Delayed onset of severe diffuse axonal injury: a case report

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ABSTRACT  Diffuse axonal injury (DAI) commonly causes immediate loss of consciousness after head injury. We report the case of a 20-year-old man who was involved in a motor vehicle accident, which his estate car ran into a truck from behind. Although he was alert on arrival at the hospital, his conscious level deteriorated approximately 7 hours after the accident. At this time point, he had a generalized tonic seizure and decorticate posturing of his arms with a Glasgow coma scale (GCS) score of 5. MRI revealed findings consistent with DAI. On the 14th day, his conscious level improved to a GCS of 9 and MRI showed chronic DAI. The patient recovered well with only mild memory deficit at discharge. There are few reports of delayed onset DAI, but in terms of its neuropathology, it is possible for it to occur after the time of injury. DAI is the result not only of direct injuries to the axon membrane and axonal sheath due to shearing force, but also of secondary injury by loss of axon transport. In the emergency department, a diagnosis of DAI should be considered in any patient who has suffered head injury by rotational forces even if there is no loss of consciousness on arrival at the hospital.

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Keywords: traumatic brain injury (TBI), magnetic resonance imaging (MRI), traffic accident, rotational force

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Introduction

Diffuse axonal injury (DAI) often occurs after cerebral injury following a road traffic accident, especially those involving high speed motor vehicles. A common clinical finding is immediate loss of consciousness, which lasts more than 6 hours, with no focal lesions on the cerebral computed tomography (CT) scan. Three categories of DAI - mild, moderate, or severe - can be defined according to the duration of the coma and presence or absence of brainstem signs. The prognosis of DAI is poor; approximately 60% of patients with severe DAI die and 20% develop vegetative states. Magnetic resonance imaging (MRI) is much more useful in the diagnosis of DAI than CT, as it visualizes better tiny hemorrhages, callosal damage and non-hemorrhagic areas of axonal damage. Furthermore, MRI may predict recovery from cerebral damage. We report a case of severe DAI whose loss of consciousness did not appear immediately after the motor vehicle accident but 7 hours later with typical MRI findings. In spite of severe DAI, the patient recovered with only mild memory deficit.

Case report

A 20-year-old man was involved in a road traffic accident on the freeway in which his estate car ran into a truck from behind. His seat belt was fastened, but the air bag did not work. When the emergency medical services arrived at the accident scene, the patient was alert and responsive with stable hemodynamics. It took 30 minutes for the emergency medical services to extract the patient from the car, and he was then transferred to our department by ambulance. On arrival at the hospital, he reported no loss of consciousness and had a Glasgow Coma Scale (GCS) score of 15. His initial systolic blood pressure was 125 mmHg with a pulse of 72/minute. He complained of
Fig. 1. Lateral cervical radiograph. Atlantodental interval is 4mm.

Fig. 2. CT scan on arrival at hospital. There were no abnormal findings.
Table 1. Clinical and laboratory data on arrival at the hospital and seven hours after the accident.

<table>
<thead>
<tr>
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<th>On arrival</th>
<th>7 hours after accident</th>
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<tbody>
<tr>
<td>Petechiae</td>
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<tr>
<td>Body temperature (°C)</td>
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<td>Heart rate (per minute)</td>
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<tr>
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<td>PaCO₂ (mmHg)</td>
<td>38.6</td>
<td>52.8</td>
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<tr>
<td>Chest X-ray</td>
<td>unremarkable change</td>
<td>infiltration in left lower field</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>16.3</td>
<td>14.1</td>
</tr>
<tr>
<td>Platelet count (x10⁹)</td>
<td>244,000</td>
<td>124,000</td>
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<tr>
<td>CRP (mg/dl)</td>
<td>0.09</td>
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Fig. 3. CT scan approximately seven hours after the accident reveals cerebral edema.

pain in his right lower extremities. Laboratory examination revealed a hematocrit of 50.2% with a hemoglobin of 16.3 g/dl. X-rays showed fractures of the right femoral shaft, the right tibia and the left forth metacarpal bone and atlantoaxial subluxation (Fig. 1). All were closed fractures and direct-traction was performed for the fractures of the lower extremities. A CT scan of the head was normal at this point in time, and the patient was drowsy with a GCS of 13 (E3V5M5) due to buprenorphine hydrochloride for analgesia (Fig. 2). Seven hours after the accident, the patient suddenly had a generalized tonic seizure and his conscious level deteriorated to a GCS of 5 (E1V1M3). The patient also developed respiratory insufficiency and required endotracheal intubation for artificial respiration. Table shows the clinical findings and laboratory data upon arrival at the hospital and 7 hours after the accident. The
head CT scan was repeated and showed only cerebral edema (Fig. 3). These changes were suspected to be a result of cerebral fat embolism because of his femur fracture. Diazepam, phenytoin and glycerin were started. The following day, an MRI was performed and T2-weighted images demonstrated small hemorrhagic lesions on the midbrain, pons and cerebellar peduncle. Small hemorrhagic lesions were also present on the white matter of the corona radiata between the thalamus and the midbrain, consecutively (Fig. 4). Accordingly, the patient was diagnosed as having DAI with MRI by neurological radiologist. Anticonvulsant medication and glycerin were continued. On the 10th day post-trauma, the patient could be weaned from mechanical ventilation and seizures were well-controlled with phenytoin. On the 14th day, his conscious level improved to a GCS of 9 (E2V1M6); at repeat MRI, there were fewer small hemorrhagic lesions than on the earlier examination and cerebral atrophy and enlarged both of lateral ventricles were noted (Fig. 5). These findings were compatible with chronic DAI. His level of consciousness gradually improved, with a GCS of 14 (E4V4M6) on the 43rd day. On the 72nd day, he had an operation for his femur fracture. On the 85th day he was alert with a GCS of 15 and was transferred to a rehabilitation center. MRI findings on the 43rd and 85th days were similar to those on day 14. Fig. 6 shows the clinical course of the patient.

Discussion

DAI occurs as a result of pivoting of the cerebrum caused by an abrupt accelerating or decelerating force. These forces directly injure the axonal sheath and membrane by a shearing or tensile force produced, in particular, where nerve fibers of different densities meet, such as junctions between white and gray matter. These partial axonal injuries then inhibit axonal conduction and cause proximal axonal edema. Commonly, DAI is associated with an immediate loss of consciousness and this unconsciousness is caused by direct axonal injury. On the other hand, there is another mechanism of DAI. Alterations in the axonal membrane also increases the edema of the axon or neuroglia by activated cysteine protease, which destroys the cytoskeleton, or by glutamate leakage through the disordered membrane. These phenomena seem to progress.
Delayed onset of DAI

Fig. 5. Small hemorrhagic lesions at corpus callosum diminished on sagittal T2-weighted MR images on 14th day after accident (a). Solid hemorrhagic lesions are decreased on mid brain and cerebral atrophy are shown (b) on axial T2-weighted MR images. Both of lateral ventricles are enlarged and hyperintense lesions are present at anterior limb of internal capsule (c). Small hemorrhagic lesions are unclear and localized on parietal lobe (d). Axial fluid attenuated inversion recovery (FLAIR) MR images show enlarged both of lateral ventricles and larger ovoid lesions at corona radiata and internal capsule (e, f: white arrows).

Fig. 6. Clinical course of the case. GCS (closed circle) and PaO2/FIO2 (P/F) ratio (open circle) are shown.
over several hours. In our patient, occurrence of DAI may have been caused by later alterations of the axonal membrane with changes in the transport of cysteine or glutamate rather than by direct axonal injuries \(^7\). There have been only a few previous reports of delayed onset of DAI. Gieron et al \(^9\) presented the case of a patient who developed severe DAI thirty hours after a jet ski accident. Another case, of moderate DAI, reported by Corbo et al \(^7\), was noticed 16 hours after arrival at hospital. All three cases, including our case, recovered their conscious level with a GCS of 15 at hospital discharge. Moreover, these patients all had fractures of the lower extremities and it is important to distinguish DAI from a cerebral fat embolism. MRI contributed to diagnostic evaluation in all these cases.

The most common MRI finding in the acute phase of DAI is multifocal areas of abnormal brightness in the temporal or parietal corticomedullary junction or the corpus callosum on T2-weighted images \(^10,11\). Typically, chronic changes of DAI on the MRI are cerebral atrophy with enlarged cerebral ventricles because of deficits in injured neuronal tissues \(^12\). However, it is often difficult to differentiate DAI from a cerebral fat embolism with MRI. Typically MRI shows multiple punctuate hemorrhage at the gray-white matter junction, along the corpus callosum, in the basal ganglia, and in the brain stem of patients with DAI \(^3\). In addition the margin of these foci is unclear in DAI, while is clear in fat embolism. In our case, when the patient’s level of consciousness decreased, a diagnosis of cerebral fat embolism was considered, because of the right femur fracture. The CT scan showed diffuse cerebral edema and compression of the lateral ventricles at that time. Furthermore, there was no low density lesion due to an occlusion of vessels to confirm the cerebral fat embolism. Twenty-four hours later, the MRI showed multiple T2 hyperintensities, but these were not compatible with occluded vessels due to a cerebral fat embolism. It is difficult to determine the dominant vessels in these lesions because those multiple hyperintensities are characteristic of many different complex lesions. In particular, hyperintensities at the corpus callosum are critical, because the branches of the anterior cerebral artery can not be infarcted by fat at a uniform distance. Furthermore, the patient must have been strongly shocked to develop an atlantoaxial subluxation. Therefore, the only diagnosis was DAI.

Moreover, when the patient’s level of consciousness altered, he had intermittent decorticate posturing in his arms. In addition, his post-traumatic amnesia continued for around 6 weeks, and his DAI was, therefore, classified as severe. Kampfl et al \(^4\), reported that corpus callosum and dorsolateral brain stem findings on MRI at 6 to 8 weeks after head injury indicated a poor neurological prognosis. In our case, the MRI on day 14 already had reduced dorsolateral brain stem findings and the patient recovered with just a mild memory deficit. Generally, DAI occurs immediately after head injury and patients are unconsciousness on arrival at the emergency department (ED); however, as seen in our patient, DAI can have a delayed onset \(^13\). In the ED, any patient with sudden rotation of the head during an accident should be considered as having latent DAI even if there are no abnormal neurological findings on arrival at hospital.

We presented this case report at the 21st annual congress of Japan Society for Critical Care Medicine.

References

症例報告

遲発性に発症した重症びまん性軸索損傷の1例

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要旨 びまん性軸索損傷（diffuse axonal injury; DAI）は，一般的には頭部外傷受傷直後に発症する。来院時は意識清明であったが，ワゴン車を運転中に2トントラックに追突し，受傷後，約7時間後，意識障害を呈した20歳男性のDAI症例を経験したので報告する。意識状態の悪化時，全身性硬直性けいれんと除皮質硬直を認め，GCS（Glasgow Coma Scale）は1113の5点であった。大腿骨骨折を合併していたため脂肪塞栓を考えたが，MRIにてDAIの所見を認め，脳幹部損傷を伴う症状があり，重症のDAIと診断した。14日目には意識状態も改善し，GCSは9点となり，MRIでもDAIの慢性所見を示した。軽度の記憶障害を伴って退院となった。遅発性のDAIの報告は少ないが，DAIの発症機序を神経病理学的に考えると，遅発性に発症する可能性はある。DAIは，軸索の膜や軸索鞘が剪断力により直接，障害されるだけでなく，二次的な障害として，軸索の腫脹や軸索膜の透過性増加により軸索伝導が起こる。よって，頭部の回旋力が加わった外傷症例においては，来院時，意識清明であっても遅発性にDAIが生じる可能性があることを念頭に置くべきと考えられた。

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キーワード：外傷性脳損傷，MRI，交通事故，回旋力

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