Serial S-100 protein serum measurements related to early magnetic resonance imaging after minor head injury

Case report

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The authors studied 24 patients with a Glasgow Coma Scale score of 14 or 15 and normal computerized tomography scans after minor head injury. The study protocol included obtaining serial measurements of S-100 protein in serum during the first 12 hours after injury and early magnetic resonance (MR) imaging. Four patients (17%) had detectable levels of S-100 protein in serum. The S-100 protein levels were highest immediately after trauma, declining hour by hour. In two patients, MR imaging revealed intracranial contusion. Levels of S-100 protein were not detectable in serum in one patient with MR-verified cerebral contusion, but the first measurements were made late, 6 hours after trauma. The highest serum level of S-100 protein (0.9 µg/L) was seen in a 73-year-old man 2 hours after injury. Magnetic resonance imaging revealed a contusion of the left cerebellar hemisphere, and the patient suffered permanent sequelae of impaired posture and dizziness.

KEY WORDS • head injury • S-100 protein • computerized tomography • magnetic resonance imaging • outcome

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Study Methods

Twenty-four patients with minor head injury were studied (13 males and 11 females ranging in age from 12 to 73 years). The following criteria were needed for inclusion in this study: 1) head injury with loss of consciousness; 2) a clinical condition equivalent to a Glasgow Coma Scale (GCS) score of 14 to 15 in the emergency room; 3) absence of focal neurological deficits; and 4) no signs of intracranial lesions on CT scan. The study was approved by the ethical committee at the University Hospital of Tromsø.

The study protocol included clinical neurological examination in the emergency room, a CT scan within 12 hours after injury, and MR imaging (T₁- and T₂-weighted) within 48 hours after injury. In four cases, MR imaging was not performed (the patient was uncooperative in two cases and there were technical problems with the imaging equipment in two cases). Blood samples for serum S-100 protein analysis were collected at admission and hourly thereafter until 12 hours after injury.

The S-100 protein serum concentrations were analyzed with a commercially available two-site immunoradiometric assay kit (AB Σangtec Medical; Bromma, Sweden). Samples were analyzed in duplicate and those with more than 10% coefficient of variation were rejected. The detection limit of the kit is 0.2 µg/L.
Results

The mean time from injury to the first S-100 protein measurement was 3.6 hours (range 1–6 hours), between injury and CT scanning 5.1 hours (range 1.5–10.5 hours), and between injury and MR examination 24.7 hours (range 12.5–48 hours).

Sixteen patients had nondetectable S-100 protein serum levels and normal MR imaging. In three other patients in whom S-100 protein could not be detected in serum, MR examination was not performed. In one patient (Case 1) with a nondetectable serum level of S-100 protein 6 to 12 hours after injury, MR imaging demonstrated a small contusion (8 $\times$ 6 $\times$ 4 mm) in the right frontal lobe 17 hours after trauma (Table 1).

In four patients (17%; Cases 2–5), S-100 protein was detected in serum. Magnetic resonance imaging in one patient (Case 2) demonstrated intracranial contusion. There was an hour-by-hour decrease in S-100 protein levels in all four patients (Fig. 1). The highest S-100 protein level (0.9 $\mu$g/L) was detected 2 hours after minor head injury (in Case 2). That patient suffered permanent neurological sequelae.

Case Report

Case 2

This 73-year-old man was admitted to the emergency room after a traffic accident in which he was hit by a car while bicycling. At the time of injury, he was still employed part-time as a fisherman. He suffered a head injury with loss of consciousness for less than 5 minutes and a scalp wound in the left occipital region, but no further injuries.

Examination. At physical examination in the emergency room 2 hours after the trauma, he was alert with a GCS score of 15. Neurological examination, including tests of coordination and cranial nerve function, showed no focal neurological deficits. The initial CT scan performed 4 hours after the trauma demonstrated a linear fracture of the left occipital bone but no intracranial lesions (Fig. 2). Magnetic resonance imaging obtained 15 hours later revealed a contusion in the left cerebellar hemisphere (Fig. 3, left). The neurological examination was repeated at discharge the day after trauma and still considered to be normal.

Laboratory Studies. Serial measurements of S-100 protein serum levels during the first 12 hours postinjury demonstrated detectable values, declining from 0.9 $\mu$g/L at 2 hours to 0.4 $\mu$g/L at 12 hours (Fig. 1).

Postoperative Course. At follow-up examination 6 weeks later, the patient complained of severe dizziness and impaired control of posture. A formal neurological investigation showed mild instability on Romberg’s test and drift toward the left side when walking with closed eyes, but the findings were otherwise normal. Magnetic resonance imaging at that time revealed a small cortical defect at the site of the previous lesion (Fig. 3, right). At final follow up 1 year after the accident, the patient reported persistent symptoms of dizziness and balance problems. He was not able to continue his previous occupation as a fisherman.

<table>
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<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Cause of Trauma</th>
<th>LOC (min)</th>
<th>GCS</th>
<th>CT Scan</th>
<th>Peak S-100 ($\mu$g/L)/ Hour After Injury</th>
<th>MRI</th>
<th>Persisting Sequelae</th>
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* Abbreviations: CT = computerized tomography; LOC = loss of consciousness; GCS = Glasgow Coma Scale score; MRI = magnetic resonance imaging.

Fig. 1. Graph depicting serial serum levels of S-100 protein ($\mu$g/L) in four patients with minor head injury during the first 12 hours after trauma. In Cases 4 and 5, the protein was detectable only at the first measurement. Asterisks = Case 2; plus symbol = Case 3; closed circle = Case 4; open circle = Case 5.
Minor head injury and S-100 protein

Discussion

In long-term follow-up studies, sequelae of isolated cerebral symptoms or psychosocial morbidity are described in 15% to 50% of patients after minor head injury.5,19 Computerized tomography scanning is less sensitive in the evaluation of diffuse brain damage in these patients.10 Magnetic resonance imaging provides more information concerning primary brain damage; however, the greater availability of CT immediately after injury means that it will remain the initial radiological investigation.4,6 Therefore, a biochemical serum marker would be of particular value in clinical practice to reveal the presence and eventual extent of diffuse brain damage, especially in those patients who present with a normal CT scan.

The S-100 protein is known to be unique to the CNS and has been detected in the CSF of patients with various neurological diseases.8,11 This protein is not detectable in serum in normal conditions.1 After glial tissue damage with subsequent disruption of the blood-brain barrier, it is reasonable to assume that the release of this organ-specific marker will occur in serum. Recently, we were able to demonstrate an increased incidence of postconcussion symptoms in minor head injury patients in whom CT scans were found to be normal but who had detectable serum S-100 protein levels.2 Sixty-seven percent of patients with detectable S-100 protein in serum reported postconcussion symptoms, compared to 36% of individuals in whom S-100 protein could not be detected in serum. Furthermore, patients with detectable S-100 protein levels in serum were hospitalized significantly longer (mean 3.4 days) compared to patients in whom S-100 protein was not detected (mean 1.1 days).1

In the present study, four patients (17%) had detectable levels of S-100 protein in serum within 12 hours after minor head injury. There was an hour-by-hour decrease in S-100 protein serum levels, and in two patients the protein was not detectable 5 hours after trauma. In the two patients with highest S-100 protein serum levels, MR imaging revealed intracranial contusions despite an initial normal CT scan. Magnetic resonance imaging in another patient revealed a small frontal right-sided contusion in spite of nondetectable levels of S-100 protein in serum. However, in this patient, the first protein measurement was taken 6 hours after trauma, probably too late for detection.

In Case 2, the serum level of S-100 protein was significantly increased, indicating the presence of structural brain damage. Magnetic resonance imaging 19 hours after minor head injury revealed a contusion in the left cerebellar hemisphere, verifying the presence of such damage. The initial CT scan failed to detect this lesion, although obviously it could have appeared during the 15-hour period between CT and MR imaging. In our opinion, this was not the case, because the S-100 protein levels declined and no further neurological deficits occurred.

Conclusions

This report reinforces the well-known fact that MR imaging is superior to CT scanning in detecting structural brain lesions after minor head injury. In addition, we believe that serum measurements of S-100 protein may be a useful tool for the detection of such lesions. The value of S-100 protein measurements in relation to outcome needs to be evaluated in further studies.

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References

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Fig. 2. Case 2. Computerized tomography scans obtained 4 hours after a minor head injury in a 73-year-old man revealing a linear fracture of the left occipital bone (left), but no intracranial lesion (right).

Fig. 3. Case 2. Left: Magnetic resonance T2-weighted image obtained 19 hours after the trauma demonstrating a 30 × 25 × 20 mm large contusion in the left cerebellar hemisphere. Right: Magnetic resonance T1-weighted image obtained at a follow-up examination 6 weeks after injury showing a small cortical defect at the site of the previous lesion.

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