Treatment of Adults with Sepsis-Induced Coagulopathy and Purpura Fulminans with a Plasma-Derived Protein C Concentrate (Ceprotin)

P. Schellongowski, U. Eidher, E. Bauer, P. Schenk and P. Knöbl

Introduction

One of the most important pathophysiological effects of sepsis and septic shock is a disturbance of the hemostatic equilibrium. A pronounced activation of the procoagulatory mechanisms, together with a shut-down of fibrinolysis, leads to the formation of fibrin microthrombi in the microvasculature. The consumption of coagulation factors and platelets enhances the bleeding tendency – the result is the clinical picture of disseminated intravascular coagulation (DIC). The resulting hypoperfusion of tissue causes damage of organs: septic patients are considerable sick, need intensive treatment and have, in part, severe compromised organ dysfunction (MODS), associated with a high mortality [1].

A distinct manifestation of sepsis-associated DIC is purpura fulminans with its typical cutaneous morphology (Fig. 1). The coagulopathic processes in the microcir-

Fig. 1. Example on skin lesions of purpura fulminans. a peripheral microembolization with inflammatory reaction; b peripheral microembolization with inflammatory reaction
calculation manifest on the one hand as microthrombosis and necrosis, and on the other hand as petechiae, ecchymosis and sometimes hemorrhagic bullae. Often, even acral gangrene develops. Furthermore, there is an accompanying enhanced inflammatory reaction. The trigger of sepsis induced purpura fulminans is often an infection with some kinds of pathogens, for example neisseria meningitidis, streptococcus pneumoniae, or others. A dysfunction of the protein C pathway is always present in purpura fulminans and a reason for coagulopathy and necrosis. Besides low levels of fibrinogen and antithrombin, a pronounced decrease of the protein C activity is obvious. This is caused either by consumption during systemic activation of blood coagulation and by reduced hepatic synthesis due to septic liver dysfunction, but also by degradation of protein C by proteolytic enzymes released by white blood cells, as elastase. This results in a markedly shortened half life time of protein C compared with healthy subjects (6 hours). Several studies demonstrated that low levels of

Fig. 1c. generalized occurrence of purpura fulminans at the skin

Fig. 1d. lower limb with skin lesions of purpura fulminans, edema, bullae, and beginning compartment syndrome