Thrombosis & Haemostasis: Research

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Perspective

Disseminated Intravascular Coagulation (DIC): What the Physician Should Know?

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Received: December 26, 2023

Accepted: January 25, 2024

Published: February 01, 2024

Perspective

Disseminated Intravascular Coagulation (DIC) can be defined as a widespread hypercoagulable state that can lead to both microvascular and macrovascular clotting compromising blood flow resulting in multiple organ dysfunction syndrome. The consumption coagulopathy and thrombocytopenia will precipitate haemorrhage which may be the presenting symptom. It typically occurs as an acute complication in patients with underlying life-threatening illnesses such as severe sepsis, haematological malignancies, severe trauma, or placental abruption [1]. While disease states that may cause many of the signs and symptoms consistent with DIC such as acute or chronic liver failure can obscure a patient's prognosis, mortality rates have been shown to double in septic patients or those with severe trauma if they are also suffering from DIC [2]. Multiple medical conditions can lead to the development of DIC either through a systemic inflammatory response or the release of pro-coagulants into the bloodstream [3-5]. The most common cause of DIC is severe sepsis occurring in up to 30 -50% cases, classically with gram-negative bacteria sepsis but the prevalence may be similar in sepsis due to gram-positive organisms. It occurs in 20% of patients with metastasized adenocarcinoma or lymphoproliferative disease, 1-5% of patients with chronic diseases such as solid tumours and aortic aneurysms. Obstetric complications such as placenta abruption, haemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome), and amniotic fluid embolism have also been known to lead to DIC. About 15% of cases of DIC have also been linked to complications occurring after surgery. Other causes of DIC include trauma, pancreatitis, malignancy, snake bites, liver disease, transplant rejection, and blood transfusion reactions [6-10]. Perhaps the manifestation of the 'macrophage activation-like syndrome' may be the entity leading to early death in sepsis [11]. As the. pathophysiology of DIC is rarely straightforward, the classification is largely arbitrary (Table 1). The differential diagnosis would include dysfibrinogenemia, haemolytic uraemic syndrome, heparin-induced thrombocytopenia, Immune Thrombocytopenia (ITC), thrombotic Thrombocytopenic Purpura (TTP) [1]. As DIC can be a complication of many medical conditions, the reported prevalence will remain greater in higher than lower acuity settings because of the higher level of clinical suspicion [1,2,6]. It is now believed that most cases result from activation of coagulation factors from both intrinsic and extrinsic pathways, i.e. consumption coagulopathy, and activation of fibrinolysis is secondary to the process. [1,2,6,12,13]. Rarely, the condition may result from a primary activation of the fibrinolytic system. The intrinsic system of coagulation is triggered from the stimulation of platelets by exposure to bacteria, immune complexes, or to endothelial damage by bacteria endotoxin. Contact activation may result from exposure to particulate matter, amniotic fluid globules, or damaged vessel wall. The extrinsic system is triggered by tissue thromboplastin liberated by trauma and disseminated malignant disease. This activation generates thrombin which aggregates platelets, leading to platelet consumption and thrombocytopenia. Intravascular thrombin generates fibrin, thus depleting fibrinogen, prothrombin and other coagulation factors. In addition, fibrinolysis is stimulated producing Fibrin Degradation Products (FDPs), which further inhibit platelet function and fibrin polymerization. If the vascular endothelium is extensively damaged, sur-

Citation: Weledji EP, Simo AW. Disseminated Intravascular Coagulation (DIC): What the Physician Should Know?. Thromb Haemost Res. 2024; 8(1): 1094.

Table 1: Some disorders contributing to DIC.

Infections	Exposure to thromboplastins	Neoplasia	Obstetric	Hypovolaemia
Sepsis with Gram-negative or Gram- positive organisms Rickettsial diseases Certain virus infections, e.g. cytomegalovirus	Some snake bites, e.g. Echis carinatus Excessive tissue trauma Burns Fat embolism Incompatible blood transfusions Heart-Lung bypass	Leukaemia (especially promyelocytic) Cancer: lung, breast, prostate, gastrointestinal tract	Septic abortion Retained dead fetus Amniotic fluid embolism Eclampsia Premature separation of the placenta	Heat stroke Hypovolaemic shock Diabetic ketoacidosis Liver failure

face contact stimulates platelet and tissue factors which then activate both coagulation and fibrinolysis. In DIC there is failure of inhibition of coagulation and fibrinolysis follows. The main problem is what causes the inappropriate activation of the haemostatic mechanism which results in widespread formation of fibrin and secondary depletion of platelets and clotting factors. [1,12,13]. The clinical presentation varies from no bleeding to complete haemostatic failure with widespread haemorrhage. This can occur from the mouth, nose or venepuncture sites, and skin shows widespread ecchymosis. The patient is often acutely ill and shocked, but the clinical severity will vary according to the initiating factors. In less severe forms of DIC a patient may show prolonged bleeding after venepuncture, or scattered ecchymosis with no other specific clinical signs. The second clinical feature is reflected by a variable degree of tissue and organ damage due to laying down of fibrin. The most serious manifestation is renal involvement, which vary in severity from reversible tubular necrosis to complete irreversible bilateral renal cortical necrosis. The skin is also vulnerable and large areas of gangrene is associated with fulminant septicaemias (purpura fulminans or gangrenosa). Adult respiratory distress syndrome (shock-lung) is associated with the diffuse fibrin deposition in the small vessels of the lung, and similarly acute liver or adrenal failure may complicate the syndrome. Microangiopathic haemolytic anaemia is common in patients with disseminated malignant disease [1,6,14].

The diagnosis and management of DIC are complex and challenging. The condition is best managed by a multidisciplinary team consisting of a haematologist, surgeon, intensivist, infectious disease specialist, pathologist and internist [15]. The key is to address the underlying disorder that ultimately led to the condition developing. However, some patients with DIC are desperately ill and the clinician has little time in which to activate a series of laboratory investigations and to start treatment. The diagnosis is initially suggested by the underlying condition. The Prothrombin Time (PT) is prolonged and the platelet count is reduced. The fibrinogen level is also reduced and FDPs are usually raised. A blood film may show fragmented cells. The principle of early goal directed therapy in sepsis holds especially as fluid resuscitation with 0.9% saline alters haemostasis in endotoxaemic shock [15,16], in addition to the optimal outcome of early source control in the management of severe sepsis and septic shock [17-19]. Bleeding requires infusion of fresh plasma and perhaps platelets until the consumptive process becomes less acute. It is essential is to treat the underlying cause, and bleeding usually stops once a septicaemia is treated by adequate antibiotic therapy, or the uterus is emptied in the syndromes of abruption placentae or the retained dead fetus. If the process is running a more chronic course and there is progressive deterioration of organ function heparin in low dosage (500-1000units per hour) is sometimes given in malignant disease, leukaemia, amniotic fluid embolism, purpura fulminans and the shock-lung syndrome to prevent intravascular coagulation, although there is still no definite proof of its efficacy. The patient should be monitored closely for evidence of increased bleeding and there should be appropriate laboratory back-up and expertise [17,20,21]. Fibrinolytic inhibitors like tranexamic acid should not be used in DIC as dangerous fibrin deposition may result. When the laboratory tests of haemostatic function are less severely abnormal in patients in whom the development of DIC may be expected, it is prudent to simply monitor changes in haemostatic function while vigorously treating the underlying condition. The premature diagnosis of DIC with possibility of potentially harmful therapeutic intervention is best avoided [17]. In conclusion, DIC is commonly associated with life-threatening illnesses and the main principles of treatment are to remove the underlying cause wherever possible with an attempt to prevent bleeding and retain organ function. It carries a very high mortality with most survivors having a prolonged recovery period because of the effects on many organ systems.

Author Statements

Author Contributions

EPW is the main author. AWS contributed to literature search

Data Availability Statement

The data that support the findings of the study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restriction.

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