Changes in coagulation condition, cytokine, adhesion molecule after repair of type A aortic dissection


Cardiovascular Surgery, National Hospital Kure Medical Center, Hiroshima, Japan

Received 16 January 2004; received in revised form 30 April 2004; accepted 3 May 2004; Available online 1 June 2004

Abstract

Objective: Because residual dissection often exists even after the repair of a type A dissection, we evaluated coagulation conditions, cytokine levels, and adhesion molecule levels in mid-term follow up after repair of type A dissections. Methods: Thrombin–antithrombin III complex (TAT), D-dimer, soluble interleukin-2 receptor (sIL-2R), soluble intercellular adhesion molecule (sICAM)-1, and type III procollagen peptide (PIIIP) were measured in 12 patients (mean age = 63 years) following the repair of a type A aortic dissection at 6–82 months after repair (median = 33 months). Results: In the chronic phase, TAT and D-dimer were significantly higher in patients following the repair of a type A dissection compared to healthy controls (TAT; 12 ± 8 vs. 2.5 ± 1.2 ng/ml, \( P \leq 0.0001 \), D-dimer; 779 ± 1384 vs. 104 ± 46 U/ml, \( P = 0.0001 \)). Cytokine was significantly higher in the affected patients (sIL-2R; 556 ± 205 vs. 398 ± 132 U/ml, \( P = 0.003 \), sICAM-1; 255 ± 131 vs. 211 ± 48 ng/ml, \( P = 0.136 \)). Collagen turnover (PIIIP) showed a significantly higher value in the affected patients (0.80 ± 0.32, vs. 0.58 ± 0.13 U/ml, \( P = 0.002 \)). sIL-2R, sICAM-1 and PIIIP showed a negative correlation with the follow-up period (sIL-2R; \( r = -0.733, P = 0.0067 \), sICAM-1; \( r = -0.61, P = 0.035 \), PIIIP; \( r = -0.692, P = 0.0126 \)). We found a positive correlation between aortic size and TAT (\( r = 0.644, P = 0.0238, n = 12 \)) as well as with D-dimer (\( r = 0.7831, P = 0.0106, n = 12 \)) and TAT showed significantly higher values in the residual dissection group compared to those without residual dissection (16.6 ± 7.9 vs. 7.45 ± 4.75 ng/ml, \( P = 0.035 \)). Conclusion: Hypercoagulation conditions continued even after repair. Both TAT and D-dimer would be good indices for following up patients having repaired aortic dissections. Furthermore, cytokine, adhesion molecules, and collagen turnover would return to a stable state unless impairment and expansion of the vessel wall occurred.

© 2004 Elsevier B.V. All rights reserved.

Keywords: Coagulopathy; Aortic dissection; Cytokine; Adhesion molecule; Collagen turnover; Follow up

1. Introduction

Aortic dissection is characterized by an acute phase and a chronic phase. In the acute phase, consumed platelets and coagulation factors, while forming a thrombus in the dissected lumen, resemble disseminated intravascular coagulation (DIC) [1–3]. In the chronic phase, a residual dissection still often exists similar to chronic type B dissections even after the repair of a type A dissection. This study was designed to clarify the coagulation conditions, and evaluate changes over time in cytokine levels, adhesion molecule production, and collagen turnover in the patients with a repaired Type A aortic dissection.

2. Subjects and methods

From 1996 to 2002, 27 patients underwent surgical procedures for Type A aortic dissections (involving the descending aorta: 20, not involving the descending aorta: 7, total arch replacement with four branched grafts: 17, graft replacement for the ascending aorta: 8, hemiarch graft replacement: 2). Twenty-one out of 27 (78%) survived the procedure. Causes of death were mesenteric necrosis: 1, cerebral infarction: 2, shock: 2, and arrhythmia: 1. Twelve of these surviving twenty-one patients were randomly selected for participation in this study (involving the descending aorta: 10, not involving the descending aorta: 2). Ages ranged from 42 to 83 years old (mean age was 63 years). Aged volunteers served as controls, and volunteer numbers were different in each test ranging from fifteen cases to seventy-two cases, with a mean age of 70 years.
Blood samples were taken from the patients with consent to measure Thrombin–antithrombin III (TAT ng/ml, by ELISA), plasma D-dimer (U/ml by ELISA), sIL-2 receptor (sIL-2R U/ml, by cell free IL-2R ELISA, EURO/DPC Ltd), soluble ICAM-1 (sICAM-1 ng/ml, by ELISA), serum type III procollagen peptide (PIIIP U/ml, by IRMA CIS bio international). Blood samples were taken at approximately the same period of follow-up during which computed tomography was examined. Dissected aortic aneurismal size was measured with computed tomography, which was sliced into 1 cm widths.

Results are expressed as mean ± SD. Data was analyzed using the student-\(t\) test. The relationship between markers and dissecting aneurismal size was assessed using linear regression analysis. A \(P < 0.05\) was considered to be statistically significant.

3. Results

In the acute phase, which we defined as just prior to operation, blood data from the patients with acute Type A dissection \((n = 4)\) showed that TAT \((45.3 ± 17.4\ ng/ml)\) as well as D-dimer \((13850 ± 20190\ U/ml)\) had tremendously higher levels than controls (\(2.5 ± 1.2\ ng/ml; n = 66, P = 0.0001, 104 ± 46\ U/ml; n = 72, P = 0.0001\), respectively).

sIL-2R showed significantly higher values in patients with acute Type A dissection compared to controls \((748 ± 250\ U/ml; n = 4, vs. 398 ± 132\ U/ml; n = 39, P = 0.0001)\). ICAM-1 did not show a difference compared to the control group \((248 ± 124\ ng/ml; n = 4, vs. 211 ± 48\ ng/ml; n = 26)\).

PIIIP showed a higher level in Type A aortic dissection \((0.77 ± 0.19\ U/ml; n = 4, vs. 0.58 ± 0.13\ U/ml; n = 15)\).

In the chronic phase, which we defined as at least six months after the operation (6–82 months), TAT and D-dimer levels were still significantly higher in patients with repaired type A dissection compared to healthy controls (TAT; \(12 ± 8\ (n = 12)\ vs. 2.52 ± 1.21\ (n = 66)\ ng/ml, \(P = 0.0001)\,\ D\text{-dimer; } 779 ± 1384\ (n = 12)\ vs. 104 ± 46\ U/ml, \(P = 0.0001)\). Blood samples were taken at approximately the same period of follow-up during which computed tomography was examined. Dissected aortic aneurismal size was measured with computed tomography, which was sliced into 1 cm widths.

Results are expressed as mean ± SD. Data was analyzed using the student-\(t\) test. The relationship between markers and dissecting aneurismal size was assessed using linear regression analysis. A \(P < 0.05\) was considered to be statistically significant.

3. Results

In the acute phase, which we defined as just prior to operation, blood data from the patients with acute Type A dissection \((n = 4)\) showed that TAT \((45.3 ± 17.4\ ng/ml)\) as well as D-dimer \((13850 ± 20190\ U/ml)\) had tremendously higher levels than controls (\(2.5 ± 1.2\ ng/ml; n = 66, P = 0.0001, 104 ± 46\ U/ml; n = 72, P = 0.0001\), respectively).

sIL-2R showed significantly higher values in patients with acute Type A dissection compared to controls \((748 ± 250\ U/ml; n = 4, vs. 398 ± 132\ U/ml; n = 39, P = 0.0001)\). ICAM-1 did not show a difference compared to the control group \((248 ± 124\ ng/ml; n = 4, vs. 211 ± 48\ ng/ml; n = 26)\).

PIIIP showed a higher level in Type A aortic dissection \((0.77 ± 0.19\ U/ml; n = 4, vs. 0.58 ± 0.13\ U/ml; n = 15)\).

In the chronic phase, which we defined as at least six months after the operation (6–82 months), TAT and D-dimer levels were still significantly higher in patients with repaired type A dissection compared to healthy controls (TAT; \(12 ± 8\ (n = 12)\ vs. 2.52 ± 1.21\ (n = 66)\ ng/ml, \(P = 0.0001,\ D\text{-dimer; } 779 ± 1384\ (n = 12)\ vs. 104 ± 46\ U/ml, \(P = 0.0001)\).
the residual dissection group compared to those without residual dissection (16.6 ± 7.9 vs. 7.45 ± 4.75 ng/ml, \( P = 0.035 \)). D-dimer, sIL-2R, ICAM-1, and PIIIP did not show significant differences (D-dimer; 434 ± 169 vs. 338 ± 138, \( P = 0.306 \), sIL-2R; 492 ± 219 vs. 621 ± 184, \( P = 0.295 \), ICAM-1; 203 ± 91 vs. 308 ± 152, \( P = 0.177 \), PIIIP; 0.70 ± 0.29 vs. 0.91 ± 0.34, \( P = 0.300 \), respectively).

4. Discussion

Several reports exist which describe disseminated intravascular coagulation with acute aortic dissection [1–3]. Clinical presentations of acute aortic dissection in laboratory findings include anemia, depleting clotting factors, and intravascular coagulopathy resulting from the consumption of platelets and clotting factors in the false lumen [1]. We confirmed coagulopathy in the acute phase of aortic dissection by TAT and D-dimer levels. We also found higher cytokine levels, indicating an inflammatory reaction in this study.

In the chronic phase after the repair of a type A dissection, there are two groups, one with and one without a residual dissection. Nakajima and colleagues [4] reported that TAT and D-dimer showed higher values in patients with residual dissection, and having aortic diameters greater than 45 mm. In our series, TAT levels in patients with residual dissection were higher after a repaired Type A dissection compared to those without residual dissection; however, differences in D-dimer did not reach significance.

Aortic diameter showed a positive correlation with both TAT and D-dimer in patients with repaired aortic dissection in this study, in Nakajima’s study [4], and with true aortic aneurysm [5]. For these reasons, the mutual relationships between aortic aneurysm with or without dissection, and with coagulation condition were investigated during the follow-up period.

Evaluation over time after the repair of Type A dissection demonstrated a significant positive correlation with sIL-2R, ICAM-1 and PIIIP, but not with TAT and D-dimer. Therefore, it might be suggested that coagulopathy still continued even after the repair of a Type A dissection; however, molecular and biological changes on aortic walls such as cytokine, adhesion molecules, and collagen turn over decreased and stabilized unless a new episode of aortic wall impairment or expansion occurred.

Time course studies of sIL-2, ICAM-1, and PIIIP after surgical repair of Type A dissection showed no differences between those with and without residual dissection in this study, which was not expected; however, during the mid-term follow-up period, after the dissected aorta was remodeled and vessels were repaired, levels of cytokine and adhesion molecules, as well as collagen turn over stabilized.

5. Conclusion

Our findings suggest that a hypercoagulation condition continues during mid-term follow-up (median of 33 months). Because sIL-2 R, sICAM-1 and PIIIP showed decreased levels as time passed, cytokine, adhesion molecule and collagen turnover would eventually stabilize in a mid-term follow up unless an impairment and expansion of vessel wall occurred. For these reasons, TAT and D-dimer would be good indices for use in the follow up of a patient with a repaired aortic dissection.

Acknowledgements

This study was partially supported by Mitsui Life Social Welfare Foundation.

References