Clinics in Surgery

Short Communication
Published: 12 Jan, 2024

Disseminated Intravascular Coagulation (DIC): What the Surgeon Should Know

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Short Communication

Disseminated Intravascular Coagulation (DIC) can be defined as a widespread hypercoagulable state that can lead to both microvascular and macrovascular clotting compromising blood flow and resulting in multiple organ dysfunction syndrome. The consumption coagulopathy and thrombocytopenia will precipitate hemorrhage which may be the presenting symptom. It typically occurs as an acute complication in patients with underlying life-threatening illnesses such as severe sepsis, hematological 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]. Systemic Inflammatory Response Syndrome (SIRS) is a massive systemic response comprising an evolution of a cytokine cascade (Tumor Necrosis Factor (TNF), Interleukins (IL-1, IL-6, IL-8), and a sustained activation of the reticuloendothelial system. It finally leads to the elaboration of secondary inflammatory mediators causing cell damage. These mediators include arachidonic metabolites (prostaglandins and leukotrienes), nitric oxide (vasodilator), oxygen free radicals, platelet activating factor causing increase platelet deposition, vasodilatation, increase capillary permeability and activation of coagulation pathways which results in end-organ dysfunction by formation of microthrombi. Once one organ system has failed, others typically follow (organ failure amplification) [5]. The most common cause of DIC is severe sepsis occurring in up to 30% to 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% to 5% of patients with chronic diseases such as solid tumors and aortic aneurysms. Obstetric complications such as placenta abruption, Hemolysis, 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 pancreatitis, snake bites, liver disease, transplant rejection, and blood transfusion reactions [6-10]. As the pro-inflammatory cytokines especially TNFα are mostly secreted by the activated macrophages and monocytes of the reticuloendothelial system the manifestation of the 'macrophage activation-like syndrome' may be the entity leading to early death in sepsis [11]. The pathophysiology of DIC is rarely straightforward, the classification is largely arbitrary (Table 1). The differential diagnosis would include dysfibrinogenemia, hemolytic uremic 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

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Received Date: *27 Dec 2023*
Accepted Date: *08 Jan 2024*
Published Date: *12 Jan 2024*

Citation:
Weledji EP. Disseminated Intravascular Coagulation (DIC): What the Surgeon Should Know. Clin Surg. 2024; 9: 3682.

Table 1: Some disorders contributing to DIC.

Infections	Exposure to thromboplastins	Neoplasia	Obstetric	Hypovolemia
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	Leukemia (especially promyelocytic) Cancer: Lung, breast, prostate, gastrointestinal tract	Septic abortion Retained dead fetus Amniotic fluid embolism Eclampsia Premature separation of the placenta	Heat stroke Hypovolemic shock Diabetic keto-acidosis Liver failure

and fibrin polymerization. If the vascular endothelium is extensively damaged, surface 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 hemostatic 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 hemostatic failure with widespread hemorrhage. This can occur from the mouth, nose or venipuncture 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 venipuncture, 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 septicemias (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 hemolytic anemia 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 hematologist, 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 hemostasis in endotoxemic shock [15,16]. In addition, the importance of early source control in the management of severe sepsis and septic shock is well known [17-19]. Bleeding requires infusion of fresh plasma and perhaps platelets until the consumptive process becomes less acute. Platelet transfusions are particularly given if there is severe bleeding and/or low platelet counts. Clotting factor replacement therapy is given for severe bleeding in patients with high PT or Partial Thromboplastin (PTT) time or low fibrinogen levels. Heparin is sometimes given if there is evidence of organ failure related to blood clotting. It is essential to treat the underlying cause, and bleeding usually stops once a septicemia is treated by adequate antibiotic therapy, or the uterus is emptied in the syndromes of abruption placentae or the retained dead fetus. Damage control surgery may be required in severe hypotension. By rapidly packing the causative bleeding source such as in postpartum hemorrhage or in severe trauma and returning after the coagulopathy is corrected will avoid the bloody vicious triad of hypothermia, acidosis and coagulopathy [20,21]. It is also important to anticipate abdominal compartment syndrome in the setting of coagulopathy and non-surgical bleeding requiring packing, extensive abdominal injury with bowel oedema, massive transfusions and fluid resuscitation [22]. If the process is running a more chronic course and there is progressive deterioration of organ function heparin in low dosage (500-1000 units per hour) is sometimes given in malignant disease, leukemia, 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 [17,23,24]. Fibrinolytic inhibitors like tranexamic acid should not be used in DIC as dangerous fibrin deposition may result. When the laboratory tests of hemostatic function are less severely abnormal in patients in whom the development of DIC may be expected, it is prudent to simply monitor changes in hemostatic function while vigorously treating the underlying condition. This will avoid a premature diagnosis of DIC with possibility of potentially harmful therapeutic intervention [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, and most survivors have a prolonged recovery period because of the effects on many organ systems.

References

1. Levi M. Disseminated intravascular coagulation. Crit care Med. 2007;35(9):2191-5.
2. Yoshimura J, Yamakawa K, Kodate A, Kodate M, Fujimi S. Prognostic accuracy of different disseminated intravascular coagulation criteria in critically ill adult patients: A protocol for a systematic review and meta-analysis. BMJ Open. 2018;8(12):e024878.
3. Gando S, Nanzaki S, Kemmotsu O. Disseminated intravascular coagulation and sustained systemic inflammatory response syndrome predict organ dysfunctions after trauma: Application of clinical decision analysis. Ann Surg. 1999;229(1):121-7.
4. Sibikova M, Zivny J, Janota C. Cell membrane-derived microvesicles in systemic inflammatory response. Folia boil (Praha). 2018;64(4):113-24.
5. Weledji EP, Assob JC. The systemic response to surgical trauma: A review. East Central Afr J Surg. 2012;17(2).
6. Okajima K, Sakamoto Y, Uchiba M. Heterogeneity in the incidence and

clinical manifestations of disseminated intravascular coagulation: A study of 204 cases. Am J Hematol. 2000;65(3):215-22.

7. Komo T, Kohashi T, Aoki Y, Hihara J, Oishi K, Tokumoto N, et al. Successful surgical management of non-perforating acute appendicitis with septic disseminated intravascular coagulation: A case report and review of the literature. Int J Surg Case Rep. 2019;55:103-6.
8. Sibai BM, Ramadan MK, Usta I, Salama M, Mercer BM, Friedman SA, et al. Maternal morbidity and mortality in 442 pregnancies with haemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Am J Obst Gynecol. 1993;169(4):1000-6.
9. Bone RC. Gram-positive organisms and sepsis. Arch intern Med. 1994;154(1).26-34.
10. Chen W, QI J, Shang Y, Ren L, Guo Y. Amniotic fluid embolism and spontaneous hepatic rupture during uncomplicated pregnancy. A case report and literature review. J Matern Fetal Neonatal Med. 2020;33(10):1759-66.
11. Karakike E, Giamarellos-Bourboulis EJ. Macrophage activation-like syndrome: A distinct entity leading to early death in sepsis. Front Immunol. 2019;10:55.
12. Thachil J. The elusive diagnosis of disseminated intravascular coagulation: Does a diagnosis of DIC exist anymore? Semin Thromb Hemost. 2019;45(1):100-107.
13. Venugopal A. Disseminated intravascular coagulation. Indian J Anaesth. 2014;58(5):603-8.
14. Matsuda T. Clinical aspects of DIC- disseminated intravascular coagulation. Pol J Pharmacol. 1996;48(1):73-5.
15. Rivers E, Nguyen S, Havstad J, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345:1368-77.
16. Passmore MR, Obonyo NG, Byrne L, Boon AC, Diab SD, Dunster KR, et al. Fluid resuscitation with 0.9% saline alters hemostasis in an ovine model of endotoxemic shock. Thromb Res. 2019;176:39-45.
17. Levi M, Toh CH, Thachil , Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for standards in Hematology. Br J Haematol. 2009;145(1):24-33.
18. Marshall JC, Maier RV, Jimenez M, Dellinger EP. Source control in the management of severe sepsis and septic shock: an evidence-based review. Crit Care Med. 2004;32:5513-26.
19. Weledji EP, Ngowe MN. The challenge of intraabdominal sepsis. Int J Surg (Lond). 2013;11(4):290-5.
20. Yoshida K, Watanabe K, Sato Y, Sumiyoshi M, Murakawa M. Successful perioperative management with damage control surgery in a patient with massive postpartum hemorrhage of more than 20,000 ml. Case Rep Anaesthesiol. 2020;2020:8872925.
21. Cosgriff N, Moore EE, Sauaia A, Kenny-Moynihan M, Burch JM, Galloway B. Predicting life-threatening coagulopathy in the massively transfused patient: hypothermia and acidosis revisited. J Trauma. 1997;43(5):857-61.
22. Saggi BH, Sugerman, HJ, Ivatury RR, Bloomfield GL. Abdominal compartment syndrome. J Trauma. 1998;45:597-609.
23. Hashimoto D, Okawa T, Maruyama R, Matsumura F, Shibata Y, Kohrogi H. Anticoagulant therapy for disseminated intravascular coagulation after gastrointestinal surgery. Anticancer Res. 2019;39(1):25-31.
24. Endo S, Shimazaki R; Antithrombin Gamma study group. An open-label, randomized, phase 3 study of the efficacy and safety of antithrobin gamma in patients with sepsis-induced disseminated intravascular coagulation syndrome. J Intensive Care. 2018;6:75.