was referred to our institution for the evaluation and treatment of coronary artery disease. Recent history included inferior myocardial infarction and postinfarction Canadian Cardiovascular Society class III angina pectoris despite adjusted anti-ischemic medications. Cardiac catheterization and coronary angiography revealed preserved ventricular function and critical lesions of the left anterior descending artery, ramus intermedius branch, and right coronary artery not amenable to interventional cardiology techniques.

The patient was scheduled for surgery despite the presence of acquired angioedema. Standard coronary artery bypass grafting with extracorporeal circulation and cardioplegia was performed in normothermic conditions with the use of a cen-

trifugal pump. The left internal thoracic artery was grafted to the left anterior descending artery, and two single saphenous vein grafts were performed on the ramus intermedius and the right posterior descending artery. Aortic crossclamp time and CPB time were 43 and 57 minutes, respectively. A hollow-fiber oxygenator was used. During the operation and the early postoperative hours, administration of tranexamic acid (10 mg/kg bolus followed by 5 mg · kg⁻¹ · h⁻¹ infusion for the first 12 hours) was the only prophylactic measure against acquired angioedema. C1-INH was available but was not used. Bleeding conditions were satisfactory (total, 490 mL), and the patient was weaned from respiratory support 5 hours after the operation with no respiratory complications before or after extubation. The following postoperative course was uneventful. The patient was discharged on the seventh postoperative day. Oral medications included ticlopidine, 250 mg, and ranitidine, 300 mg. Measurement of complement components throughout the procedure demonstrated a stable depletion of the components of the classical pathway (C1q and C4) and of its regulator (C1-INH) as expected in patients with acquired angioedema. On the other hand, the levels of C3, the key component of the system in which all complement-activating pathways converge, showed a progressive decrease from a preoperative level of 99% of normal value to a level of 73% at the end of CPB.

Discussion. Acquired angioedema is characterized by deficiency of C1-INH, resulting in continuous activation of the classical complement pathway, leading to consumption of its components, and impairing the regulation of the complement and contact systems, coagulation, and fibrinolysis. Cardiac operations requiring CPB in patients with acquired angioedema are considered potentially at increased risk because of complement activation related to contact of blood with artificial surfaces and may result in increased vascular permeability, adult respiratory distress syndrome, and coagulopathy.

A successful case presented in recent years was performed with adjunctive measures against potential complications related to acquired angioedema, such as aprotinin administration⁴ and prophylactic infusion of C1-INH and antithrombin III.

Some aspects of surgical strategy must be stressed and may have important implications:

1. Despite relatively young age and the absence of classical specific contraindications, bilateral internal thoracic artery harvesting was avoided to minimize dissection of tissues, surgical trauma, and potential bleeding sources.

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2. A hollow-fiber oxygenator and a centrifugal pump were selected to reduce complement activation, denaturation of plasma proteins, and impairment of platelet function. In fact, a case report concerning an unsuccessful operation³ relates to the use of a bubble oxygenator. The only moderate consumption of C3, indicating activation of the alternative pathway, did not cause side effects of clinical relevance.
3. Normothermic CPB was performed to maintain more physiologic conditions.
4. To overcome the possibility that massive protease activation in the absence of C1-INH could lead to activation of the contact system causing complications, such as bleeding, angioedema, or both, tranexamic acid was administered intraoperatively. This antifibrinolytic agent was proved to be effective in long-term prophylaxis of angioedema in patients with acquired angioedema⁵ and has been used to prevent bleeding after CPB, particularly since aprotinin became unavailable in Europe.
5. Considering the satisfactory bleeding conditions at the end of the operation, antithrombin III was not used.

In conclusion, cardiac operations with CPB are probably not at high risk of complications related to acquired angioedema, and adjunctive routine (ie, in the absence of specific complications, namely bleeding and respiratory failure related to acquired angioedema) prophylactic measures may be reduced to intraoperative antifibrinolytic therapy. However, definitive conclusions cannot be stated considering the low number of cases.

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