Case Report

Pulmonary Thromboembolectomy in Congenital Antithrombin III Deficiency Associated with Acute Pulmonary Embolism–Report of a Case–

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Antithrombin III (AT III) deficiency is a rare hereditary disease that predisposes to thromboembolic complications. We report a case of AT III deficiency complicated with acute pulmonary thromboembolism, successfully treated with emergency pulmonary thromboembolectomy after insertion of an inferior vena cava filter. AT III activity before treatment was found to be 44% of normal value and remained less than 50% of normal throughout the postoperative course. In his family line, both the patient's aunt and deceased father had a history of pulmonary infarction. AT III activity of the patient's aunt was 47 to 58% of normal value. The patient was discharged on the 15th day after surgery and has been doing well for four years receiving warfarin as anticoagulant therapy. Careful follow-up is essential for early detection of the recurrent pulmonary thromboembolism resulting in pulmonary hypertension and/or right heart failure. (Ann Thorac Cardiovasc Surg 2003; 9: 192–6)

Key words: antithrombin III (AT III) deficiency, pulmonary thromboembolism, pulmonary thromboembolectomy, coagulopathy

Introduction

Antithrombin III (AT III) deficiency is a rare hereditary disease that predisposes to thromboembolic complications.[1-3] Pulmonary thromboembolism, which is also liable to complicate AT III deficiency, is a serious complication that may lead to circulatory collapse. In the presence of shock due to massive clot, surgical treatment is usually undertaken to resuscitate the patient. We report a case of AT III deficiency complicated with acute pulmonary thromboembolism, successfully treated with emergency pulmonary thromboembolectomy.

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Case Report

In April 1998, an 18-year-old man visited our hospital with chest pain and dyspnea that had lasted since the day before. He did not have a history of pulmonary embolism, but his father had died of pulmonary infarction and his aunt also had a history of pulmonary infarction. On physical examination, there was no anemia, jaundice, or disturbance of consciousness. A mild hypotension was noted with systolic blood pressure of 94 mmHg and regular pulse at a rate of 110 beats/min. A 3/6 systolic murmur was heard in the tricuspid area. A chest X-ray examination showed a cardiothoracic ratio (CTR) of 52%. An electrocardiogram (ECG) showed a regular sinus rhythm at a rate of 114 beats/min with inversion of T wave in the III and aVF leads.

Arterial blood gas collected under 3 L/min oxygen inhalation showed hypoxemia [partial pressure of oxygen (PaO_2), 53.7 Torr] and hypocapnia [partial pressure of carbon dioxide ($PaCO_2$), 31.0 Torr]. An echocardiography revealed a dilatation of the right ventricle (RV) with grade 3 tricuspid regurgitation (TR), indicating that estimated

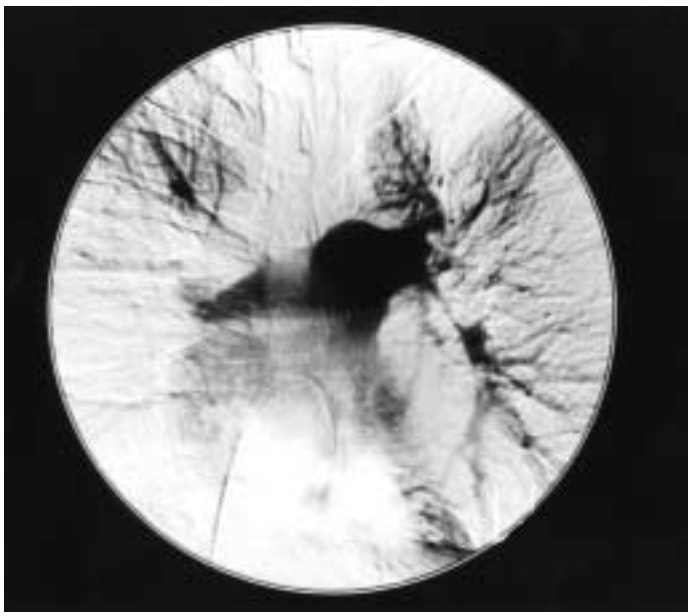

Fig. 1. Preoperative pulmonary arteriography. Occlusion of the right pulmonary artery trunk and stenosis in the left pulmonary branches in the upper and lower lobes are noted.

RV pressure was higher than 80 mmHg. The patient immediately underwent a pulmonary arteriography (PAG), which demonstrated occlusion of the right pulmonary artery trunk and stenosis in the left pulmonary branches in the upper and lower lobes (Fig. 1). The right heart catheterization (RHC) performed simultaneously demonstrated a marked elevation of the RV pressure > 100 mmHg. An inferior vena cava (IVC) filter was inserted concomitantly with PAG. Subsequently, emergency pulmonary thromboembolectomy was contemplated since the patient continued to present with hypoxemia and hypotension which may have led to a circulatory collapse. Table 1 shows preoperative data of laboratory tests, indicating polycythemia and lowered AT III activity of 44% of normal value.

Surgery was started one hour after the completion of PAG. After conducting median sternotomy, bicaval cannulation with a 32 French venous cannula for the superior vena cava (SVC) and 34 French for the IVC, and arterial cannulation with an arterial cannula of 6.5 mm in diameter were performed. Extracorporeal circulation (ECC) was started and the patient was moderately cooled to have a rectal temperature of 32°C. An incision was made in the trunk of the pulmonary artery, through which pulmonary thromboembolectomy in the bilateral pulmonary arteries was performed using Kelly forceps and curved clamp forceps. After removal of the thrombus in the pulmonary artery, the patient was rewarmed and weaned from ECC without any difficulties. Concentrated AT III was not supplemented during the course of operation. The patient was extubated in the operation room and the postoperative course was uneventful. Arterial blood gas after the operation returned to normal levels and anticoagulant therapy with warfarin was started after the operation.

Postoperative evaluation with PAG and RHC was performed on the 14th day after surgery. PAG revealed a residual occlusion of the segmental artery of the branch in the right upper lobe and demonstrated canalization of the trunk of the left pulmonary artery and its branches and trunk of the right pulmonary artery trunk (Fig. 2). The pressure data (mmHg) were as follows: PCWP (10), PA 36/14 (18), main PA 37/12 (20), RV 38/1, RA (9), AO 98/

Table 1. Preoperative laboratory data

WBC	11,400	(/μL)	Thrombotest	44	(%)
RBC	627×10^4	(/μL)	Prothrombin time	66	(%)
Hb	17.3	(g/dL)	Fibrinogen	234	(mg/dL)
Plt	22.8×10^4	(/μL)	FDP	43.4	(μg/mL)
TP	7.6	(g/dL)	D-dimer	1,500	(ng/dL)
GOT	58	(IU/L)			
GPT	134	(IU/L)	AT III	44	(%)
LDH	766	(IU/L)	Protein C	109	(%)
CK	106	(IU/L)	Protein S	115	(%)

WBC, white blood cells; RBC, red blood cells, Hb, hemoglobin; Plt, platelet counts; TP, total protein; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; LDH, lactic dehydrogenase; CK, creatinine phosphokinase; FDP, fibrin degeneration products; AT III, antithrombin III.

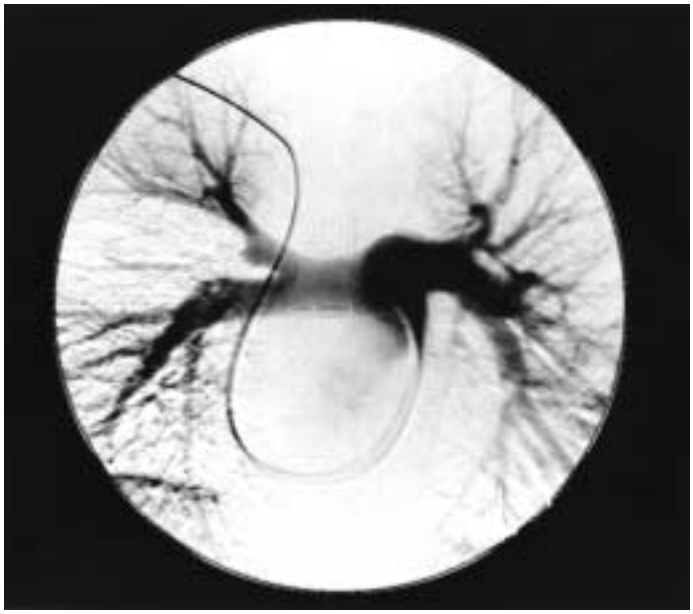

Fig. 2. Postoperative pulmonary arteriography. The trunk of the left pulmonary artery and its branches and trunk of the right pulmonary artery trunk are canalized but the segmental artery of the branch in the right upper lobe is occluded.

62 (PCWP, pulmonary capillary wedge pressure; PA, pulmonary artery; RV, right ventricle; RA, right atrium; AO, aorta). Pressures in the PA and RV that had been elevated preoperatively were remarkably reduced after surgery. Venography of the lower extremity, performed concomitantly with PAG and RHC, revealed deep venous thrombi in the left femoral vein which were considered a source of pulmonary thromboembolism. Repeated measurements of AT III levels demonstrated the persistent reduction of AT III activities less than 50% of normal value. The patient was discharged on the 15th day after surgery on foot and has been doing well for four years of the follow-up period.

Figure 3 shows the family history of the patient. So far as we have investigated, development of pulmonary infarction and sudden death was common in the patient's family line. AT III activity of the patient's brother is normal, but that of the patient's aunt, who has a history of pulmonary infarction, is 47% to 58% of normal value in repeated measurements.

Discussion

It has been reported that thrombi formed in the deep veins of the lower extremities may cause acute or chronic pulmonary thromboembolism which results in pulmonary hypertension.[4] These thrombi may develop without apparent cause, but may be caused by hemostatic anomalies such as antiphospholipid syndrome (APS) and deficiency of AT III, protein C, protein S in some cases.[4]

AT III, a serine protease inhibitor, plays an important

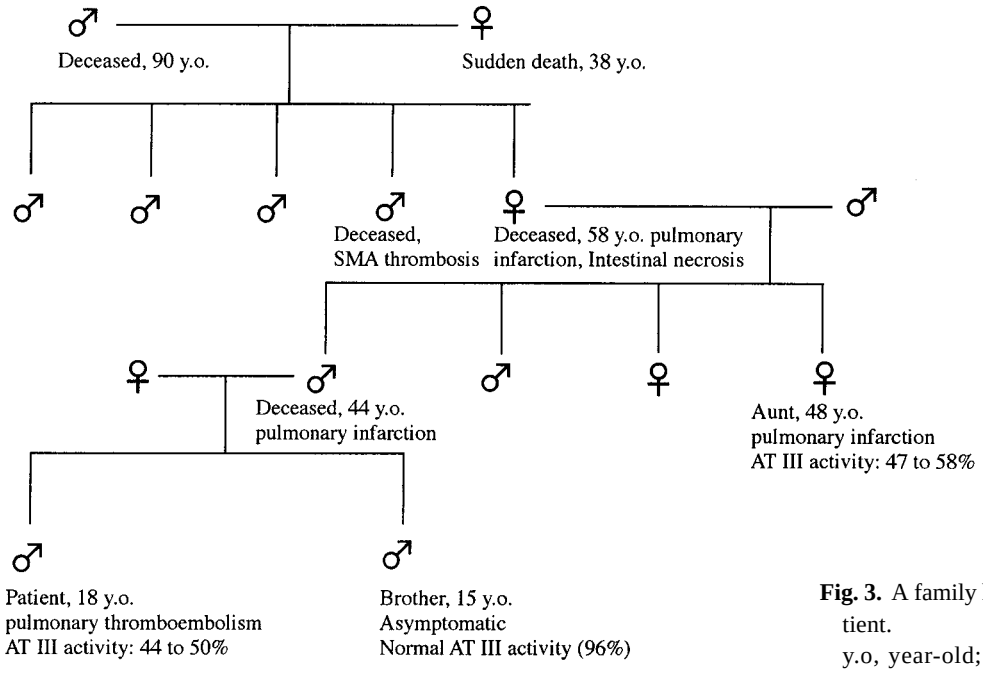

Fig. 3. A family history of the patient.
y.o, year-old; SMA, superior mesenteric artery.

role in the blood coagulation mechanism. Congenital AT III deficiency is inherited as an autosomal dominant trait and known to have an incremental risk for thromboembolism among hemostatic anomalies.[1-3] Martinelli and associates reported that there were higher risks for thrombosis for subjects with AT III deficiency at a risk ratio of 8.1 (3.4 to 19.6 by 95% confidence interval) than for individuals with normal coagulation.[3] The reported incidence of congenital AT III deficiency ranged from 1/2,000 to 1/20,000.[1,5] AT III deficiency is found in 4 to 6% of young patients with venous thrombosis, which is similar to but slightly lower than the prevalence of protein C and protein S deficiency in young subjects with thrombosis.[1] The chance of finding an AT III deficiency is increased if there is a history of familial or recurrent venous thrombosis.[6] In the present case, both the patient's aunt and deceased father had a history of pulmonary infarction. Although a decrease in the AT III activity was documented only in the patient and his aunt, occurrence of pulmonary infarction and sudden death was common in the patient's family line (Fig. 3). There have been 29 families with congenital AT III deficiency reported previously in Japan.[7] According to the reports describing clinical features of these families, the male-to-female ratio is about 1:1 and thrombosis may appear as pulmonary thromboembolism, mesenteric vein thrombosis, deep vein thrombosis, intracranial venous sinus thrombosis, or habitual abortion.[7]

Thrombotic events may occur in 30 to 80% of the carriers with AT III deficiency.[1] Thrombosis is uncommon in the first decade, but the risk rises sharply between the ages of 15 and 30.[1,2] Pabinger and associates reported that a 50% probability for the first thromboembolic episode was reached at the age of 21 years in patients with AT III deficiency.[2] They also reported that the most common site of the first thrombotic event was pulmonary thromboembolism with or without deep vein thrombosis, as was seen in the present case.[2] AT-III-deficient females tend to develop thrombosis earlier in life due to a high thrombotic risk during pregnancy.[2] In addition to pregnancy, trauma and surgery can be also predisposing factors. After 14 years of age thromboembolic events may occur after abdominal surgery or leg injury in approximately one third of patients.[2] The major clinical manifestations of AT III deficiency are young age at onset, idiopathic thrombosis, family history, and recurrent venous thromboembolism. Clinical features of the present case were in accord with these manifestations.

Surgical treatment was apparently indicated for the present case exhibiting hypoxemia, hypotension, and marked pulmonary hypertension. AT III deficiency caused acute pulmonary thromboembolism in this case, but may often cause chronic pulmonary thromboembolism in some cases.[8-10] Surgical indications for chronic pulmonary thromboembolism may include a mean pulmonary artery pressure of 30 mmHg or more, a pulmonary vascular resistance of 300 dyne or more, and thrombi that can be approached surgically.[11] The present patient had undergone insertion of an IVC filter for prevention of pulmonary thromboembolism due to thrombi formed in the deep veins of the lower extremities. However, thromboembolism will occur spontaneously in the pulmonary arteries in AT III deficiency.[1] Thus the patient has a considerably high likelihood of developing pulmonary hypertension due to chronic pulmonary thromboembolism which requires surgical treatment. The potential for recurrent pulmonary thrombosis should be kept in mind during the follow-up period of this patient.

For chronic pulmonary thromboembolism, pulmonary thromboendarterectomy under deep hypothermic circulatory arrest is recommended to achieve a blood-free field.[8,11-13] In this procedure, organized thrombi adherent to the pulmonary artery wall should be carefully resected in the media with the intima.[8] In the present case of acute pulmonary thromboembolism, thromboembolectomy was performed under complete ECC with moderate hypothermia. Although an occlusion of the segmental artery of the branch in the right upper lobe was left, hypoxemia and pulmonary hypertension were remarkably improved immediately after surgery. The patient was discharged on the 15th day after surgery without sequelae, thus the surgical result seemed to be clinically acceptable.

In conclusion, we have successfully treated a case of acute pulmonary thromboembolism due to AT III deficiency with emergency pulmonary thromboembolectomy. The patient underwent the insertion of an IVC filter to prevent recurrence of pulmonary thromboembolism due to thrombi formed in the deep veins of the lower extremity. However, thromboembolism may occur spontaneously in the pulmonary artery itself in this hemostatic anomaly. Careful follow-up is essential for early detection of the pulmonary thromboembolism resulting in pulmonary hypertension and/or right heart failure.

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