Disseminated intravascular coagulopathy (DIC)

Clotting-Guide
vom Labor zur Diagnose

Description:

Disseminated intravascular coagulopathy (DIC) is a rare but often serious and life-threatening blood clotting disorder. While the hemostatic system is designed to ensure the integrity of the blood vessel system and to minimize blood loss in the event of injuries, it must also be ensured that the clotting processes only take place in a controlled and limited manner at the site of the injury in order not to impede circulation in the unaffected flow areas. This interaction between rapid closure of vascular injuries and ensuring undisturbed microcirculation requires subtle regulation of the mechanisms involved.

DIC is a condition in which coagulation processes are not localized but rather disseminated throughout the entire circulation. As a result, the physiological control and modulation of hemostasis is no longer guaranteed and excessive fibrin formation and deposition in the microcirculation and disturbances in organ function occur. In later stages, the consumption of coagulation factors can no longer be compensated for and a severe clinical tendency to bleeding occurs (consumption coagulopathy).

Non-overt and overt coagulopathy:

In certain situations there is a mismatch between the intensity of coagulation activation and the ability of the organism to adequately control it or to reproduce the factors used. Individual, genetically determined or acquired differences also play a major role. The resulting coagulopathy can be transient and stop simply by treating the underlying disease, but can also develop progressively from massive fibrin formation with thrombosis and microcirculation disorders to manifest, severe consumption coagulopathy with an insatiable tendency to bleeding.

Early signs of a serious coagulopathy are reduced levels of platelets, PT and fibrinogen (although fibrinogen levels must always be assessed in context with other acute phase parameters), as well as increased D-dimer values. In addition, a reduction in inhibitors (antithrombin, protein C) can be observed. The fibrinolytic system is often downregulated, leading to persistence of fibrin microthrombi and organ dysfunction.

In the early phase of DIC, massive fibrin formation is often found. Clinical signs include thrombosis, embolism, poorly perfused areas, especially on the skin, but also in other organs, and even necrosis. If there is no response to therapy, progression occurs with increasing consumption of coagulation factors, platelets and inhibitors, as well as insufficient new synthesis with often concurrent liver dysfunction. An early sign of clotting factor consumption is a decrease in PT. If there is a simultaneous acute phase reaction, the fibrinogen levels can remain in the apparently normal range for a longer period, but the D-dimer values increase sharply. Hyperfibrinolysis can often occur parallel to DIC (especially in paraneoplastic coagulopathy), which then manifests itself in very low fibrinogen levels and extremely elevated D-dimer values. The reduction of inhibitors (antithrombin, protein C) is a poor prognostic sign.

The extreme case of DIC is purpura fulminans, a very rapidly progressive disease with typical skin lesions, which, depending on the individual constitution, can occur acutely with certain infections (meningococci, pneumococci, gram-negative sepsis, post-splenectomy infections). There is always a severe coagulopathy, which is primarily characterized by a (local or systemic) failure of the protein C system. Supplementing standard therapy by substituting protein C improves outcome and long-term damage.

Treatment options:

General measures:

Standardized sepsis therapy:	fluids, antibiotics, vasopressors, etc. according to guidelines. Hemodynamic monitoring, intensive care treatment
Declaration of consent	for possible inclusion in clinical studies for off-label therapy with Ceprotin®
Advanced laboratory samples:	Protein C activity, PAI levels, muscle enzymes, research
Scoring and close monitoring:	Use ISTH score for manifest and latent DIC, note sources of error
Erythrocyte concentrates:	Target: Hb >7.0 g/dL

Coagulation inhibitors:

Antithrombin concentrates:	approx. 50 U/kg/d (if antithrombin levels significantly lower than PTZ). Goal: Antithrombin level >50%
Protein C concentrate (Ceprotin®):	100 U/kg bolus, 10 U/kg/h continuous infusion. Target: plasma protein C level 100%; off label for purpura fulminans
Plasma infusions:	20-40 ml/kg/d (be careful with hypervolemia or hyperproteinemia)
Unfractionated heparin:	200-1000 IU/h continuous infusion, controlled by APTT (60-80 sec.), TCT (40-60 sec.) or Anti-Xa (0.3-0.5 U/mL)
or low molecular weight heparin:	e.g. 1-2 mg/kg enoxaparin/d, anti-Xa trough level 0.3-0.5 U/mL
Recomb. Thrombomodulin (Remodulin®):	only available in Japan

In case of bleeding prohemostatic therapy:

Fibrinogen concentrate (Fibryga®):	2-4 g/d iv. Goal: fibrinogen >0.5 g/L (even higher in case of bleeding)
Platelet concentrates:	1-2 units/d, not more! Only with sufficient response! Target: platelet counts >30 G/L (for bleeding >50 G/L)
Prothrombin complex concentrates:	approx. 30 U/kg/d. Goal: PTZ >30% (also higher in case of bleeding)
rhFVIIa (Novoseven®):	90 µg/kg repetitive single doses for life-threatening bleeding

Surveillance:

ISTH score for overt DIC:

Score only to be used if the patient has a predisposing underlying disease (e.g. sepsis, severe infection, trauma, organ failure, severe pancreatitis, malignancies, pregnancy complications, vascular anomalies, liver failure, severe toxic or immunological reactions, snake venom, drugs, medications, transfusion reactions, transplant rejection)

Parameter	0	1	2	3	SUM
Platelet count (G/L):	>100	50-100	<50		
D-Dimer (mg/L):	<0,4		0,4-4,0	>4,0	
Prothrombin time (%)	>60	40-60	<40		
or INR:	<1,4	1,4-1,8	>1,8		
Fibrinogen (g/L):	>1,0	<1,0			

Result:

If score > 4 points: compatible with manifest DIC. Repeat score daily

If score <5 points: DIC not proven, apply ISTH score for latent DIC. Repeat score daily.

ISTH score for non-overt DIC:

Parameter	-1	0	1	2	SUM
Predisposing underlying disease		no		yes	
Platelet count (G/L)		>100	<100		
Dynamic:	rising	stable	falling		
D-Dimer (mg/L)		<0,4	>4.0		
Dynamic:	falling	stable	rising		
Prothrombin time (%)		>60	<60		
Dynamic:	rising	stable	falling		
or INR		<1,4	>1,4		
Dynamic:	falling	stable	rising		
If available:					
Antithrombin	normal		low		
Protein C	normal		low		
TAT-complex	normal		high		
F1+2 (?)	normal		high		

Result:

If score > 4 points: compatible with latent DIC. Repeat score daily

If score <5 points: DIC unlikely. Repeat score daily if clinically indicated.

In case of questions please contact a coagulation specialist.

References:

Thomas L, Laboratory and Diagnosis, 2023, Release 5: https://www.labor-und-diagnose.de/index.html

Parameter catalog of the Clinical Institute for Laboratory Medicine, Med.Univ.Wien and AKH Vienna: https://www.akhwien.at/default.aspx?pid=3982

List of services for clinical chemistry, Univ.Klinikum Ulm: https://www.uniklinik-ulm.de/zentrale-einrichtung-klinische-chemie/leistungskatalog.html

According to (Taylor et al. Thromb Haemost 2001; 86(05): 1327-1330. DOI: 10.1055/s-0037-1616068 2001)