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Coagulation factor deficiency apparently related to the Fitzgerald trait: the first cases in Japan.

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Abstract

A blood coagulation deficiency was found at the contact phase in identical Japanese female twins. Of the four possible factors involved, Factor XI or XII can be ruled out according to cross-correction studies. The problem factor was probably not Fletcher factor, because the abnormal partial thromboplastin time was not significantly shortened by increasing the incubation period of plasma with kaolin. The deficiency is most likely due to the lack of Fitzgerald factor.

KEYWORDS: fitzgerald trait, HMW-Kininogen, fletcher factor, factor XI, factor XII

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— BRIEF NOTE —

**COAGULATION FACTOR DEFICIENCY APPARENTLY
RELATED TO THE FITZGERALD TRAIT :
THE FIRST CASES IN JAPAN**

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Abstract. A blood coagulation deficiency was found at the contact phase in identical Japanese female twins. Of the four possible factors involved, Factor XI or XII can be ruled out according to cross-correction studies. The problem factor was probably not Fletcher factor, because the abnormal partial thromboplastin time was not significantly shortened by increasing the incubation period of plasma with kaolin. The deficiency is most likely due to the lack of Fitzgerald factor.

Key words: Fitzgerald trait, HMW-Kininogen, Fletcher factor, Factor XII, Factor XI

Fletcher factor (prekallikrein) deficiency is characterized by abnormal partial thromboplastin time and the absence of hemorrhagic diathesis. Saito *et al.* (1) reported a new coagulation factor deficiency which is different from Fletcher factor deficiency. This new coagulation factor deficiency lacks kininogen of high molecular weight and was termed Fitzgerald trait. Only three families have been reported with this disorder in the literature (1, 2, 3). In the present paper, we report on two additional possible cases. The patients were 56-year-old identical Japanese female twins without previous hemorrhagic tendencies. However, in 1971, one twin (Case 2) developed massive postoperative hemorrhage after hysterectomy due to uterine myoma. The family history revealed no consanguinity, although three women in the family had hysterectomy operations.

Table 1 shows the coagulation studies on the patients. Activated partial thromboplastin time (APTT) was greatly prolonged with kaolin and ellagic acid. No circulating anticoagulants were detected. The thromboplastin generation tests were highly abnormal; the abnormal thromboplastin formation was corrected by normal serum whereas partially corrected by normal BaSO₄-adsorbed plasma. Factor XII concentration was normal. Factor XI activity decreased to 28% of normal by the one-stage method in which bovine Factor XI-deficient

plasma was used as a substrate, whereas the same factor decreased to 2-8% of normal by the Margolis method. On the other hand, the prolonged APTT was completely corrected by adding Factor XII-deficient plasma or XI-deficient plasma to patient plasma (Table 2). According to Hathaway *et al.* (4), the prolonged APTT was normalized with Fletcher plasma by increasing the incubation period with kaolin up to 15 min. Table 3 shows the effect of clotting time in our two patients after incubation with kaolin and ellagic acid. The abnormal APTT was only partially corrected after incubation. The addition of kallikrein did not correct the abnormal APTT.

These findings appear nearly identical to the reported findings on Fitzgerald trait (1). However, for confirmatory diagnosis, cross-correction studies of APTT with Fitzgerald plasma (1) and Passovoy plasma (5) are required.

TABLE 1. BLOOD COAGULATION DATA ON PLASMA OF IDENTICAL TWINS

| | Case 1 | Case 2 |
|--|---------|--------|
| Whole blood clotting time (min) | 19.5 | ND |
| Recalcification time (min) | Over 10 | ND |
| Prothrombin time (sec) | 13.0 | 11.6 |
| Activated partial thromboplastin time (APTT) with ellagic acid (sec) | 243.4 | 209.0 |
| Activated partial thromboplastin time (APTT) with kaolin (sec) | 628.0 | 434.6 |
| Thrombin time (sec) | 11.6 | 13.8 |
| Serial thrombin time (sec) | 16.0 | 17.6 |
| Factor | | |
| I (mg/dl) | 330.0 | 292.0 |
| II (%) | 90 | ND |
| V (%) | 130 | ND |
| VII-X complex (%) | 110 | ND |
| VIII (%) | 70 | ND |
| IX (%) | 70 | ND |
| XI (%) | 28 | 28 |
| XII (%) | 80 | 76 |
| XIII | Normal | Normal |

ND, Not determined

TABLE 2. CROSS-CORRECTION STUDIES ON PLASMA APTT OF IDENTICAL TWINS

| Condition | Case 1 (sec) | Case 2 (sec) |
|---|--------------|--------------|
| Patient plasma (Pt-pl) | 261.8 | 290.0 |
| Pt-pl + Factor VIII deficient pl. (8:2) | 30.8 | 31.4 |
| Pt-pl + Factor IX deficient pl. (8:2) | 40.2 | 29.0 |
| Pt-pl + Factor XI deficient pl. (8:2) | 39.6 | 36.0 |
| Pt-pl + Factor XII deficient pl. (8:2) | 31.6 | 30.2 |

TABLE 3. EFFECT ON CLOTTING TIME (SECONDS) AFTER PROLONGED INCUBATION WITH KAOLIN AND ELLAGIC ACID

| | Kaolin | | | Ellagic acid | |
|------------------------|-----------------------|-------|-------|-----------------------|-------|
| | Incubation time (min) | | | Incubation time (min) | |
| | 2 | 5 | 15 | 2 | 15 |
| Case 1 | 628.0 | 379.0 | 192.6 | 241.1 | 152.5 |
| Case 2 | 434.5 | 266.3 | 150.4 | 209.0 | 165.8 |
| Pooled normal subjects | 64.2 | 64.6 | 63.6 | 32.0 | 30.4 |

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