Persistent Inflammation, Immunosuppression Catabolism Syndrome

Subjects: Pathology | Nutrition & Dietetics

Contributor: Christopher Rugg

Combining new immunological insights with great clinical experience is how the Persistent Inflammation, Immunosuppression and Catabolism Syndrome (PICS) was first described in 2012 [1]. The attempt to translate fundamental research into readily available surrogates in order to describe a clinical condition is how biomarkers and their cut-offs were determined. In the recent past, PICS has more and more become an acknowledged concept regarding ICU patients on their transition to chronic critical illness.

Keywords: PICS ; MDSC ; DAMPs ; inflammation ; immunosuppression

1. Introduction

Since its first description by Gentile et al. in 2012[1], the concept of PICS has been validated and is becoming more and more accepted as the underlying pathophysiology of chronic critical illness (CCI)[2][3][4][5][6][7][8].

2. Clinical Markers

The paradigm implies that, following the simultaneously triggered pro- and anti-inflammatory responses to a major inflammatory insult (e.g. trauma, burns, sepsis, acute pancreatitis, etc.) the increasing number of acute survivors either proceed to a fairly rapid recovery or a prolonged trajectory partially ending in CCI[2][3]. Clinically spoken these patients present with a prolonged ICU stay (typically > 14 days) under the coexistence of ongoing inflammation and immunosuppression resulting in persistent catabolism and organ dysfunction[2][3][4]. Besides an ICU length of stay (LOS) of over 14 days, applied clinical markers defining the diagnosis are a c-reactive protein (CRP) over 0.15 mg/dl as sign of inflammation, a total lymphocyte count under 0.800 G/l as sign of immunosuppression and a serum albumin concentration under 3.0 g/dl, a creatinine height index under 80% or a weight loss over 10% as signs of ongoing catabolism[1]. Regarding sepsis patients on a surgical ICU an observational study was able to show that more than half of the acute survivors ended up developing CCI. This was associated with an older age, an increased rate of hospital acquired infections and a 6-month survival of merely 63%[9]. On a cellular level initial emergency myelopoiesis also inducts a primarily beneficial expansion of so-called myeloid-derived suppressor cells (MDSC)[10][11]. However, a prolonged expansion of these MDSCs promotes the suppression of adaptive immunity and the evolvement of chronic inflammation[12][13][14]. The concomitant tissue damage of trauma, major surgery or sepsis with the release of damage associate molecular patterns (DAMPs) can amplify the above mentioned[15][16]. Even mere muscle wasting – itself triggered by the ongoing inflammation – has been shown to propagate systemic inflammation through liberation of mitochondria derived DAMPs[17][18]. Monocyte paralysis with reduced phagocytosis and HLA-DR expression as well as a reduced T-cell proliferation with elevated expression of suppressor molecules (e.g. programmed death ligand – 1; PDL-1) are only a few of the known inhibitory results, lastly predisposing for recurrent infections and therefore feeding this viscous cycle[4][9][19][20].

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