EARLY DIAGNOSIS OF DIC DEVELOPMENT INTO THE OVERT PHASE

Jan Urge^a, Jan Strojil^b

^a 2nd Internal Clinic, University Hospital Olomouc, Czech Republic

^b Department of Pharmacology, Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic
e-mail: urgejan@fnol.cz

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Background: Disseminated intravascular coagulation (DIC) is a syndrome characterized by over-activation of intravascular coagulation, accompanied by consumption of coagulation factors. It is a pathologic systemic inflammatory response accompanied by release of coagulatory substances into the circulation.

Aim: The aim of this paper is to emphasize the importance of early the early diagnosis of DIC and to present a case report of a successful early diagnosis and treatment.

Method: A case report giving a detailed account of clinical and laboratory presentation of a case of DIC in a patient with sepsis. Relevant laboratory results and other tests are presented, treatment is described in detail.

Conclusions: DIC remains an important and potentially life-threatening complication of severe disease and states. Early diagnosis is vital for the success of treatment, and in severely ill patients, the possibility of DIC should always be kept in mind in order to detect early signs and initiate treatment as soon as possible.

According to the ISTH (International Society for Thrombosis and Hemostasis), disseminated intravascular coagulation (DIC) is a syndrome characterized by over-activation of intravascular coagulation, accompanied by consumption of coagulation factors. The absence of clear localization and damage to microcirculation are typical, which leads to severe organ damage.¹

The most common causes are trauma and surgical operations, especially if accompanied by devastation of tissues, longer duration, or massive blood loss (over 2 liters). Other significant and common causes are complications of labor, malignant diseases, sepsis, infections, metabolic disturbances, giant hemangiomas, aneurysms of abdominal aorta, and liver disease.

The exact incidence of DIC is not known. It was estimated that DIC develops in one in every 1,000 patients admitted to hospital.²

Pathophysiologically, DIC is a pathologic systemic inflammatory response accompanied by release of coagulatory substances into the circulation.³

When the body has intact endothelium, it is able to neutralize any generated thrombin via antithrombin and bound thrombomodulin. When the endothelium is damaged, for example in sepsis, this protective function is diminished^{4,5} and a large amount of tissue factor is released into the lumen of the vessel, which increases the generation of thrombin.

The course of DIC has three consecutive stages:

1. The stage of active coagulation with hypercoagulable state.
2. The stage of exhaustion of coagulation.
3. The stage of hyperfibrinolysis, previously called defibri-

nation syndrome. (In this stage, multiple unstoppable hemorrhagic diathesis with total breakdown of coagulation develops, with very little chance of reversal.)

The clinical symptomatology of DIC is very variable, and it consists of two dominant presentations, which can overlap and even convert from one to the other. The first is a hypercoagulable state, and the second is the hemorrhagic diathesis state.

Bleeding symptoms are multiple and varied. They can have the form of petechial bleeding, presenting with large ecchymoses and suggillations, or present by bleeding into the skin, muscles, body cavities, or the brain. Bleeding from wound surfaces is very common – after operations, labor, decubitus, and so on.

The course and severity of the syndrome depends on the responsible cause, how rapidly the syndrome develops, and how dramatic it is, is directly proportional to the cause. It often ends fatally. Severe disturbances of coagulation cannot be compensated for by the body, or can only be compensated with difficulty.

This course of the syndrome is the so-called “overt syndrome”. It is frequently seen in shock, sepsis, obstetrics, major trauma, post-operative and peri-operative states, and malignant diseases. Incidence of DIC in solid tumors is estimated to be between 15–20 %.⁶

However, most bleeding disorders in malignant diseases are not a clinical sign of DIC. According to the latest published literature, the incidence of DIC in patients with tumors is about 6.8 %.⁷

In contrast to this, the so-called “non-overt DIC syndrome (chronic, compensated)” often runs undetected.

DIAGNOSIS OF DIC

The most important thing is to correctly recognize individual phases of the syndrome and assess the damage to individual organs and identify the cause of the syndrome.^{4,8}

The bases of the diagnosis are coagulation tests with targeted examination of coagulation parameters.

The basic set includes, besides APTT, AT, and PT, the examination of the platelet count, fibrinogen, anti-thrombin, and fibrin degradation products (FDP) and D-dimers (DD).

From the diagnostic point of view, D-dimers are important because their levels reflect fibrin breakdown.

TREATMENT OF DIC

Treatment of DIC is focused on:

- The underlying disease
- The life-threatening circumstances
- The DIC itself

The treatment is different depending on the specific characteristics of DIC, and on the etiologic cause, and on the stage of DIC at a given moment.

The treatment has to account for the symptoms and clinical complications of the patient.^{9,10}

In light of the proven over-activation of coagulation, it is a logical requirement to introduce anti-thrombotic measures. For this purpose we mostly use heparins, direct and indirect inhibitors of thrombin and factor X, and inhibitors of blood coagulation.

Views on heparins use are divided, but we administer them when there are conclusive signs of coagulation and no symptoms of insufficient coagulation or exhausted coagulation factors.

Currently, we mainly use low molecular weight preparations. In order for the heparin treatment to be effective, it is necessary to ensure sufficient binding capacity, i.e. a sufficient level of antithrombin. For this reason, anti-thrombin levels need to be supplemented when they drop significantly (under 40–50 % of normal values).

For substitution, we use fresh frozen plasma, a complex concentrate of coagulation factors of the extrinsic coagulation pathway. Currently in development is a new preparation, drotrecogin alpha, a recombinant activated protein C.¹¹

Plasma itself is probably the most balanced preparation. When individual systems and mechanisms of coagulation regulation fail, we are often forced to take extreme measures, including administering antifibrinolytics, universal hemostatics such as rFVIIa, and other new therapeutic options.

CASE REPORT

A female patient Z.N. was admitted to the 2nd Internal Clinic in the University Hospital in Olomouc on

December 2, 2005 for general deterioration in state and a history of enterorrhagia. In the previous 2 weeks she had complained of weakness, dull pain in the lumbar region bilaterally, and pain in the lower limbs. For several days she had been practically immobile.

She had long-term urinary incontinence and recently had dysuric symptoms. Sometimes she vomited acids without blood. She had not measured her temperature, and did not have chills or shivering.

HISTORY

Personal history: In May 2003 she had an abdominal hysterectomy for carcinoma of the uterus with adjuvant radiotherapy. She had been treated for several years for hypertension and ischemic heart disease, and had a history of thrombosis of the right lower limb.

Family history: Negative

Social and occupational history: Retired housewife.

Pharmacologic history: Diacordin, Anavenol, Anopyrin, Rhefluin, Verospiron

Allergies: None

EXAMINATION ON ADMISSION

An obese patient with global heart failure, edema of the lower limbs up to the knees, two decubiti in the sacral region. The patient was afebrile, temperature 36.7 °C, abdominal examination without any abnormalities, rectal exam without abnormalities, brown stool.

On December 5th, 2005 a temperature of 38.3 °C (100.9 °F) was measured in the afternoon and massive enterorrhagia appeared, unstoppable with a rectal tampon with epinephrine. Because of the febrile state, decubiti and urine tests, a diagnosis was made of an insipient DIC, which was later confirmed. Abdominal pain appeared with maximum intensity in the left mesogastrium, where an elastic resistance could be palpated, approximately 10×5 cm in size. The patient was transferred to the ICU for further treatment.

Laboratory findings:

Sedimentation: 70/114

Blood count	Initially	First day of clinical worsening
Leukocytes (4.0–10.0 10 ⁹ /l)	13.2	33.2
Erythrocytes (4.3–5.7 10 ¹² /l)	4.96	4.3
Hemoglobin (120–170 g/l)	138	117
Hematocrit (0.39–0.52)	0.41	0.34
Platelets (150–400 10 ⁹ /l)	499	154

Further trend for normalization up to normal level at dismissal

Coagulation:

(1st day of clinical worsening)

Quick: 26 % (85–1.21 %) INR: 3.31 (0.9–1.15) aPTT: 81.7" (24.0–34.0 s) fibrinogen: 0.3 (1.8–4.5 g/l) ATIII: 115 % FDP: positive

D-dimers: positive FDP quant.: over 20 (pod 10 g/l)

Selected biochemical parameters:

Na: 120 (130–144 mmol/l) K: 5.1 (3.6–5.4 mmol/l) Cl: 84 (95–110 mmol/l) Ur: 9.5 (2.8–8.3 mmol/l) Creat.: 93 (53–124 µmol/l) Bilirubin: 14 (0–23 µmol/l) ALT: 0.74 (0–0.75 µkat/l) AST: 0.76 (0–0.94 µkat/l) ALP: 3.49 (0–2.5 µkat/l) GMT: 3.73 (0–0.6 µkat/l) LD: 8.66 (3.9–7.8 µkat/l) AMS: 0.71 (0.47–0.67 µkat/l) CK: 0.64 (0.2–2.9 µkat/l) CB: 65 (65–85 g/l) ALB: 36 (35–50 g/l) CRP: 126 (0–5 mg/l) glucose: 7.7 (3–5.6 mmol/l)

Urine cultivation: *E. coli* 10^{6–7}/ml repeatedly

Chest X-ray: Lungs without infiltration, heart border size

Abdominal CT – disfigurement of the left psoas muscle and irregular enlargement, reaches the posterior thoracic wall, vertebral bodies, and aorta, lateral abdominal wall, dislocation of the left kidney ventrally and to the right

Abdominal CT excluded a relapse of a malignant tumor; a hematoma of left psoas muscle was diagnosed.

Rectoscopy and colonoscopy confirms diverticulosis of sigmoid colon, without a clear source of bleeding.

All criteria for the diagnosis of DIC were met.

After treating the DIC syndrome with frozen plasma, transfusions of erythrocytes, application of low molecular weight heparin, and complex nursing care including monitoring of vital functions, the critical condition was resolved. Concomitant urinary tract infection was treated with antibiotics according to the MIC profile (gentamicin and amoxicillin).

Repeated CT scan showed no progression of the hematoma and laboratory values returned to normal.

Since the patient had several other conditions requiring intensive nursing care even after the critical condition had subsided, she was transferred back to the ward, realimented and rehabilitated. She was then transferred for further treatment to the geriatric clinic.

DISCUSSION

It is necessary to keep DIC in mind each time we see a hemorrhagic complication, as was proven true in our patient hospitalized for enterorrhagia in diverticulosis. She was scheduled for a routine GI examination, with no anticipation of the need for an urgent intervention. Her history included enterorrhagia several weeks earlier, without any drop in blood count. While preparing for

colonoscopy, a lower GIT bleeding appeared that could be considered to be a complication of the underlying disease. In view of the patient's febrile condition, enterorrhagia not responding to local treatment, and decubiti in sacral region and the urinary finding, DIC was considered as a possible diagnosis.

The suspicion was confirmed and the patient was transferred to the ICU for intensive therapy, including rational hemotherapy.

Thanks to the rigorousness of the doctor on duty, a potentially fatal complication was avoided, since if the patient had remained on a standard ward, she would have been in danger of potentially fatal blood loss. The DIC syndrome was diagnosed relatively early by laboratory tests and its pathological course was able to be reversed by intensive therapy.

CONCLUSION

DIC remains a feared complication of many acute and chronic states. Its high mortality is often caused by late diagnosis and treatment. It is therefore necessary to keep reminding physicians that a most important factor is to keep the condition in mind at all times.

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