Posterior Reversible Encephalopathy Syndrome and Septic Encephalopathy: Neuroimaging, Inflammation and Neurodegeneration Findings

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is known to be associated with septic encephalopathy. The pathophysiology of septic encephalopathy is thought to involve inflammatory immune response pathways. We are reporting a patient with septic encephalopathy and PRES with well documented inflammatory biomarkers and neuroradiological findings.

Keywords: Septic encephalopathy, posterior reversible encephalopathy syndrome, neuroimaging, inflammation, neurodegeneration

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INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a well-recognized clinical and radiological syndrome comprising of mental status changes, seizures, focal neurological signs as well as edema in the posterior cerebral vascular territory (1, 2). Although originally described in patients with abrupt systemic hypertension, currently the list of possible etiology is much longer, recently including sepsis and septic encephalopathy (3, 4). It is now widely accepted that the underlying mechanism in PRES involves activation of the immune system such as activation of T cells and the production of inflammatory cytokines (1, 5). A better understanding of the immune mechanisms on a cellular level established with laboratory markers and possibly radiological data is necessary. We are reporting a patient with septic encephalopathy and PRES with well documented inflammatory biomarkers and neuroradiological findings.

CASE REPORT

A 56-year-old male patient was admitted with fever, tachycardia and low blood pressure to our intensive care unit (ICU) on the 14th day of abdominoperineal resection for rectum cancer. He had no known history of systemic or neurological disease. In the initial assessment of the patient, his consciousness was alert and oriented, blood pressure was 80/35 mmHg, heart rate 130 beats-per-min, respiratory rate 24 breaths/min, oxygen saturation 94% on room air, temperature 39.2

°C. He had widespread rough rales in the respiratory examination and distension was detected in the abdominal examination. There was no lateralizing sign in the neurological examination. Laboratory work up revealed elevated leukocytes count 14200/mm³, C-reactive protein was 311 mg/L, procalcitonin levels 10.39 ng/L, creatinine 1.9 mg/dL, lactate dehydrogenase 391U/L and serum ammonia level was 43 mg/dL. Liver enzymes, coagulation tests and serum electrolyte levels were normal. Computed tomography of the thorax and abdomen showed bilateral pneumonic infiltrations and multiple abscesses in the abdomen. Patient was taken into urgent laparotomy for drainage of the abscesses and a broad spectrum antibiotic regimen was started. Shortly after admission in the ICU, patient developed hemodynamic instability requiring vasopressor agents, acute renal failure, disturbance of liver function and coagulopathy. Hemofiltration was started. Endotracheal aspirate cultures and intraabdominal fluid cultures showed *Acinetobacter spp.* growth and there was *Klebsiella pneumoniae* in the blood cultures whereupon suitable antibiotic treatment regimen was administered. On the seventh day of ICU hospitalization, when sedation was stopped, neurological examination showed that the patient was confused with left sided focal neurological deficit. There was bilateral hypodensity in parieto-occipital areas on non-enhanced brain computed tomography. Electroencephalogram showed diffuse slowing of electrical activity (Figure 1). Three days after the detection of acute neurologic dysfunction, brain magnetic resonance imaging was performed. This investigation showed vasogenic edema in the cortical gray and subcortical white matter in bilateral parietal and occipital regions extending anteriorly into the frontal areas, also involving the corpus callosum splenium and deep gray matter. A similar but less enhanced involvement was also present in the cerebellar hemispheres (Figure 2). Clinical and neuroradiological diagnosis of PRES associated with septic encephalopathy was thus established. Cerebrospinal fluid analysis was not possible due to the acquired coagulopathy. Biomarker levels associated with septic encephalopathy were investigated with ELISA method. IFN- γ : 5.1 pg/ml (0.0-2.6), C5a: 0.2 ng/ml (5.5-31.1), C4d: 6837.4 μ g/ml (241.5-1128.0) and iC3b levels: 1.0 μ g/ml (5.1-6.1) were noted. Neurodegeneration and gliosis related biomarkers (amyloid β peptides 1-40, 1-42, total tau, phosphorylated tau, S100 calcium-binding protein B and neuron specific enolase) were within normal ranges. There was no improvement in the physical and neurological condition of the patient in the ICU care and he passed away on the 38th day.

Figure 1. Electroencephalogram showing diffuse theta-delta slowing of electrical activity. Recording: 10 cm/sec, sensitivity: 100 μ V/cm; filter settings: 0.500 Hz–70Hz.

Figure 2. Representative images of posterior reversible encephalopathy syndrome (PRES) on magnetic resonance imaging. PRES findings in a 56 year-old septic shock patient who developed focal neurological signs. Flair images show high signal in the subcortical and deep white matter as well as deep gray matter in both cerebral hemispheres and similar symmetrical high signal in cerebellar deep white matter. Extensive vasogenic edema in this patient is highly suggestive of PRES.

DISCUSSION

Understanding the neurological pathology in the critically ill patient has been a major challenge for the ICU physician. Septic encephalopathy was long known but relevant laboratory and neuroradiological data only recently accumulated (6, 7). PRES is one of the patterns of brain involvement in sepsis or septic shock patients (3, 4). Although PRES is not common in this group of patients, it should be distinguished as part of a potentially morbid or even mortal disease where ‘reversible’ radiology and favorable disease course is uncommon.

From a neuroradiological perspective PRES is an easily distinguished disease mostly starting in the cortical and subcortical regions of the posterior halves of the cerebral hemispheres. It is mostly in the form of vasogenic edema, but cytotoxic and even mixed forms of edema may be

detected on imaging. Hemorrhage and breaking down of the blood brain barrier with subsequent contrast enhancement is possible (5, 8). Although PRES typically involves parieto-occipital regions, it may extend to involve the anterior regions of the brain hemispheres, deep gray matter and cerebellar hemispheres (5, 8). A limited form of PRES with involvement of the posterior vascular territory is the common form and has been associated with sudden hypertensive episodes with favorable disease prognosis (9). However, from our previous experience with a larger group of septic encephalopathy patients, we have observed both typical and atypical and more extensive forms of PRES involvement with variable disease courses (10). This patient showed an extensive PRES radiology with uncommon regions of involvement such as the splenium and posterior fossa and significant changes in the corresponding biomarkers. It is very premature to correlate neuroradiological PRES findings with

disease progress and prognosis but larger series with well documented cases will be significant.

Increased IFN- γ levels, decreased C5a and iC3b levels, and increased C4d levels were associated with pathological imaging findings and adverse events in septic encephalopathy patients (10, 11). Significance of C5a is well known in sepsis and sepsis-associated brain damage (12) and C5a has been associated with increased blood-brain barrier disruption, hyperactivation of inflammatory mediators, enhanced gliosis and consumptive coagulopathy (13, 14). The latter mechanism might particularly explain reduced C5a and iC3b levels in septic encephalopathy patients with brain lesions. Overactivation of the complement system by pathogens might trigger the coagulation pathways leading to both reduced complement levels due to overconsumption of complement factors and brain lesions due to occlusion of small brain vessels (14, 15). Normal levels of neurodegeneration and gliosis markers suggest that neuronal loss does not play a role in the pathogenesis and poor prognosis of septic encephalopathy (11). The biomarker changes in our patient were compatible with inflammatory pathway and showed no indication of neurodegeneration or neuronal loss.

The pathophysiology of septic encephalopathy is not fully understood. Laboratory biomarkers and neuroimaging patterns may provide some insight and larger well documented series of patients have to be observed.

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