Brain Enzyme May Help to Flag Severity of Traumatic Injuries

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — An enzyme found in brain cells may become the first bedside biomarker for assessing the severity of traumatic brain injury, according to Dr. Linda Papa.

In a multicenter trial, levels of the enzyme ubiquitin C-terminal hydrolase (UCH-L1) rose significantly in severely injured brains, an increase that paralleled the rise in cerebral spinal fluid and correlated with the Glasgow Coma Scale (GCS) score. Dr. Papa said at the annual meeting of the Society for Academic Emergency Medicine, "We know that biomarkers can provide diagnostic and prognostic information, give us insight into the pathophysiology of the brain injury, and guide therapy in both the emergency department and intensive care unit," said Dr. Papa, director of academic clinical research at Orlando (Fla.) Regional Medical Center.

If further study confirms the value of UCH-L1 as the first clinical biomarker in traumatic brain injury (TBI), physicians will be better able to identify targets for drug therapy and guide the timing of treatment with such agents as tissue plasminogen activator, he explained.

This prospective case-control study enrolled consecutive adult patients presenting to two tertiary care teaching hospitals following severe TBI, defined by a GCS score of less than 8 and requiring invasive intracerebral monitoring.

The primary outcome was severity of injury as measured by postresuscitation and 24-hour dichotomized GCS score. Secondary outcome included the presence of evolving lesions on CT scan at 24 and 72 hours post injury. Over 16 months, 41 patients with severe TBI were enrolled. Their mean age was 38 years, and four-fifths were men. Patients were excluded if they did not have ventriculostomy, which is necessary to obtain cerebrospinal fluid (CSF).

Ventricular CSF was drained from each patient at 6, 12, 24, 48, 72, and 96 hours after TBI and was measured by enzyme-linked immunosorbent assay for UCH-L1 levels.

The control group consisted of uninjured patients who required CSF drainage for other reasons. Mean 12-hour UCH-L1 levels were 145 ng/ml for patients with GCS scores of 3-5, and 38.5 ng/ml in those with GCS scores of 6-8. Similarly, 24-hour levels were 76 and 36 ng/ml, respectively.

The largest increase in the experimental biomarker occurred during the first 48 hours after injury. "Then we found that patients with evolving lesions had significantly higher levels of the biomarker" than did patients with non evolving lesions at both 48 and 72 hours, she said.

"There is a significant increase in CSF UCH-L1 following severe human TBI compared to uninjured controls, associated with severity of injury measured by GCS and the presence of evolving lesions on CT," Dr. Papa said, adding that these data suggest that UCH-L1 is a potential TBI biomarker. Dr. Papa said more than 5 million Americans live with TBI disabilities, and the hospital and fatality costs related to TBI exceeded $48 billion annually.

Brain Injuries Difficult to Diagnose in U.S. Troops

BY KRISTINA R. ANDERSON
Contributing Writer

CAMP PENDLETON, CALIF. — Brain injuries may be the most common wounds suffered by American troops in Iraq, but they can also be the most difficult to diagnose, Mark McDonough, Ph.D., said at an international conference on civilian and military combat stress.

Such trauma is tough to spot on CT scans and can often result in soldiers or Marines wrongly thinking that they have emerged from a roadside bombing or ambush relatively unscathed, said Dr. McDonough, a clinical neuropsychologist in Encinitas, Calif., who specializes in brain injuries and rehabilitation.

"They’re next to a blast, but nothing happened to them," he said. "There’s no fragmentation [shrapnel]; their arms are not blown off; they don’t have missiles in their chests. They look fit for duty; but that is not necessarily the case.

Soldiers often suffer multiple concussions, and the effects can be cumulative. “I think we’re dealing with the signature injury of this war, which is going to be the traumatic brain injury,” he observed. “But I don’t think we have a clue as to how many people have actually suffered through these injuries.”

Modern Kevlar helmets are far better able to prevent penetrating head wounds than are the steel models worn from World War I through the Vietnam era, but they are not as effective in protecting the brain from closed injuries, he said.

And while the survival rate of wounded troops in Iraq and Afghanistan is much improved over World War II and even Vietnam, the level of traumatic brain injury (TBI) affecting white matter is, in fact, much higher.

Dr. McDonough urged the military to keep a close eye on personnel who are suspected of having suffered a TBI, however slight, so that they are not assumed to be healthy and sent back into combat. Such troops could pose a threat to their units if they are unable to react as quickly or if they experience some level of confusion in the midst of a combat situation.

Soldiers suffering from TBI can often be susceptible to leading questions and can even be implanted with false memories, he noted. Symptoms may also be similar to those seen in posttraumatic stress disorder and, in fact, the two may overlap. Making the situation more difficult is a level of malinger- ing, which, he said, can often be uncovered by asking the patient a seemingly off-the-wall question such as, “Do you experience pain behind your eye when you urinate?” He told audience members that they would be surprised at the number of positive responses.

Criteria Inadequate for Postconcussional Disorder

BY JANE SALOODOF MCNEIL
Senior Editor

SANTA FE, N.M. — The suggestions for diagnosing postconcussional disorder that appear in the text revision of the DSM-IV are inadequate for the assessment of mild traumatic brain injury, Dr. Stephen D. Anderson said at the annual meeting of the American College of Forensic Psychiatry.

Numerous studies have shown that people do not have to be unconscious after a head trauma or experience more than 1 hour of posttraumatic amnesia to suffer from postconcussional disorder, said Dr. Anderson of the University of British Columbia, Vancouver.

Yet the DSM-IV-TR would require that they fulfill two of the following three criteria to meet a threshold for closed head injuries: more than 5 minutes of unconsciousness; more than 12 hours of posttraumatic amnesia, or seizures. As seizures rarely follow a mild traumatic brain injury (TBI), most people would have to meet the first two overly rigorous criteria to satisfy the definition proposed in the manual, he said.

Dr. Anderson also listed a multitude of symptoms as missing from the DSM-IV-TR discussion of postconcussional disorder.

He cited the omission of nausea; decreased balance and coordination; tinnitus; and sensitivity to light and noise as physical symptoms, and noted that cognitive defects in initiation and planning; judgment and perception; information-processing speed; and communication ability are not discussed. Likewise, increased sensitivity to lack of sleep, fatigue, stress, drugs, or alcohol is not mentioned, and loss of libido and decreased appetite are not included under psychological symptoms.

"It is easier to make a diagnosis of dementia [resulting from head trauma] than postconcussional disorder," Dr. Anderson said.

The definition of postconcussional disorder “does not cut it,” he summarized in an interview after his talk. “It is in an appendix, so it is not fully accepted, but the fact that it is included in DSM IV lends it some legitimacy.”

Mild TBI is a real but under-diagnosed condition, according to Dr. Anderson, who offered as examples impairments in football, soccer, and hockey players. The same problems have been observed in patients with severe traumatic brain injuries, but the effect is less obvious in mild TBI.

Despite concerns about people using mild TBI to excuse malingering, researchers have shown that unemployment and underemployment can occur, and that some people ask for neurocognitive tests. Patients with mild TBI have performed comparably with control groups in several studies, but imaging showed that their brains worked harder to achieve the same results. This may help explain why fatigue is a common complaint, Dr. Anderson said.

He also cited a study of brains taken from five people who died of causes not related to their mild TBI. The researchers found multifocal axonal injury and axonal damage to fornices in all five patients.

Unless structural damage is clearly seen, neither MRI nor CT is a good measure of mild TBI. Without images taken before the trauma, imaging cannot compare brain function before and after the injury, Dr. Anderson said.

An hour or more of posttraumatic amnesia is one of the best predictors of mild TBI, Dr. Anderson said. He recommended the Glasgow Coma Scale-Extended (GCS-E) amnesia scale but volunteered that results are rarely available. “It is great, but no one uses it,” he said. “You never see it in an ambulance report.”

The largest increase in the experimental biomarker occurred during the first 48 hours after injury. “Then we found that patients with evolving lesions had significantly higher levels of the biomarker” than did patients with non evolving lesions at both 48 and 72 hours, she said.

“There is a significant increase in CSF UCH-L1 following severe human TBI compared to uninjured controls, associated with severity of injury measured by GCS and the presence of evolving lesions on CT,” Dr. Papa said, adding that these data suggest that UCH-L1 is a potential TBI biomarker. Dr. Papa said more than 5 million Americans live with TBI disabilities, and the hospital and fatality costs related to TBI exceeded $48 billion annually.