Serum S-100b levels predict brain death after traumatic head injury

Dimopoulou et al. performed serial measurements of serum S-100b levels in patients with severe traumatic brain injury. They showed that S-100b on admission was an independent predictor of brain death, in the presence of advanced age and low Glasgow Coma Scale score.

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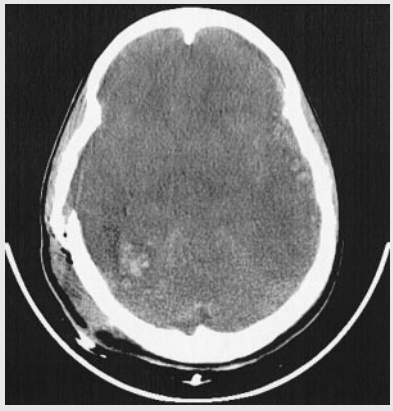
Serum markers for traumatic brain injury

Commentary by Jeffrey J. Bazarian, MD, MPH

Traumatic brain injury is an important cause of preventable death and neurologic disability worldwide. Of the 1.5 million Americans who have a traumatic brain injury each year, 15 to 20% are severe (GCS ≤8). Despite advances in medical and surgical management, severe traumatic brain injury mortality has remained at 30 to 40%. The inability to accurately identify those at high risk for brain death has been a major obstacle both to clinicians trying to decide who warrants early and aggressive management and to researchers who have been unable to reduce mortality with available neuroprotective agents. Trials of such treatments should be limited to traumatic brain injury patients whose prognosis is poor.

Serum markers offer the possibility of quantifying traumatic brain injury severity and stratifying risk within hours of an injury. S-100b, the most widely studied marker, is a calcium-binding protein found in supporting CNS cells, but not neurons. S-100b levels correlate with traumatic brain injury severity, CT abnormalities, and long-term cognitive outcome.[1,2] In this issue of *Neurology*, Dimopoulou et al. have demonstrated that S-100b also predicts brain death after traumatic brain injury. Among 47 severe traumatic brain injury patients, the mean admission S-100b level of those who deteriorated to brain death was over twice that of survivors (2.32 vs 1.04 μg/L). Initially low but increasing S-100b levels also predicted brain death. After controlling for confounders, admission S-100b levels were a strong independent predictor of brain death.



Enthusiasm for integrating S-100b into clinical practice has to be tempered by reports showing levels as high as 10 μg/L among patients with multiple trauma without head injury.[3] Small amounts of S-100b have been found outside the brain in melanocytes, adipocytes, chondrocytes, and epidermal cells. The refinement of assays for proteins more specific to neuronal injury, such as cleaved-tau, should enhance our ability to quantify traumatic brain injury and to predict not only brain death but also disability.[4] In the meantime, an initially elevated or rising S-100b level in selected severe traumatic brain injury patients without extensive, multiple trauma elsewhere can be considered a risk factor for poor outcome and an indication for early and aggressive TBI management.

References

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2. Herrmann M, Curio N, Grubich C, et al. Release of biochemical markers of damage to neuronal and glial brain tissue is associated with short and long term neuropsychological outcome after traumatic brain injury. J Neurol Neurosurg Psychiatry 2001;70:95–100.
3. Anderson RE, Hansson LO, Nilsson O, Dijlai-Merzoug R, Settergren G. High serum S-100b levels for trauma patients without head injuries. Neurosurgery 2001;48:1255–1260.
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Progressive supranuclear palsy

Clinical features and prognosis

Nath et al. studied the case records of 187 progressive supranuclear palsy patients and personally examined 62 cases. Seventy-five patients died during follow up. The onset of falls, speech problems, or diplopia within 1 year and swallowing problems within 2 years predicted a worse prognosis.

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Milestones of progressive motor impairment

Goetz et al. examined 50 subjects with probable progressive supranuclear palsy defined by National Institute of Neurological Disorders and Stroke–Society for Progressive Supranuclear Palsy workshop criteria from first visit to a tertiary care center until death or in an on-going fashion. They examined a series of predefined key motor impairments based on standardized rating scales that involved assessments of gait, speech, and feeding. The median time from disease onset to the first key motor impairment was 48 months, 24 months after first consultation. As a composite end point, speech/gait impairment accounted for 98% of the sample's first key motor impairment.

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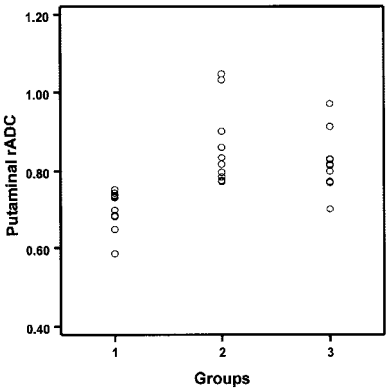

Group 1: PD, Group 2: MSA-P, Group 3: PSP

Diffusion-weighted MRI in progressive supranuclear palsy

Seppi et al. report that DWI detects basal ganglia abnormalities in PSP patients early in disease onset, discriminating patients with PSP from those with PD based on putaminal rADCs but not separating PSP patients from those with multiple system atrophy.

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"Patients with PSP know it is an inexorably progressive and largely untreatable condition. . . ."

The Editorial by Siderowf and Quinn accompanying these three papers notes that there are three steps in the development of treatment for progressive supranuclear palsy: 1) establishing the natural history of progressive supranuclear palsy; 2) improving accuracy of diagnosis; and 3) determining clinical and other objective surrogate markers to track disease progression.

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Premonitory symptoms in migraine

Migraine patients often remark on symptoms that can be very noticeable before the onset of aura or pain—premonitory symptoms. Giffin et al. used an electronic diary for patients to record premonitory symptoms. Feeling tired/weary, having difficulty concentrating, stiff neck, and yawning predicted migraine in 72% of attacks.

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Opioids: a therapeutic option in painful diabetic neuropathy

Opioids have played a limited role in the management of painful diabetic neuropathy. In a randomized, controlled study, Gimbel et al. report significant analgesia with controlled-release oxycodone in subjects with painful diabetic neuropathy. Opioids can be an option for therapy in patients with neuropathic pain.

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"The[se] findings reassure physicians. . . . That opiate use in neuropathy patients . . . is evidence based."

The accompanying editorial by Zochodne and Max notes that oxycodone was beneficial at relatively low daily doses. However, it was not dramatically better than tricyclics or gabapentin since it did not eliminate pain and since 30 to 40% of patients had dose-limiting G1 and CNS side effects. They also note that the site of action of opiates is not necessarily in the CNS; peripheral receptors at sites of tissue injury or in peripheral nerve may respond to opioids and offer new approaches to pain treatment.

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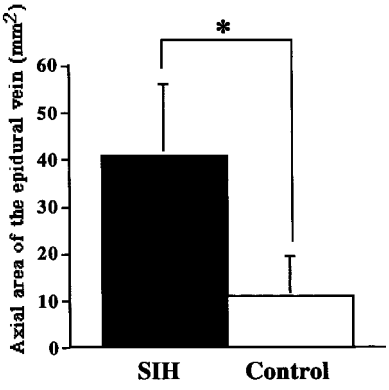
CSF hypovolemia in "SIH syndrome"



Miyazawa et al. suggest that CSF hypovolemia, not intracranial hypotension, causes "spontaneous intracranial hypotension (SIH) syndrome." MRI evidence of CSF leakage, venous engorgement, and dilatation of epidural veins suggests CSF hypovolemia in an appropriate clinical setting.

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N-acetyltransferase 2 and PD in Hong Kong Chinese

Chan et al. examined the association between the *N*-acetyltransferase 2 slow acetylator genotype and PD in Chinese. The frequency of the slow acetylator genotype was significantly higher in the PD group (n = 99) than in controls (n = 126) (odds ratio = 5.53).

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AMT PET can detect epileptogenic cortex even when MRI and FDG PET are nonlocalizing

In a PET study of 27 children with intractable neocortical epilepsy, Juhász et al. show that increased cortical uptake of α[^{11}C]methyl-L-tryptophan (AMT) is highly specific for EEG-defined epileptogenic regions. Increased AMT uptake was strongly associated with cortical developmental malformations; with 80% sensitivity, AMT PET may be of value in presurgical evaluation epilepsy, even when MRI and 2-deoxy-2[^{18}F]fluoro-D-glucose (FDG) PET fail to provide adequate localizing information.

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APOE and diabetic neuropathy

In a cross-sectional study of diabetic patients, Bedlack et al. showed that *APOE* 3/4 or 4/4 genotype was an independent risk factor for neuropathy severity.

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