Abstract

The purpose of this article is to understand pediatric sepsis, activation of the innate immune system and a synergistic relationship between the loss of organ functions and sepsis pathophysiology. Many complex factors such as genetics, physical agents, mediators and effectors are involved in the development of organ failure both in sepsis in children and neonates. The patient’s immune surveillance could fail to eliminate the pathogens with a release with inappropriate activation. These topics are very important for pediatricians, immunologists, and neonatologists.

Keywords: Pediatric sepsis; Protein C deficiency; Neonatal sepsis; Innate: Immunity

Introduction

Sepsis

Injury due to trauma can induce immune function changes, which can lead to both pro-inflammatory activation known as Systemic Inflammation Response Syndrome (SIRS) and an anti-inflammatory reaction with immune suppression known as Compensatory Anti-Inflammatory Response Syndrome (CARS). SIRS with proven infection is referred to as sepsis, however clinically it is often difficult to isolate the microbial inoculum, making the differential diagnosis between SIRS and sepsis difficult[1]. This differential diagnosis is in turn crucial for further therapeutic decisions: is an antimicrobial therapy and aggressive search for a septic focus with all its side-effects necessary or is a focused symptomatic therapy of the SIRS the adequate treatment concept[1]?

Previous reports on Emergency Medical Services (EMS) transportation of pediatric patients have demonstrated a high rate of overutilization. However, there is also a concern that pediatric patients may underutilize EMS for emergencies that might benefit from EMS. This article compares EMS utilization rate between adult and pediatric patients for high-acuity patients and for the most common reasons for transport[2]. As compared with adults, pediatric patients are less likely to utilize EMS for transport to the hospital for both routine and emergent complaints. The definition of inappropriate utilization of EMS for pediatric transport, which has largely focused on inappropriate overutilization, should also incorporate the potential of underutilization for critical patients[2].

Systemic Inflammation Response Syndrome and Sepsis

Systemic Inflammation Response Syndrome (SIRS) vital signs are common among medical pediatric patients presenting to an ED, and critical illness is rare. The majority of patients with SIRS vital signs were discharged without IV therapy and without readmission. Patients with SIRS vital signs had a statistically significant increased risk of critical care requirement, ED IV treatment, ED laboratory tests, admission, and readmission[4].

However, SIRS vital sign criteria did not identify the majority of patients with mortality or need for critical care. SIRS vital signs had low sensitivity for critical illness, making it poorly suited for use in isolation in this setting as a test to detect children requiring sepsis resuscitation[4].

Plasma gelsolin levels in premature infants at 72 hours and were significantly lower in patients with respiratory distress syndrome and in patients who were administered surfactant therapy and in patients who developed sepsis[5] Plasma gelsolin levels at 28 days were significantly lower in patients who developed bronchopulmonary dysplasia and retinopathy of prematurity (P
concentrate together with continuous veno-venous hemodiafiltration assessed the effects of early replacement therapy with protein-C and also has important anti-inflammatory activity. These authors pointed out that failure are not uncommon. Protein C is a natural anticoagulant that can be brought to bear on an invading pathogen, including neutrophilic cells possessing an impressive array of microbicidal weapons that can be brought to bear on an invading pathogen, including a variety of toxic oxygen radical species and proteolytic enzymes.

Innate Immunity and Sepsis

The cell-regulated innate immune system often contributes to posttraumatic multiple organ dysfunctions or even multiple organ failure. With a cell fraction of 50-60% of all leukocytes, polymorphonuclear leukocytes have been shown to be key effector cells within the innate inflammatory immune reaction.

The innate immune system is an immune monitor and has a very prominent role in organ failure after trauma. Polymorphonuclear phagocytes and monocytes are the main effector-cells of the innate immune system that are involved in organ failure and are controlled by cytokines. Neutrophils play an essential role in the body’s innate immune response to infection. To protect the host, these phagocytic cells possess an impressive array of microbicidal weapons that can be brought to bear on an invading pathogen, including a variety of toxic oxygen radical species and proteolytic enzymes.

Newborn Hypoxia and Reactive Oxygen Species

A review on hypoxia inducible factor (HIF) signaling and experimental persistent pulmonary hypertension of the newborn was conducted. Mitochondrial Reactive Oxygen Species (ROS) levels and nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) activity are increased in an animal model of Persistent Pulmonary Hypertension of the Newborn (PPHN). These events can trigger Hypoxia Inducible Factor (HIF) signaling in response to hypoxia and complex physiological and biochemical processes facilitate the fetal to newborn transition, and abnormal lung development and/or vascular dysfunctions may disrupt these events.

The authors stated increased HIF signaling in PPHN is triggered by stretch, via mechanisms involving mitochondrial ROS and NFκB. Hypoxia substantially amplifies HIF activity in PPHN vascular cells. Targeting these signaling molecules may attenuate and reverse pulmonary vascular remodeling associated with PPHN. This study identified components of the HIF signaling pathway that may contribute to the pathogenesis of PPHN and further studies are warranted in vivo and in vitro to investigate the mechanisms involved to improve current detection and treatment strategies for babies with PPHN.

Figure 1: Pathophysiology Sepsis.

Stage I: Bacteremia Fibrin.

A recent paper by one of the authors stated marked increase in serum procalcitonin during the course of a septic process often indicates an exacerbation of the illness, and a decreasing level is a sign of improvement. Integrating use of procalcitonin into pediatric practice in the early golden hours of sepsis diagnosis and antibiotic stewardship program would be beneficial.

During sepsis, there is an increase in CALC-1 gene expression which causes a release of procalcitonin and, more importantly, their levels persist for relatively long periods of time and correlate with sepsis severity and mortality.
Pediatric Sepsis

State II: Macrophages Responses if the Host Coagulation, Complement, Organ Dysfunction and Death.

Septic children aged between 28 days and 14 years were divided into sepsis and septic shocks. CRP and Procalcitonin (PCT) were measured at admission. CRP levels were not statistically different for groups and time points. PCT was better than CRP for diagnosing sepsis and septic shock, mainly at admission, and is related to disease severity[13].

Conclusion

Sepsis, protein C deficiency, biomarkers to identify neonatal sepsis were reviewed in this article. Defense mechanisms and physiological functions of the immune system were also covered and the pathophysiology of sepsis. These areas are very important for pediatricians, neonatologists and immunologists on the floor and in the hospital.

References