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Perioperative Mannan-Binding Lectin (MBL) Patterns in Cardiac Surgery May Correlate with the Clinical Outcomes in MBL Deficient Patients

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Abstract

Previously we reported a case of abrupt change of postoperative mannan-binding-lectin (MBL) in a patient with preexisting MBL deficiency who expired shortly after cardiac surgery. Herein we report additional cases of 3 more patients with preexisting MBL deficiency who underwent cardiac surgery. Analysis of their blood samples from the perioperative period showed their MBL levels were abruptly increased at 24 hours after surgery. However, 2 patients had a subsequent drop of MBL at 48 hours, and both expired. These data indicated that the postoperative decrease of MBL may have been related with an unfavorable outcome after cardiac surgery.

There are three pathways in the complement system: (1) the classical pathway, (2) the alternative pathway, and (3) the lectin pathway. Each is activated by specific initiators: C1 for the classical pathway, factor B for the alternative pathway, and mannan-binding-lectin (MBL) for the lectin pathway. All three pathways converge to C3 and are then followed by a common cascade [1].

To further elucidate the pattern of MBL activity in cardiac surgery and their potential correlation with outcome, we studied the perioperative pattern of MBL in 3 patients with MBL deficiency and who underwent cardiac surgery. Early factors in the other two complement pathways were also studied.

We previously reported a postoperative pattern of abrupt increase followed by decrease of complement MBL in a patient with preexisting MBL deficiency who expired 10 days after successful cardiac surgery [2]. Our interpretation was that fresh frozen plasma MBL transfusion was consumed in mediating a lethal systemic inflammation. A recent study also found that fresh frozen plasma transfusion in patients with MBL deficiency was associated with MBL reconstitution and multiple organ dys-function syndrome [3].

This study was approved by the institutional review board of the State University of New York Downstate Medical Center. Three adult patients had consented to undergoing elective open heart surgery with cardiopulmonary bypass (CPB) and were enrolled into the study. All 3 patients were female African Americans (age: patient 1, 73 years; patient 2, 46 years; patient 3, 65 years). Patient 1 was diagnosed with aortic insufficiency and mitral

regurgitation. Patient 2 was diagnosed with severe mitral regurgitation, moderate pulmonary hypertension, and systemic lupus erythematosus. Patient 3 was diagnosed with left main coronary artery disease with occluded percutaneous coronary intervention right coronary artery stent, post-transient ischemic attack, and hypertension.

Peripheral blood samples were obtained from all 3 patients at 7 predefined time points in the preoperative, intraoperative, and postoperative periods: (1) preoperatively before the skin incision, (2) after the skin incision and prior to the sternotomy, (3) 5 minutes after CPB was started, (4) 5 minutes after stopping aortic cross clamping, (5) 5 minutes after CPB cessation, (6) postoperatively on day 1, and (7) postoperatively on day 2. Plasma levels of MBL were measured by an enzyme-linked immunosorbent assay kit from Cell Sciences (Caton, MA). Active fragment of factor B, Bb, was measured by an enzyme-linked immunosorbent assay kit from Quidel (San Diego, CA). C1q enzyme-linked immunosorbent assay was adapted from the method developed by Quidel.

Three patients with deficient MBL levels underwent open heart surgery (1,000 ng/mL is considered sufficient for full activity of MBL pathway). These patients had normal levels of C1q (the initial component of the classical complement pathway) and factor B (an early component of the alternative complement pathway). The MBL levels of all patients peaked on postoperative day 1 (Fig 1). Surge values ranged from approximately threefold (patients 1 and 3) to 93-fold (patient 2). By postoperative day 2, there were 2 patients (ie, patients 1 and 2) who showed an abrupt drop of MBL and experienced postoperative complications, and thus expired within 4 months after surgery. The increased MBL levels in patient 3 were sustained by postoperative day 2. She had no significant postoperative complications and was discharged on postoperative day 7. She recovered uneventfully.

Comment

We previously reported a postoperative pattern of abrupt MBL increase and decrease in a patient with preexisting MBL deficiency who expired 10 days after successful coronary artery bypass grafting surgery [2]. Herein we report additional cases of 3 patients who had preexisting MBL deficiency and who underwent cardiac surgery with CPB. Two of these patients expired with similar postoperative changes of MBL. Taken together, our results indicated the postoperative pattern of abrupt increase followed by decrease of MBL may be related with an unfavorable outcome after cardiac surgery.

One possible mechanism to explain our findings is that the sudden influx of exogenous MBL into these MBL deficient patients activates a complement cascade, thus leading to systemic inflammation. The MBL may target certain patterns of carbohydrate structures or natural immunoglobulin-M ischemic antigen complex [4], which are likely exposed during the global heart ischemia through aortic cross clamping. This hypothesis is supported by a recent report that reperfusion of regionally ischemic hearts had a favorable clinical outcome in MBL-deficient patients [5]. It is interesting to note that reperfusion in these patients were achieved without blood transfusion; thus no exogenous MBL were infused.

In our study, the patient who had favorable recovery had a sustained postoperative MBL level, indicating that infused exogenous MBL was not consumed and activated as with the other patients. A possible explanation is that in this patient the target(s) for MBL was not fully exposed in cardiac surgery. Supporting this hypothesis is that this patient had the shortest aortic clamping duration and CPB time. Therefore, the patient had the least global heart ischemia in comparison with the others. Although this study is descriptive, it cannot claim causality, as our interpretation of findings merely supports previous experimental models and justifies the need for future studies.

The MBL deficiency is not uncommon and occurs in about 5% of normal human population [6,7]. However, MBL deficiency is not routinely tested before open heart surgery. If our hypothesis is true that MBL deficiency may affect the outcomes of patients undergoing open heart surgery with aortic cross clamping, preoperative screening for MBL deficiency will become important, and necessary perioperative management should be implemented. Further investigations are needed to delineate the correlation and possible predictive value of MBL-mediated inflammatory response with clinical outcomes.

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Fig 1.

Perioperative mannan-binding-lectin (MBL) changes in patients who had MBL deficiency and who were undergoing cardiac surgery. Plasma samples were collected at 7 time points preoperatively, intraoperatively, and postoperatively: (1) preoperatively before skin incision, (2) after skin incision and prior to the sternotomy, (3) 5 minutes after cardiopulmonary bypass (CPB) started, (4) 5 minutes after stopping aortic cross clamping, (5) 5 minutes after CPB cessation, (6) postoperatively on day 1, and (7) postoperatively on day 2. The MBL enzyme-linked immunosorbent assay (ELISA) was performed using a human MBL ELISA kit according to the instructions by the manufacturer (Cell Sciences, Caton, MA).