1.8 Effect of Antithrombin III Concentrate for DIC in Obstetrics and Gynecology: The Changes of Prostanoids in Plasma Before and After Administration

HIROSHI SUZUKI¹, MAYUMI KASAI¹, KEN SATOH¹, HAJIME IIDA¹, HIROKI SUZUKI², and IWAO NISHIYA²

Introduction

Obstetrical disseminated intravascular coagulation (DIC) is frequently acute and sometimes life threatening. However, early diagnosis and prompt treatment often save lives. We have shown in patients with gestosis that changes in vasoactive substances such as prostaglandin and prostanoid are associated with progression of the disease that induces chronic DIC [1–3]. On the other hand, DIC complicating gynecological malignant tumors are mostly seen at the terminal stage of the disease, and, therefore, active treatment for DIC has been rarely performed. However, recent advances in the anti-cancer therapy and radiotherapy for gynecological malignant tumors have prolonged the life of some patients. During chemotherapy with anti-cancer drugs, DIC sometimes develops, and active treatment for DIC is often required. In this study, we administered an antithrombin III concentrate (AT-III) to 7 patients with obstetric DIC and 10 of 15 patients treated for gynecological malignant tumors who had DIC or were expected to develop DIC. To evaluate the usefulness of this drug, the AT-III activity and various effects, especially on prostanoid, were studied.

Materials and Methods

Subjects

Obstetrical DIC

The subjects were 7 patients referred to the Iwate koji Emergency Center (Iwate Prefecture) between November 1984 and April 1986 who scored 8 or

¹Department of Obstetrics and Gynecology, Iwate Prefectural Central Hospital, 1-4-1 Ueda, Morioka, 020 Japan
²Department of Obstetrics and Gynecology, Iwate Medical University, 19-1 Uchimaru, Morioka, 020 Japan
more according to the diagnostic criteria for obstetrical DIC established by Maki et al. [4]. The underlying disease was DIC type third-stage bleeding in 2 patients, uterine rupture in 1, abruptio placentae in 2, and eclampsia in 2 (Table 1). The test drug was BI 6013 (AT-III concentrate, 500 unit vial, Berling Research Center, Hoechst Co.). One vial of BI 6013 was dissolved in distilled water (10 ml), and 3000 units (6 vials) per day was mixed with lactic acid (500 ml) and administered by drip injection for 2 h. Patients 1–4 were treated at a dose of 3000 units only on the first disease day, and patients 5–7 were treated on the first and second disease days at a total dose of 6000 units.

**Gynecological DIC**

The subjects were 15 patients who were admitted to the Department of Obstetrics and Gynecology of Iwate Prefectural Hospital because of gynecological malignant tumors between 1984 and 1987 and who had received chemotherapy and radiotherapy. After these therapies, all these patients scored 5–9 according to the Diagnostic Criteria for DIC established by the Ministry of Public Welfare [5]. The underlying disease was ovarian carcinoma in 12 patients, choriocarcinoma in 1, and cervical carcinoma in 2 (Table 2). Six vials of the AT-III concentrate (3000 units) was mixed with lactic acid (500 ml) and administered by drip infusion for 2 h to 10 of the 15 patients. The remaining 5 patients used as controls were not treated with this drug. Though transfusion was performed in some patients with anemia, in principle, aprotinin or heparin was not used in combination with this concentrate; and fresh frozen plasma, platelets, or fibrinogen was not administered.

**Examination Items**

Before as well as 1, 3, 6, 12, 24, and 48 h after the drug administration, scoring according to the diagnostic criteria for DIC was carried out. In addition, a general blood analysis, a blood chemistry test, and an examination of electrolytes and the blood clotting system [platelet count, prothrombin time (PT), fibrinogen (Fbg), fibrinogen degradation product (FDP), α2-plasmin inhibitor (α2-PI), plasma protamine paracoagulation test (FMT), AT-III antigen, and prostanoid (6 keto-PGF1α, thromboxane B2)] were done [2,3].

**Evaluation and Side Effects**

The efficacy of the drug was evaluated (effective or ineffective) comprehensively based on clinical symptoms, values of the coagulation test, and improvement in the prostanoid values. The safety was evaluated (presence or absence of side effects) based on clinical symptoms and changes in the values of clinical chemical examinations such as general blood analysis, blood chemistry test, and examination of electrolytes.