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CASE REPORT

S. Uchigasaki · H. Takahashi · T. Suzuki

A case of delayed death after accidental intravenous injection of thrombin

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Abstract A delayed death which occurred after accidental injection of thrombin into the right subclavian vein is described. The patient was given heparin intravenously after an erroneous intravenous injection of thrombin and died from lobar pneumonia 3 months afterwards without any apparently ill effects on the circulation of the body except for the brain. At autopsy, however, a large thrombus was observed extending continuously from the superior vena cava to the pulmonary trunk, via the right atrium and ventricle. From the results it was concluded that there was a causal relationship between the inadvertent intravenous administration of thrombin and death.

Key words Thrombin · Thrombus · Medical malpractice

Introduction

Thrombin is a valuable aid applied topically to control bleeding. It is used as oral treatment for gastric bleeding and acts by converting fibrinogen into fibrin to initiate the clotting process [1]. Most clinicians know that thrombin may cause massive intravascular coagulation if administered by intravenous injection. However, a few cases of erroneous intravenous injection of thrombin during hospitalization for gastric bleeding have been reported. All died 2–3 h after the thrombin injection and the postmortem examination confirmed total intravascular coagulation including the cavity of the heart and pulmonary vasculature [2, 3]. We report a case where 5,000 U of thrombin was erroneously administered intravenously and death occurred 3 months later from lobar pneumonia.

S. Uchigasaki (✉) · H. Takahashi · T. Suzuki
Department of Forensic Medicine,
Yamagata University School of Medicine,
Yamagata 990-9585, Japan

Case histories

A 54-year-old male was admitted to hospital for a bypass grafting operation of the coronary arteries and after the operation was hospitalized in the intensive care unit (ICU). The patient suffered hematemesis 10 days after the operation and 5,000 U of fluid thrombin (one vial) was prescribed to be given orally to stop bleeding from the stomach. A nurse took the fluid thrombin in a syringe from the thrombin vial and erroneously injected it in the cannula connected to the right subclavian vein, which had been set for the central venous hyperalimentation. Immediately after the injection, the deceased suffered from a convulsion and lost consciousness followed by respiratory and heart failure. He was given energetic cardiopulmonary resuscitation for 30 min and the respiration and heart recovered. Immediately after resuscitation 1,000 U of heparin was administered intravenously and an additional 600 U of heparin was given by drip infusion over the following 12 h. Spontaneous respiration ceased 2 days after the thrombin injection and breathing was maintained by a respirator. The patient died 3 months after the episode without regaining consciousness in a state of brain stem death.

Autopsy findings

An autopsy was carried out 13 h after death. The deceased measured 165 cm in length, weighed 79.5 kg and the skin was jaundiced. There were surgical scars along the midline of the chest (37 cm) and on the right iliac area (6 cm). In the centre of the neck there was a small defect at the site of insertion of the tracheotomy tube. There were two small incised wounds in the right subclavicular area for the central venous hyperalimentation.

On sectioning the brain was softened and discoloured pinkish gray by autolysis. There were tight fibrous adhesions between the anterior surface of the heart and the pericardium. The heart showed three transplanted vessels on the anterior surface of the left ventricle. A large thrombus was observed extending continuously from the superior vena cava to the pulmonary trunk, via the right atrium and ventricle (Figs. 1 and 2). The thrombus was firm but brittle with a mottled appearance and distinct linear markings on the surface from fibrin lamination. The thrombus was grayish-red and was variegated in colour. It appeared to produce a cast of the entire length of the circulatory system from the superior vena cava to the pulmonary trunk (Fig. 3a, b). Thrombi were not formed in any other vessel including in the right subclavian vein and bilateral major pulmonary arteries. The heart was very hypertrophic and weighed 780 g. The wall of the left ventricle was thickened and there were many small intramural myocardial scars. The dimen-

Fig. 1 Thrombus in the right atrium and ventricle

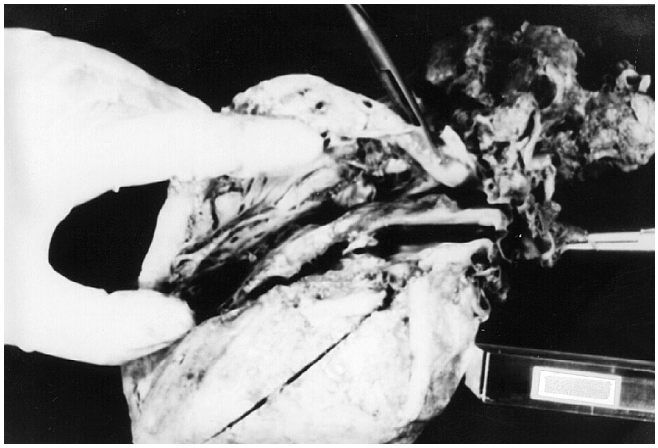

Fig. 2 Thrombus in the right ventricle and pulmonary trunk

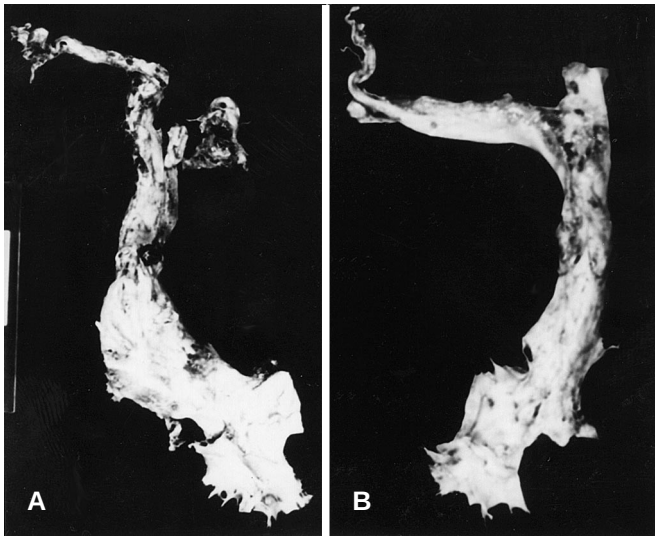

Fig. 3 A, B Thrombus appeared like a cast of the lumen of the circulatory system extending from the superior vena cava to the pulmonary trunk. **A**: the part extending from the superior vena cava to the right ventricle, **B**: the part extending from the right ventricle to the pulmonary trunk

sions of the lumina of the descending branches of the left coronary artery were reduced to pin-hole size.

The left and right lungs were oedematous weighing 1,100 g and 1,400 g, respectively and were marked by impressions of the ribs and intercostal spaces. The cut surfaces were mottled and yellowish-red and dirty brown and a large amount of frothy yellow creamy fluid could be squeezed from them. Microscopically, in the lumina of some alveolar spaces the fluid was replaced by densely packed neutrophils and in others a large amount of fibrin was present. Intravascular coagulation could be found in only a few arterioles. The liver weighed 2,400 g and showed moderate fat accumulation and lymphocyte infiltration in perisinusoidal areas. Each kidney weighed 270 g. Moderate lymphocyte and plasmacytic infiltration was seen in the interstitial tissue. The spleen weighed 500 g and moderate leukocyte infiltration was observed in the white pulp.

Discussion

Liquid thrombin is valuable for hemostasis and can be given orally to patients suffering from gastric bleeding. Because liquid thrombin is dispensed in a 5 ml vial, it can be mistaken for injectable material and erroneously taken up in a syringe and accidentally given intravenously. The patient in the present case was injected with 5,000 U of thrombin into the right subclavian vein through a tube placed there for central venous hyperalimentation instead of being applied topically i.e. by oral ingestion.

One unit of thrombin is defined as the amount of thrombin required to clot 1 ml of standardized fibrinogen solution in 15 s [4]. Therefore 5,000 U of thrombin may clot 2.5 l of oxalated human plasma in 15 s [5]. The previously reported cases died 2–3 h after an injection of 10,000 U of thrombin with total intravascular coagulation, including the cavity of the heart and pulmonary vessels [2, 3]. Although convulsion and loss of consciousness were noted immediately after the thrombin injection in this patient, 1,000 U of heparin was given intravenously 30 min after the injection and an additional 600 U of heparin by drip infusion over the following 12 h, the patient survived on a respirator for 3 months. The delayed death after the injection of thrombin in the present case seemed to be due to the effects of the heparin injection on the clotting mechanism.

One of the actions of heparin is as an inhibitor of the thrombin-fibrinogen interaction [4, 6]. Wesley and Wesley [7] showed that a rabbit injected with thrombin at 14.3 U/kg body weight (equivalent to 1,000 U of thrombin per 70 kg body weight) died within 30 s due to total intravascular coagulation and three additional rabbits injected with thrombin but treated with heparin at 143 U/kg body weight (equivalent to 10,000 U of heparin per 70 kg body weight) intraperitoneally 40 min before the thrombin injection, intravenously 30 min before thrombin, and intravenously immediately after thrombin injection, survived without any ill-effects being noted over the next month. They suggested that intravenous heparin should be given as soon as possible to counteract an accidental injection of thrombin. The fact that the present patient survived for 3 months without any apparent circulatory ill-effects except for brain ischemia after the thrombin injec-

tion, suggests that thrombin-fibrinogen interaction might have been inhibited by heparin. In addition, it is said that thrombi also tend to spontaneously dissolve as a result of the combined effects of fibrinolysis and lysosomal enzymes released from the trapped leukocytes [8].

The lobar pneumonia of the deceased was so severe that it was considered to be the cause of death. The extent and severity of the lobar pneumonia may in part be due to the insufficient blood supply to the lungs due to a massive thrombus found continuously between the superior vena cava and the pulmonary trunk.

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