CASE REPORT

Disseminated Intravascular Coagulation in a Horse with Postpartum Ulcerative Colitis and Laminitis

I. B. JOHNSTONE AND T. E. BLACKWELL

Department of Biomedical Sciences (Johnstone) and Department of Clinical Studies (Blackwell), Ontario Veterinary College, University of Guelph, Guelph, Ontario N1G 2W1

Summary

Hemostatic studies were conducted on a five year old Belgian mare presented two days postpartum with colic and laminitis that was unresponsive to treatment.

The mare was moderately thrombocytopenic with plasma fibrinogen levels more than twice that of a normal control horse. Platelet function as evaluated by aggregometry indicated that the circulating platelets were markedly hyporesponsive. Activated partial thromboplastin times and prothrombin times were prolonged. Para-coagulation tests (prothrombin time and ethanol gelation) were strongly positive and fibrin degradation products were significantly elevated in the serum.

The laboratory data suggested that the clinical bleeding was the result of the development of disseminated intravascular coagulation. The data were compatible with intravascular activation of the clotting mechanism, consumption of hemostatic factors, inhibition of platelet function and enhanced stimulation of the fibrinolytic mechanism.

This report illustrates the complexity of the hemostatic abnormalities associated with pathological overactivation of the hemostatic mechanism. Factors such as tissue thromboplastins and/or endotoxins can stimulate disseminated intravascular coagulation, particularly during pregnancy or in the early postpartum period when a physiological "hypercoagulable" state already exists.

Key words: Equine, disseminated intravascular coagulation, laboratory diagnosis, pathology.

Résumé

Coagulation intravasculaire dis-séminée associée à une colite ulcéreuse et à une fourbure puerpérales, chez une jument

Les auteurs ont effectué des études hémostatiques chez une jument Belge, âgée de cinq ans, qu'il fallut hospitaliser deux jours après la parturition, parce qu'elle souffrait de coliques et de fourbure insensibles au traitement. Elle affichait une thrombocytopenie modérée et un taux de fibrinogène plasmatique équivalent à plus du double de celui d'un cheval témoign. L'utilisation d'un agrégomètre permet de constater une fonction plaquettaire très affaiblie. Les temps de la thromboplastine partielle activée et de la prothrombine s'avérèrent prolongés. Les tests de paracoagulation, à l'aide de sulfate de protamine et de gélatine à l'éthanol, donnèrent des résultats fortement positifs et les produits de dégradation de la fibrine affichèrent une élévation appréciable dans le sérum.

Les résultats de ces épreuves de laboratoire laissaient sous-entendre que le saignement clinique résultait du développement d'une coagulation intravasculaire disséminée. Ils étaient compatibles avec l'activation intravasculaire du mécanisme de coagulation, l'épuisement des facteurs hémostatiques, l'inhibition de la fonction des plaquettes et l'accroissement de la stimulation du mécanisme fibrinolytique.

Ce rapport illustre la complexité des anormalités hémostatiques qui accompagnent une activation excessive du mécanisme de l'hémostase. Des facteurs tels que les thromboplastines tis-
sulaires et/ou les endotoxines peuvent stimuler la coagulation intravasculaire disséminée, surtout durant la gestation et au début de la période puerpérale, alors qu'existe déjà un état physiologique d'hypercoagulabilité.

Mots clés: équin, coagulation intravasculaire disséminée, diagnostic de laboratoire, pathologie.

Introduction

Disseminated intravascular coagulation (DIC) is probably a more common complication of systemic disease in horses than reports in the literature would indicate (1,2). Disseminated intravascular coagulation can be triggered by a wide variety of stimuli which are capable of inducing vascular injury and/or activation of blood platelets and coagulation proteins. Such stimuli include endotoxemias, viremias, acidosis, circulating antigen-antibody complexes and tissue thromboplastins from injured or devitalized tissue (3,4,5,6).

Signs of DIC often include petechiae and purpura, oozing from surgical or traumatic wounds, bleeding from venipuncture sites, or evidence of internal bleeding (hematuria, melena). Usually there is bleeding from multiple unrelated sites (7). The physiological "hypercoagulable" state associated with late pregnancy and the early postpartum period predisposes to the development of DIC (8,9).

Fulminating DIC is almost invariably fatal. In its earlier stages of development however, DIC may be reversible with intensive supportive therapy and removal of the inciting cause (10). The early recognition of DIC is difficult since there is no specific labora-
tory test that is diagnostic of the condition. Diagnosis is dependent on evaluation of multiple aspects of hemostasis (11).

The purpose of this paper is to describe the history, clinical signs and laboratory findings in a postpartum mare which developed DIC in conjunction with ulcerative colitis and laminitis. The hemostatic profile in this mare illustrates the complexity of the hemostatic defects which develop in DIC and which predispose to the hemorrhagic diathesis. Early laboratory evaluation of high risk patients may be of significant prognostic value.

**History**

A five year old Belgian mare with foal was admitted to the Ontario Veterinary College with a history of colic and laminitis of 36 hours duration. The mare had foaled unevenly two days prior to admission but was observed to be in distress the morning after foaling. A diagnosis of laminitis and mild abdominal pain was made by the attending veterinarian and the mare was administered mineral oil and diocital sodium sulfosuccinate by stomach tube, and steroids, antihistamines, antibiotics and nonsteroidal anti-inflammatory drugs parenterally over the following 36 hours. Improvement was not noted and the mare was referred to the Ontario Veterinary College.

On admission the mare showed signs of mild abdominal pain and was reluctant to move. The rectal temperature was 38.4°C, pulse 60/min and respiratory rate 64/min. The mare was moderately dehydrated, had a mild metabolic acidosis (pH 7.33) and had a bounding pulse in all four feet. Rectal palpation revealed no abnormal findings and the mare’s feces had a “pasty” consistency. The mare was treated with intravenous fluid therapy (Lactated Ringers and 5% sodium bicarbonate) to correct the dehydration and acidosis and with intravenous phenylbutazone for the laminitis.

The following day the mare appeared more painful in both forefeet and was still mildly acidotic (blood pH 7.30). Treatment with intravenous fluids and phenylbutazone was continued.

On day 3 the mare developed a profuse watery diarrhea. Rectal temperature, pulse and respiratory rate were unchanged from day 1. The intravenous catheter had to be removed because of apparent thrombosis of the left jugular vein.

On day 4 the mare showed increased signs of discomfort including pawing and occasional rolling. Blood pH was 7.27. Bleeding from the skin above the hoof wall of both front feet was now apparent. Blood was collected for evaluation of hemostatic parameters prior to treatment on day 4.

The mare’s condition continued to deteriorate on day 5. Abdominal pain was severe and the diarrhea became blood tinged. Euthanasia was performed on day 5 when she was no longer able to stand.

**Hemostatic Evaluation**

Blood samples were collected from the mare and from a healthy adult control horse on day 4.

The mare was moderately thrombocytopenic (Table I). Plasma fibrinogen was elevated to more than twice normal (12,13), and the venous packed cell volume was 0.37 L/L at this time.

Platelet function was evaluated by in vitro platelet aggregometry (14). Adenosine diphosphate (ADP) and collagen are considered to be two important stimulants of platelet aggregation in vivo. Platelet aggregation responses to ADP and collagen are shown in Figure 1. It is apparent that the mare’s platelets were hyporesponsive to ADP and totally nonresponsive to collagen. Additional aggregometric studies (tracings not shown) indicated that the aggregation response of normal horse platelets to collagen could be significantly depressed by preincubation with the mare’s serum but not serum from normal control horses. These observations suggested the presence of a circulating platelet inhibitor.

The integrity of the blood coagulation mechanism in the mare was evaluated by the activated partial thromboplastin time (APTT) and prothrombin time (PT) tests, and simultaneous thrombokinograms (TKG) (14,15,16). Thrombokinogram profiles are graphic depictions of the optical density changes occurring in plasmas during the actual clotting process. They therefore provide additional information concerning how the clot forms after fibrin generation is initiated (17).

Typical APTT- and PT- TKG profiles for the mare and for the normal control horse are shown in Figure 2. The left base line components of the APTT-TKG profiles correspond in length to APTT clotting times of 132.9 s and 67.1 s in the mare and control plasmas respectively. Likewise, the left baseline components of the PT-TKG profiles (mare and control horse) cor-

![Figure 1. Platelet aggregation responses of the mare's platelets (M) and those of the normal control horse (C) to collagen and ADP. Final drug concentrations are given. The arrow represents the point at which the aggregating agent is added to a stirred platelet suspension (platelet-rich plasma). Aggregation is indicated by an increase in light transmission through the platelet suspension after stimulation of the platelets.](image)

**Table I**

<table>
<thead>
<tr>
<th>Hemostatic Parameters in the Mare With DIC as Determined on Day 4</th>
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<tbody>
<tr>
<td>Mare</td>
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<tr>
<td>------</td>
</tr>
<tr>
<td>Platelet count ((\times 10^{11} / L))</td>
</tr>
<tr>
<td>Fibrinogen ((g/L))</td>
</tr>
<tr>
<td>Ethanol gelation</td>
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<tr>
<td>Protamine sulfate</td>
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<td>FDP ((\mu g/mL))</td>
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change following intrinsically indicated by the optical density of the plasma (double asterix). This is the clotting time. The wave pattern following the double asterix depicts the rates of change in plasma optical density during fibrin production and polymerization and reflects how fibrin forms.

respond to 41.2 s and 23 s respectively. It is apparent from the TKG profiles that there were significant differences in the kinetics of fibrin production as indicated by the optical density changes following the onset of fibrin generation. Not only did it take significantly longer for fibrin production in the mare's plasma to be initiated by intrinsic and extrinsic pathways, but the events associated with fibrin production and polymerization took significantly longer than normal.

Fibrinolysis was evaluated by the measurement of fibrin degradation products (FDP). The mare's serum had significantly elevated levels of FDP (> 40 µg/mL) while the control serum had less than 10 µg/mL FDP (Table I).

Paracoagulation tests (ethanol gelation and protamine sulfate tests) were performed in order to determine the presence or absence of soluble fibrin monomer. Both tests were strongly positive using the mare's plasma and negative with the control plasma (Table I).

Postmortem Findings

The postmortem findings were primarily associated with the gastrointestinal tract. The entire tract contained blood and blood tinged fluid. The mucosa from the cecum to the small colon was ulcerated with extensive thrombosis of submucosal veins evident. A 60 cm length of lower large colon was red-black in colour and friable. In this area there was extensive thrombosis and infarction of the full thickness of the mucosa with extensive hemorrhage and blood pooling. The ulcerative colitis appeared to be chronic while the infarcts were thought to be recent.

The skin above the hoof wall on the right hind and both forefeet was necrotic and separated from the wall. There was considerable congestion, hemorrhage and thrombosis of the dermal pegs.

Extensive adrenal cortical hemorrhage was evident and there was considerable thrombosis of venous channels in the adrenal medulla.

Focal infarction and thrombosis was apparent in the kidneys.

Discussion

The early detection of DIC is likely critical for effective reversal of this syndrome. This early detection however, is made difficult by the lack of a specific diagnostic test for the condition. In this mare the diagnosis of DIC was made on the basis of laboratory evidence of a quantitative and qualitative platelet deficiency concurrent with indications of intravascular activation of clotting proteins and the accumulation of products of clot lysis.

Disseminated intravascular coagulation is rarely a primary disease process but is more commonly secondary to other pathology (5). In this horse the stimulus for DIC was probably a hypercoagulable state due to the recent pregnancy exacerbated by endotoxin and/or tissue thromboplastin released from the lesions in the gastrointestinal tract. Elevations in plasma clotting factors such as factor VIII, factor XII and fibrinogen, and increased platelet aggregatability are thought to contribute to the physiological hypercoagulable state of late pregnancy (8,9). Acidosis also predisposes to a hypercoagulable state (5,7).

A white cell count performed on day 3 indicated that the mare had a mild neutropenia with a left shift, possibly as a result of endotoxia.

The laboratory data obtained suggested that the condition had progressed to the consumptive phase. Disseminated intravascular coagulation in its early phase is characterized by a hypercoagulable stage which ultimately leads to consumption of hemostatic factors. The hypercoagulable stage is rarely diagnosed in animals and it is the hemorrhagic consumptive phase that is more commonly recognized. In retrospect the thrombosis of the jugular vein and the circulatory deficits to the extremities (likely causing the laminitis) in this patient may have been clinical reflections of the hypercoagulable state due to the recent pregnancy and/or to the gastrointestinal disorder (11,18). Extensive thrombosis of renal, cutaneous, adrenal and intestinal tissues was apparent at postmortem.

The moderate thrombocytopenia and prolonged intrinsic and extrinsic clotting times in the mare were indicative of platelet/clotting factor activation and consumption exceeding replacement by body reserves. Hypofibrinogenemia, a common feature of consumptive coagulopathies, was not evident in this horse (19). The elevated fibrinogen concentration (6.07 g/L) in the mare's plasma may have been a reflection of an acute stress response associated with pregnancy and parturition plus the extensive inflammation associated with the gastrointestinal lesions.
Intravascular activation of the coagulation mechanisms was indicated by the strongly positive para-coagulation tests confirming the presence of circulating soluble fibrin monomer (20). Normally fibrin monomers polymerize into fibrin, however, in the presence of fibrinogen/fibrin degradation products, the monomers complex with these substances before much polymerization can occur (6,21). Circulating soluble fibrin monomer is abnormal and indicates activation of the clotting sequences. The abnormally high level of FDP (>40 µg/mL) was compatible with accelerated activation of the fibrinolytic mechanism; a defensive response to accelerated fibrin production.

In addition to impaired coagulation mechanisms in the mare, the hemostatic studies indicated that the kinetics of fibrin production were abnormal. Soluble fibrin monomers may have contributed to these thrombokinetic abnormalities since they can interfere not only with fibrinogen to fibrin conversion, but also with the polymerization of fibrin monomers (22,23).

The platelet function studies indicated that the platelets which were circulating were hyporesponsive. Although some of the drugs administered to the mare prior to blood sampling are known to affect platelet function (particularly the nonsteroidal anti-inflammatory drugs), it is unlikely that they alone produced the significant qualitative platelet deficiency detected by aggregometry (24). Fibrin degradation products may have contributed to the platelet function deficit by binding to and coating platelet membranes thus interfering with surface receptors necessary for platelet aggregation (21,22).

In this mare the hemostatic abnormalities were significantly advanced at the time of laboratory examination. Incompetence of both primary and secondary hemostatic mechanisms predisposed to the clinically evident hemorrhagic diathesis (15). The laboratory diagnosis of DIC is dependent on the evaluation of multiple hemostatic parameters. Which tests are of the greatest diagnostic value for early detection of developing DIC has yet to be determined (19,21). Early evaluation of high risk patients however, may be beneficial both in detecting early changes associated with intravascular coagulation and in establishing the prognosis in developing DIC.

Acknowledgments

The authors are indebted to Mr. S. Crane for his technical assistance and expertise and to Dr. I. Wilkie (Department of Pathology) for performing the postmortem examination.

Financial support from the Ontario Racing Commission and the Ministry of Agriculture and Food is gratefully acknowledged.

References