Predictors of delirium in post-transplant patients: S-100β and other inflammatory markers

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Abstract

Delirium is a common complication of critically ill surgical patients, particularly those having undergone lung transplant surgery. The aim of this study was to assess the association between the CAM-ICU (confusion assessment method for the intensive care unit) and a serum marker of blood-brain barrier (BBB) integrity (protein S-100β) as well as other analytes affected by anoxia and brain metabolism.

21 Patients participating in this study were part of a prospective, observational, cohort study conducted at the Cleveland Clinic. The CAM-ICU was obtained at baseline and daily for 4 days after transplant. In addition, blood was collected and processed to obtain serum from which S-100β and several analytes were measured. All data were compared in patients with and without delirium diagnosed by CAM-ICU criteria. Those analytes that yielded the greatest significant difference between the 2 groups (p < 0.05) also included IL-6, white blood cell (WBC) counts, pH, pCO2, sodium, blood urea nitrogen (BUN) and creatinine.

Based on CAM-ICU, 19% of patients were diagnosed at some point with delirium, S-100β increased in all patients after transplantation, however, by day 4, the delirium group presented with levels of S-100β statistically elevated (p<0.01), compared to the non-delirium group once glomerular filtration rate (GFR) was factored into the serum concentrations. Analytes significantly elevated in the delirium group (p<0.05) in which GFR was factored included IL-6 at day 4, sodium at days 3 and 4, BUN at 12 hrs, days 3 and 4, creatinine at day 4 and WBC count at days 3 and 4. Those analytes with significant differences between the delirium and non-delirium groups in which GFR was not a factor, included pH at days 1 and 3, and pCO2 at day 3. Good correlation was observed between baseline S-100β and absolute lymphocyte count (ALC) at day 2 (r=0.837). Comparison of mean values of S-100β, 12 hrs post transplant of all study patients vs. normal controls were significantly elevated (p<0.05) as were baseline values for IL-6, WBC, ANC, and ALC. These results are remarkable given all the patients were immune suppressed (with Prograf, CellCept, etc.) and therefore elevated levels of cells and serum markers of inflammation were unexpected.

We hypothesize that the significant difference for GFR factored S-100β seen between delirium and non-delirium subjects on day 4 is due to BBB disruption and may be related to the inflammatory response indicated by higher WBC and serum IL-6 levels. The finding that baseline S-100β values correlated well with ALC levels at day 2 may emphasize the connection between inflammatory response and BBB disruption. Also, elevated IL-6 and leucocyte counts in transplant recipients may indicate a primed immune system causing an underlying susceptibility to BBB disruption.

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Lung Transplantation Procedure

Delirium vs. Non-delirium of Key Analytes

Transplants vs. Controls for Key Analytes

Conclusions

• S-100β values, when corrected for GFR yield a significant difference between delirium and non-delirium lung transplant recipients on day 4 post transplantation.

• Baseline S-100β values correlation with ALC levels at day 2 may emphasize a connection between inflammatory response and BBB disruption leading to delirium in lung transplant recipients.

• Elevated IL-6 and leucocyte counts in transplant recipients may indicate a primed immune system causing an underlying susceptibility to BBB disruption.