馬の血小板無力症の一例

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A Case of Equine Thrombasthenia

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Thrombasthenia is a hemorrhagic disease caused by impaired platelet function [3]. This is characterized by bleeding tendencies, an absence of clot retraction, and a lack of platelet aggregation in the presence of inducers such as adenosine diphosphate (ADP), collagen, or thrombin. Among the inducers, the complete lack of platelet aggregation in the presence of ADP at any concentration is one of the most important diagnostic criteria in human thrombasthenia.

There have been few reports about this disease in animals except for an otterhound family reported by Dodds [1, 2] and bassethounds reported by Johnstone *et al* [6]. In the otterhound cases, the presence of high proportion of giant bizarre platelets suggested that they might be classified as a mixed type of thrombasthenia along with another thrombocytopathy such as Bernard-Soulier syndrome.

Recently, we observed a 6-month-old female thoroughbred foal having shown numerous bleeding tendencies such as hematoma or hemarthrosis formation, spontaneous subcutaneous or mucosal hemorrhages, melena, and prolonged bleeding even with mild trauma or horsefly bites. Her growth rate was slow compared to other foals of the same age.

In order to provide controls, all diagnostic procedures were carried out on the patient as well as the dam and 3 other thoroughbred foals (1 female and 2 males) of the same age and from the same farm. The blood specimens were collected from the jugular vein through a single venipuncture using 2 different plastic syringes. Initially, 7 m*l* of whole blood was withdrawn for observation of clot retraction and platelet counting. Then, 18 m*l* of blood was withdrawn into a syringe with 2 m*l* of 3.8% sodium citrate for the preparation of platelet rich plasma (PRP) and platelet poor plasma (PPP). The PRP was prepared by centrifugation of the citrated blood at 850 rpm for 5 min, and then the rest was centrifuged again at 2800 rpm for 5 min for the preparation of PPP. The aggregation tests were carried out within 4 hrs. For the determination of prothrombin time (PT), partial thromboplastin time (PTT), and fibrin/fibrinogen degradation product (FDP), another venipuncture was carried out to collect 10 m*l* of citrated blood and 2 m*l* of blood with aprotinin.

The clot retraction was observed in a water bath at 37°C. Platelet aggregations were evaluated with a Sienco Aggrecometer (Model DP-247E) connected to a recorder. The PRP was adjusted to approximately 2×10^5 platelets/μl using PPP and incubated for 3 min before the aggregation inducers were added. Thirty μl of various concentrations of inducers were added to 270 μl of incubated PRP and the changes in transmittance were recorded [10]. ADP (Sigma) and collagen prepared from equine tendon (Horm) were used as the inducers. The final concentrations of ADP and collagen were 1, 2, 10, and 100 μM/m*l* and 2, 5, and 10 μg/m*l*, respectively. PT was determined by a quick one-stage method and PTT was determined using rabbit brain thromboplastin (Hokken). FDP was assayed by the latex-agglutination method (Teikoku Zoki).

The results of the coagulatory examinations are shown in Table 1. The PT and PTT values of the patient were 9.2 sec and 115.6 sec respectively, and there were no significant differences compared to those of the control foals and the dam. FDP values were below 5 μg/m*l* in all the horses examined. These results suggest that the cause of the bleeding tendencies was not an abnormality in intrinsic or extrinsic coagulation mechanisms nor was it abnormal fibrinolysis.

The results of the platelet function tests are shown in Table 2. The platelet counts of the patient ($136\times10^3/\mu l$), the control foals ($108\times10^3-191\times10^3/\mu l$), and the mother horse ($104\times10^3/\mu l$) were all within the normal range [4]. Most of the patient's platelets appeared

Table 1. Results of blood coagulation tests

	Control foals			Mother horse	Patient
	No. 1	No. 2	No. 3		
PT (sec)	9.5	8.9	9.7	8.7	9.2
PTT (sec)	104.5	124.7	101.9	108.5	115.6
FDP (μg/m*l*)	5>	5>	5>	5>	5>

Table 2. Results of platelet function tests

		Control foals			Mother horse	Patient
		No. 1	No. 2	No. 3		
Platelet count ($\times 10^3/\mu l$)		191	108	132	104	136
Clot retraction		+(1hr)	+(1hr)	+(1hr)	+(1hr)	−(12hr)
Platelet aggregation						
	1	+[a)]	+	N	+	−
ADP	2	++	+	+	+	−
(μM/m*l*)	10	++	++	+	++	−
	100	N[b)]	N	N	N	−
	2	−	−	N	−	−
Collagen	5	±	−	N	−	±
(μg/m*l*)	10	++	±	++	++	±
	20	N	±	++	++	±

a) ++: Irreversible aggregation, +: Reversible aggregation, ±: Only a small initial change in transmittance, −: No aggregation.
b) Not done.

isolated on blood smears but the shape and the size were nearly normal.

Clot retraction began within 1 hr of incubation in all of the control foals and the mother horse, whereas it was not observed even after 12 hrs of incubation in the patient.

As for the platelet aggregation tests, ADP induced reversible aggregation at 1–2 μM/m*l* and irreversible aggregation at final concentration of 2–10 μM/m*l* in the control foals (Fig. 1) and the mother horse. All of their aggregation patterns were monophasic. The platelets of the patient, on the other hand, did not demonstrate any aggregation pattern with the addition of ADP at final concentrations of 2, 10, and 100 μM/m*l* (Fig. 2). Though Meyer *et al* reported that bovine collagen initiated irreversible platelet aggregation at 10 μg/m*l* or more [7], equine collagen did not consistently induce platelet aggregation in control foals (Table 2). In 2 of 3 control foals and the dam, irreversible aggregation patterns were obtained (Fig. 3), whereas it was not induced in control foal No.2. In the patient, no aggregation was induced at any concentration of collagen (Fig. 4). The initial decrease in transmittance just after adding collagen observed in almost all the samples including the patient's was thought to result from the adhesion of platelets to the collagen.

The results of these examinations indicate that the bleeding tendencies of this patient were the results of platelet dysfunction. This fulfills the minimal diagnostic criteria for thrombasthenia in the human. This finding is significant in that such a hemostatic problem could be an important consideration in the breeding of thoroughbred horses. Many thrombasthenia cases are thought to be congenital with autosomal recessive or

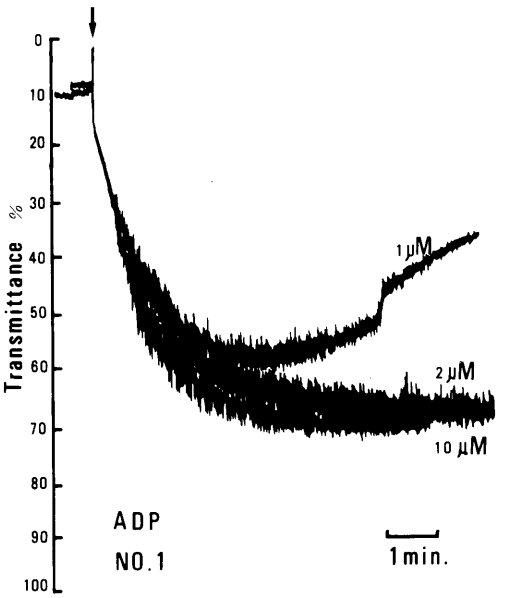

Fig. 1. ADP-induced aggregation patterns of a control foal (No.1).

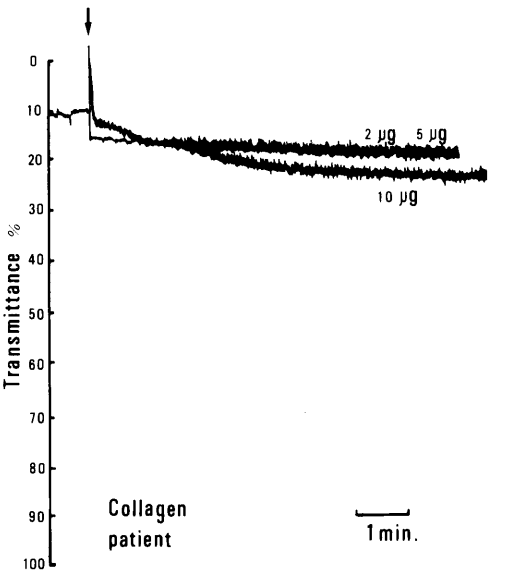

Fig. 2. ADP-induced aggregation patterns of the patient. No aggregation was initiated at any concentration of ADP.

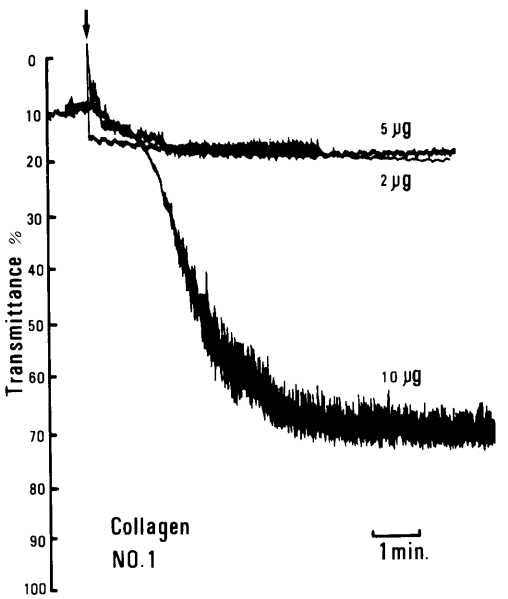

Fig. 3. Collagen-induced aggregation patterns of a control foal (No. 1).

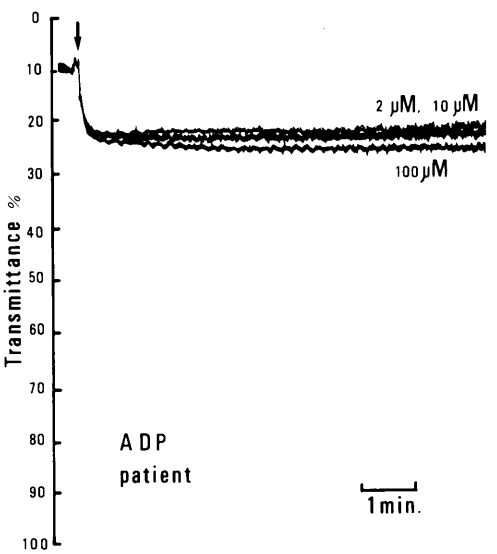

Fig. 4. Collagen-induced aggregation patterns of the patient.

imcompletely dominant trait of inheritance in the human and in the otterhounds as well [1]. However, the precise function of the platelet in animals may differ from that of the human, thus further examinations such as determination of abnormal platelet glycoprotein patterns [5, 8, 9] would be necessary to give a diagnosis of Glanzmann's thrombasthenia.

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要　　約

馬の血小板無力症の一例（短報）：三浦　昇・仙波裕之[1)]・小川博之・佐々木伸雄・大石秀夫[1)]・大橋文人・竹内　啓・臼井和哉（東京大学農学部家畜外科学教室，[1)]日高地区農業共済組合）——血腫形成，粘膜の出血など，種々の出血傾向を呈した6カ月齢のサラブレッド種雌馬について，血液凝固検査および血小板機能検査を行ったところ，血餅退縮が欠如し，いずれの濃度のADPにおいても血小板凝固が誘起されず，血小板無力症と診断された。