Disseminated intravascular coagulation in an ambulatory young woman

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We are reporting the case of an ambulatory young woman with a 10-year history of recurrent venous thrombosis who presented to us with diffuse intravascular coagulation (DIC). After excluding the recognized causes of DIC, we examined the possibility that her clinically quiescent ulcerative colitis might be the underlying stimulus. We documented sepsis-range endotoxemia in this patient at a time when she was afebrile and had a normal C-reactive protein level. In vitro her serum upregulated tissue factor in cultured endothelial cells. We postulate that she had become tolerant to the systemic effects of endotoxin leaking from her inflamed colon but that the endotoxin stimulated her endothelium and/or monocytes to produce tissue factor that made her intensely hypercoagulable. Her prothrombotic state may have been compounded by the fact that she was heterozygous for prothrombin G20210A and that her plasma clotting time demonstrated resistance to activated protein C. (J Lab Clin Med 2005;146:192–196)

Abbreviations: APC = activated protein C; DIC = disseminated intravascular coagulation; DVT = deep vein thrombosis; ELISA = enzyme-linked immunosorbent assay; HUVECs = human umbilical vein endothelial cells; IBD = inflammatory bowel disease; PT = prothrombin time; SD = standard deviation

DIC is always secondary to an underlying and usually obvious disease. Acute DIC is typically associated with sepsis or extensive trauma, whereas chronic expressions of the syndrome occur with metastatic malignancy, giant hemangiomas or venous malformations, and retained dead fetuses.[1] Recently, however, we encountered an ambulatory outpatient with DIC who had none of these pathologies. Her case was sufficiently instructive that we felt it should be reported.

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CASE PRESENTATION

Our patient was evaluated at the W. G. Magnuson Clinical Center at the National Institutes of Health under a protocol approved by the Institutional Review Board of the National Heart, Lung, and Blood Institute. Her investigation was carried out according to principles of the Declaration of Helsinki.

She was a 34-year-old Caucasian woman who was seen in consultation on August 15 because of extensive ecchymoses for several months and inexplicable coagulation test results. She claimed to be otherwise asymptomatic. Although she gave a history of recurrent DVT and ulcerative colitis, she was taking no anticoagulants, and her colitis was well controlled with mesalamine. She specifically denied recent diarrhea.

Three months earlier, however, she had had a bout of bloody diarrhea at a time when she was taking warfarin.

Table I. Laboratory data

	August 15	September 3	September 30	March 18
PT (11.8–14.7 s)	18.7	13.7	13.0	13.4
APTT (23.4–34.3 s)	43.6	34.5	32.5	28.3
Fibrinogen				
Functional (170–460 mg/dL)	56	123	212	269
Immunologic (180–310 mg/dL)	45			
D-dimer (<0.5 μg/mL)	8–16	2–4	<0.5	8–16
FDP (<5.0 μg/mL)	80–160	5–10	5–10	20–40
Platelets (160–380 K/μL)	113	349	446	340
Antithrombin (75–127%)	98			95
Protein C (72–150%)	76			83
Protein S (64–130%)	56			74
Homocysteine (0–13 μmol/L)		7.5	9.3	
APC resistance ratio (2.2–3.4)		1.6		1.4
Plasminogen (77–130%)	56			98
Antiplasmin (80–120%)	69			
Factor II (60–150%)	74			112
Factor V (55–140%)				107
Factor VII (55–160%)	77			
Factor VIII (55–175%)	59			104
Factor X (60–450%)	64			
TAT (1.3–4.0 μg/L)	47			
Functional tPA (0–0.9 IU/mL)	0.2			
Functional PAI-1 (0.1–60 U/mL)	8.7			
Tissue factor (5–650 pg/mL)	172			

Her PT then was >100 s, which was attributed to over anticoagulation, and she had thrombocytopenia (45,000/μL), which was felt possibly to be secondary to mesalamine. The warfarin was discontinued, and her gastrointestinal symptoms came under control with corticosteroids, but the ecchymoses persisted. Over the subsequent months, her thrombocytopenia also continued, and her PT remained prolonged. Eventually she was found to have a plasma fibrinogen level of 59 mg/dL, which prompted the referral to our clinic.

Ten years before consultation, the patient had her first DVT in her left leg while taking an oral contraceptive. She stopped the contraceptive and took warfarin for 6 months. But 6 months after discontinuing warfarin, she developed a DVT in her right leg and a pulmonary embolus. After this she was prescribed lifelong anticoagulation. She was found to be heterozygous for prothrombin G20210A, as was her father, who had never had a thrombosis, nor had anyone else in her family.

Four years later, the patient began bruising spontaneously and developed a hematoma in her right elbow. She also developed symptoms of gastroenteritis and apparent sepsis. In an intensive care unit, a catheter was inserted in her right radial artery, which subsequently thrombosed. It led to a compartment syndrome and amputation of her right hand. During that hospitalization, her fibrinogen fell precipitously, and her D-dimer level became extremely elevated. However, she recovered and resumed warfarin.

A year later, the patient developed bloody diarrhea and was found to have ulcerative colitis by colonoscopy. She was treated successfully with corticosteroids and mesalamine. Two years later, while on warfarin, she again developed bloody diarrhea, accompanied by bruising and hematomas. The warfarin was discontinued until her colitis was controlled. She remained stable until the hospitalization described above 3 months before our consultation.

Our initial laboratory evaluation of the patient is summarized in Table I (August 15). She also underwent computerized tomography of the chest, abdomen, and pelvis, which revealed no evidence of malignancy or vascular malformations, although it did show a left hydronephrosis that had also been documented several years earlier. Blood cultures were sterile. Pancreatic enzymes, C-reactive protein, and ceruloplasmin were within normal limits.

Because her laboratory data were consistent with DIC, the patient was given low-molecular-weight heparin (60 mg/d enoxaparin). Within 2 weeks, her ecchymoses resolved, and her laboratory values had improved significantly (Table I, September 3). Approximately 8 weeks after presenting to us, however, our patient developed bloody diarrhea and discontinued her low-molecular-weight heparin. She was given corticosteroids and