From chickenpox to purpura fulminans: a case report on acquired protein S deficiency in the aftermath of a varicella zoster infection in a child.

F. Verbeke[1], B. De Wilde[2,3], J. Willems[4], K. Devreese[1]

[1]Dept of Laboratory Medicine, Ghent University Hospital, [2]Dept of Pediatric Hematology, Oncology & Stem Cell Transplantation, Ghent University Hospital, [3]Cancer Research Institute Ghent, Ghent University, [4]Dept of Pediatric Intensive Care, Ghent University Hospital, Corneel Heymanslaan 10 Ghent, Belgium (Corresponding author: Frederick.Verbeke@UZGent.be).

BACKGROUND

The prevalence of protein S deficiency in the general population ranges from 0.03 to 0.13% [1]. Protein S deficiency can be either inborn or acquired, with acquired protein S deficiency linked to, among others, pregnancy, liver disease, sepsis, and multiple myeloma [2]. Varicella zoster is also a possible cause of acquired protein S deficiency, with in extreme cases resulting in purpura fulminans. Purpura fulminans is a disseminated intravascular coagulation-subtype, characterized by skin necrosis, and is mainly confined to children [3]. Hospitalization due to post-varicella zoster coagulopathy in children is rare with 0.04/100 000 per year in the United Kingdom and Ireland [4], but debilitating sequelae, including necrosectomy and even amputation can occur.

CASE PRESENTATION

In this case report, a 4-year-old girl was confronted with varicella zoster with spontaneous resolution. Seven days later, she suddenly experienced profound pain in both legs and substantial purpuric lesions became visible on both legs. Coagulation tests were indicative of a coagulopathy (fibrinogen level below 40 mg/dL (reference interval (RI): 200-400 mg/dL), prothrombin time (PT) (36%; RI: 70-120%), activated partial thromboplastin time (aPTT) (44.7 s; RI: 28.9-38.1 s), protein C activity 46% (RI: 59-168%), antithrombin exceeded 145% (RI: 75-145%), and free protein S antigen of 10% (RI 50-134%)). Her risk to develop purpura fulminans was further increased since she was diagnosed as heterozygous carrier of factor V Leiden [5]. She was transferred to the paediatric intensive care unit (PICU) where fresh frozen plasma was administered with successful normalization of both PT and aPTT. However, over the course of the disease she experienced twice a relapse. The first relapse was preceded by disturbed coagulation parameters and massive gluteal purpuric lesions occurred at day 3. At day 8, the second and last relapse occurred with new, purpuric lesions on the anterior side of both upper legs. Plasmapheresis was started and continued for 2 days in total. On day 18 she left the PICU and she was discharged home at day 20. During follow-up visits, her free protein S antigen levels were 33%, 76%, and 87% at day 23, 49, and 70 respectively. The girl fully recovered and was not confronted with major sequelae due to the fast recognition of the acquired protein S deficiency.

References:

[1] Mannucci PM and Franchini M. Classic thrombophilic gene variants. Thromb Haemost. 2015;114:885-889.

[2] Deitcher SR, Erban JK, Limentani SA. Acquired protein S deficiency associated with multiple myeloma: a case report. Am J Hematol. 1996;51:319–23.

[3] Fonkoua LK, Zhang S, Canty E, et al.Purpura fulminans from reduced protein S following cytomegalovirus and varicella infection. Am J Hematol. 2019;94:491-495.

[4] Cameron JC, Allan G, Johnston F, et al. Severe complications of chickenpox in hospitalised children in the UK and Ireland. Arch Dis Child. 2007;92:1062–1066.

[5] Woods CR and Johnson CA. Varicella purpura fulminans associated with heterozygosity for factor V leiden and transient protein S deficiency. Pediatrics. 1998;102:1208–1210.