

Laparoscopic Splenectomy in a Patient with Acquired Angioneurotic Edema

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ABSTRACT

Background: We report the case of a 77-year-old female with acquired angioneurotic edema, C1 esterase inhibitor level = 4mg/dL, who was scheduled to undergo a laparoscopic splenectomy.

Methods: In the operating room, we administered on call 500 units (UI) of C1 esterase inhibitor concentrate intravenously. Intraoperative hemodynamic instability and generalized blood oozing improved following the administration of aprotinin 250 000 UI intravenous (IV) drip.

Conclusion: We recommend the administration of an antifibrinolytic agent in addition to C1 esterase inhibitor concentrate in patients with acquired angioneurotic edema.

Key Words: Laparoscopic splenectomy, Acquired angioneurotic edema, Aprotinin.

INTRODUCTION

Angioneurotic edema is a demarcated painless, nonpruritic, nonpitting edema of the deep dermis and subcutaneous tissue. It usually involves the face, upper airway, gastro-intestinal tract and extremities.¹ Osler² in 1888 demonstrated the hereditary nature of the disease. In the early 1960s, hereditary angioneurotic edema (HAE) was shown to be caused by deficiency of C1 esterase inhibitor, also called C1 inhibitor (C1INH).^{3,4} In 1972, an acquired form of C1INH deficiency (AAE) was first reported.⁵

We report the case of a woman with acquired angioneurotic edema who underwent laparoscopic splenectomy and experienced intraoperative hemodynamic instability and bleeding in the immediate postoperative period.

CASE REPORT

A 77-year-old female who weighed 60 kg and had splenomegaly associated with anemia and neutropenia was scheduled to undergo a laparoscopic splenectomy. Two years prior to the present admission, she had an episode of upper airway edema following a tooth extraction. She also suffered from recurrent episodes of abdominal pain and swelling of the upper extremities and the face, which was diagnosed as angioneurotic edema. The diagnosis was confirmed by a low level of C1 esterase inhibitor (C1INH) of 4 mg/dL (normal =11-26 mg/dL).

On the morning of the scheduled laparoscopy, 500 units (UI) of C1INH concentrate was given intravenously on call in the operating room. The patient was premedicated with glycopyrrolate 0.2 mg intramuscular (IM) and diazepam 5 mg per os. Anesthesia was induced with propofol 2 mg/kg, vecuronium 0.1 mg/kg, fentanyl 2 mg/kg, and midazolam 1 mg, and was maintained with isoflurane 1% in nitrous oxide:oxygen (2:1). The patient was stable during the first hour of surgery; her systolic blood pressure varied between 110-115 mm Hg, and her heart rate varied between 50-60 beats/min. Suddenly, her heart rate dropped to 30 beats/min, and her systolic blood pressure dropped to 30 mm Hg. Two units of

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packed red blood cells and two units of Hemacel were rapidly infused. Also, multiple doses of ephedrine (a total of 30 mg) and phenylephrine (a total of 100 mg) were administered. The blood pressure was only raised to 60/20 mm Hg. Epinephrine 0.2 mg was then administered as a bolus, which increased the blood pressure to 90 mm Hg. Epinephrine drip was then started and titrated according to the blood pressure. Also, the patient received an additional dose of C1INH concentrate (1000 UI), two units of blood, and two units of fresh frozen plasma. The spleen was completely mobilized, placed in a bag, and brought out through the umbilical trocar. The incision was widened so that the spleen could be removed. The size of the spleen was 27 x 13 x 7 cm. At the end of the procedure, neuromuscular blockade was reversed with a mixture of neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg, and the trachea was extubated.

In the recovery room, extensive bleeding from the abdominal drain was observed. Exploratory laparotomy did not reveal any surgical bleeding, but generalized oozing from the raw surface was discovered. Aprotinin 250 000 UI was administered as an IV drip for 30 minutes and was followed by a significant decrease in bleeding. The epinephrine drip was decreased progressively and was stopped at the end of surgery. The trachea was extubated during the evening of the surgery, and the patient was discharged 3 days later.

DISCUSSION

HAE is caused by a defective C1INH gene that produces either no C1 esterase inhibitor (type I) or dysfunctional C1INH (type II), which is measurable for antigen but is inactive.⁶ C1INH inhibits the first component of activated complement. In addition, it inhibits the clot-promoting and kinin-releasing plasma enzymes, including activated Hageman factor (factor XIIa), factor XIa, plasma kallikrein, and the fibrinolytic enzyme plasmin.^{7,8} Also, it may be a secondary inhibitor of tissue plasminogen activator.⁹

Acquired C1INH deficiency is caused by the consumption of C1INH or by autoantibodies directed against C1INH. Also, two types of acquired C1INH deficiency have been identified. Type I is induced by malignancy that activates complement or produces idiotype anti-idiotypes or other immune complexes. In contrast, type II is not associated with underlying disorders, except for the presence of an autoantibody that interferes with C1INH activity.¹⁰

Our patient has a case of acquired type I C1INH deficiency as evidenced by the onset of the angioneurotic edema at an old age, absence of a positive family history, and the association with a lymphoproliferative disease.¹¹ The pathology of the excised spleen of the patient manifested non-Hodgkin's lymphoma.

Two events were striking in this case: the intraoperative hemodynamic instability and the postoperative bleeding. These events may be attributed to the activation of the contact phase (factor XII, prekallikrein and high molecular weight kininogen) by surgery¹² and to fibrinolysis. Patients with AAE display signs of activation of the contact phase and the fibrinolysis during basal conditions as well as during attacks. Such activation cannot be explained by a deficiency of C1INH alone, which does not activate the contact phase or fibrinolysis as shown in patients with HAE. Therefore, in addition to C1INH deficiency, some other mechanism for C1 depletion and contact activation must be acting in patients with AAE.¹³ This may explain why the infusion of C1 inhibitor concentrate in our patient did not prevent the intraoperative hemodynamic instability and the postoperative bleeding. Cicardi et al¹⁴ described the high effectiveness of the antifibrinolytic agent tranexamic acid (trans-4-aminoethylcyclohexane-1-carboxylic acid) [AMCA] for prophylaxis in patients with AAE. The effectiveness of AMCA in AAE is significantly greater than that reported for patients with HAE. The mechanism of action of AMCA in AAE patients probably depends on its antiplasmin activity that impairs the release of vasoactive mediators.^{13,15} In our patient, the infusion of aprotinin 250 000 UI was highly effective in providing hemodynamic stability and controlling the raw surface oozing, probably through its antiplasmin and its antikallikrein effects that inhibit the contact phase of coagulation.¹⁶

In conclusion, we present a case of AAE in a patient undergoing laparoscopic splenectomy. The diagnosis of AAE was evidenced by a low level of C1 inhibitor, the onset at old age, absence of a positive family history, and the association with non-Hodgkin's lymphoma as manifested by the pathology of the spleen. The patient was treated prophylactically with C1INH concentrate. Intraoperative hemodynamic instability and postoperative bleeding were controlled successfully with aprotinin. The effectiveness of aprotinin is probably due to its antikallikrein and its antiplasmin effects. We recommend that patients with AAE undergoing elective surgery receive an antifibrinolytic agent in addition to C1INH concentrate.

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