INNOVATING CROSS-DOMAIN SOLUTIONS TO DETECT EMERGING BIOLOGICAL THREATS

Rapid Detection Of Blood Based Biomarkers For Emerging Biological Threats That Cause Brain Injury

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The ability to rapidly detect infection-induced brain injury is critical since central nervous system (CNS) infections are a major burden of disease worldwide that cause high rates of morbidity and mortality. Military personnel are frequently stationed in areas where they may be at risk of exposure to neurotropic pathogens and specific diagnostic assays are lacking. Brain injury caused by neurotropic pathogens usually requires a combination of clinical assessment, neuroimaging studies, analysis of the cerebrospinal fluid, and other laboratory testing which is invasive and time-consuming. Blood biomarkers of brain injury could provide a rapid diagnosis of CNS injury caused by infections. Brain injury biomarkers have been studied more extensively for traumatic brain injury (TBI). An FDA-approved assay for mild TBI measures glian fibrillary acidic protein (GFAP) and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), which signal astrocyte and neuronal injury, respectively. Here, we assessed the applicability of this biomarker assay for determining infection-induced brain injury. We measured serum levels of GFAP and UCH-L1 retrospectively in serum samples from three study populations: 1) human cases infected with Venezuelan equine encephalitis virus (VEEV) and Madariaga virus (MADV) (n = 73), 2) human sepsis patients who were severely ill or diagnosed with encephalitis (n = 66), and 3) sepsis cases that were subsequently evaluated for cognitive impairment (n = 64). In the virus infection group, we found elevated GFAP for VEEV (p = 0.014) and MADV (p = 0.011) infections, which correlated with seizures (p = 0.006). In the bacterial sepsis group, GFAP was elevated in cases diagnosed with encephalitis (p = 0.0007) and correlated with headaches (p = 0.0002). In the bacterial sepsis cases with a later cognitive assessment, elevated GFAP (p = 0.0057) at study enrollment was associated with cognitive impairment six months later with a positive prognostic capacity of 79% (CI: 66–95%; p = 0.0068). GFAP and UCH-L1 levels measured using an FDA-approved assay for TBI may indicate brain injury resulting from viral or bacterial infections and could predict the development of neurological sequelae. This simple and rapid assay could be used to support the Warfighter in austere environments to determine if a higher echelon of care is required for military personnel potentially exposed to neurotropic pathogens.

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