Acute subdural hematoma and diffuse axonal injury after severe head trauma

JUAN SAHUQUILLO-BARRIS, M.D., JOSE LAMARCA-CIUIRO, M.D., JORGE VILALTA-CASTAN, M.D., ENRIQUE RUBIO-GARCIA, M.D., AND MANUEL RODRIGUEZ-PAZOS, M.D.

Department of Neurosurgery, Ciudad Sanitaria Valle de Hebrón; Department of Neuropathology, Hospital Nuestra Sehora del Mar; and Department of Forensic Pathology, Hospital Clinico, Barcelona, Spain

The association of acute subdural hematoma (SDH) and diffuse axonal injury has received little attention in the literature. The authors report the clinicopathological findings in six patients who died of severe head injury in whom computerized tomography revealed acute SDH as the predominant lesion. All patients were injured in road traffic accidents and lost consciousness on impact. The mean total contusion index was 17.4 and severe contusions were seen in only two cases. All patients presented histological criteria of intracranial hypertension (pressure necrosis focus in one or both parahippocampal gyri). Hypoxic brain damage was evident in the postmortem examination of three patients. In three cases, macroscopic hematic lesions were observed in the corpus callosum. All patients had widespread axonal retraction balls disseminated in the white matter. Three patients who survived for more than 11 days had microglial clusters. In some patients with a head injury, acute SDH may be only an epiphenomenon of a primary impact lesion of variable severity: that is, a diffuse axonal injury. In these cases, the final outcome is fundamentally dependent on the severity of the subjacent diffuse axonal injury.

KEY WORDS • acute subdural hematoma • head trauma • diffuse axonal injury

Acute subdural hematoma (SDH) and diffuse axonal injury (DAI) are posttraumatic lesions carrying high morbidity and mortality rates. Strich first described DAI in 1956; his report was followed by studies by several other authors, notably those by Adams and Gennarelli and their colleagues. Diffuse axonal injury is a primary lesion, which Gennarelli, et al., described as caused by rotational acceleration/deceleration, principally in the coronal plane. Macroscopically, the lesion in its most severe form is characterized by the presence of foci of hemorrhage in the corpus callosum and in the dorsolateral part of the rostral brain stem.

Histologically, patients with a short survival time present axonal retraction balls disseminated throughout the white matter. Patients who survive for several weeks (an intermediate survival time) have hypertrophic microglial clusters. Longer surviving patients exhibit foci of demyelination on specific staining. The classification of focal and diffuse head injury proposed by Gennarelli, while useful from a physiopathological viewpoint, sometimes may not correspond to the actual situation. Adams, et al., reported that 11% of all patients with DAI present associated intracranial hematomas. Although this has been also observed by other authors, no investigations have been specifically addressed to the study of coexisting acute SDH and DAI. The present paper describes the clinicopathological findings in six patients who died of acute SDH and in whom pathological study revealed DAI of varying severity.

Clinical Material and Methods

Comprehensive neuropathological studies were undertaken in 31 patients with fatal nonmissile head injuries. These were derived from a series of 91 patients who died from severe head injury at the Valle de Hebron Hospital, Barcelona, between December, 1984, and November, 1985. Plain computerized tomography (CT) was performed on all patients within 24 hours after injury. Intracranial pressure (ICP) was continuously recorded epidurally* in the majority of patients.

* Epidural intracranial pressure monitor manufactured by Ladd Industries, Burlington, Vermont.
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and some also underwent multimodality evoked potential studies.

All postmortem examinations were performed by one of the authors (M.R.P.). The brain was removed and fixed in formal 10% for at least 3 weeks, after which the brain-stem was sectioned at the midbrain level. Coronal brain, axial cerebellum, and brain stem sections approximately 10 mm thick were cut for gross examination. All the brains were assessed with the contusional index described by Adams, et al. For microscopic study, representative blocks were obtained from the corpus callosum (splenium, genu, and body) and bilaterally from the internal capsule, centrum ovale, parahippocampal gyri, calcarine cortex, frontal and temporal cortex, cingulate gyrus, and cerebellum. Representative blocks from the midbrain, pons, and medulla were also obtained. All blocks were embedded in paraffin and 10-μm sections were stained with hematoxylin and eosin, Nissl-Luxol fast blue, Woelcke's, Bielchowsky's, and Palmgren's stains.

The presence or absence of histological signs of intracranial hypertension was evaluated in all cases according to the criteria described by Adams and Graham1 for pressure necrosis in the parahippocampal gyri. All histological preparations were examined by one of the authors (J.L.C.). Macro- and microscopic pathological alterations were recorded photographically.

In 10 of the 31 cases studied, acute SDH's were the predominant lesion. In six of these, there were histological signs of DAI of varying severity. The clinicopathological study of these six cases prompted this paper.

Results

Clinical Findings

Of the six patients studied, four were men and two women. The age range was 23 to 66 years (mean 39.5 years). All six patients sustained their injuries in road traffic accidents and all lost consciousness immediately on impact and remained in coma until death. At admission, five patients had a Glasgow Coma Scale score of 5 or less and one scored above 5 points. According to the criteria of Miller, et al.,7 four of the six patients in our group had extracranial insults (such as hypoxia and hypotension). A clinical summary of these patients is given in Table 1.

Four patients had fractures visible on plain skull films, in three ipsilateral and in one contralateral to the hematoma. A plain CT scan showed SDH on the left in four cases and on the right in two. In all patients, analysis of the CT scan demonstrated a more or less pronounced shift of the midline with partial or total obliteration of the basal cisterns and third ventricle in four.

All six patients underwent continuous extradural ICP monitoring; five presented with an initial ICP of 20 mm Hg or higher. Only one patient had a pressure on admission below 20 mm Hg; after evacuation of the hematoma the ICP rose to levels that were uncontrollable with routine therapeutic measures. Surgical treatment was performed within 15 hours after sustaining the injury in all six patients. In four cases the SDH was evacuated via burr holes and in two an osteoplastic flap was turned. The survival time in these patients was variable. None died within the first 24 hours after treatment; three died within the 1st week, and the other three survived for 11, 28, and 48 days (Table 1).

Neuropathological Findings

The gross neuropathological findings are summarized in Table 2. Five patients suffered associated subarachnoid hemorrhage, bilateral in three and unilateral in two cases. The mean total contusion index (MTCI), evaluated according to the criteria of Adams, et al.,6 was 17.4. One patient had an MTCI of 0, while two had severe contusions (MTCI > 30). The most frequent sites for contusion were the frontal poles (mean contusion index (MCI) 8.2), followed by the temporal poles (MCI 6.5). In all cases contusion was minimal in the parietal and occipital lobes and in the sylvian sites. None of the patients presented foci of contusion in the cerebellum (Table 3).
TABLE 3
Distribution of severity of contusions

<table>
<thead>
<tr>
<th>Location</th>
<th>Mean Contusion Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>17.4</td>
</tr>
<tr>
<td>rt hemisphere</td>
<td>9.7</td>
</tr>
<tr>
<td>lt hemisphere</td>
<td>7.7</td>
</tr>
<tr>
<td>frontal lobe</td>
<td>8.2</td>
</tr>
<tr>
<td>temporal lobe</td>
<td>6.5</td>
</tr>
<tr>
<td>sylvian fissure</td>
<td>1.0</td>
</tr>
<tr>
<td>occipital lobe</td>
<td>0.7</td>
</tr>
<tr>
<td>parietal lobe</td>
<td>1.0</td>
</tr>
<tr>
<td>cerebellum</td>
<td>0</td>
</tr>
</tbody>
</table>

All six patients had signs of raised ICP, manifested by pressure necrosis in one or both parahippocampal gyri (Fig. 1). Four patients presented bilateral necrotic foci, while in the remaining two necrosis was seen only ipsilateral to the SDH (Table 2). In four cases gross hemorrhages were seen in the medial or paramedial brain stem, generally involving the midbrain, the more rostral part of the pons, or both. The two other cases had a macroscopically normal brain stem (Table 2). Besides the foci of necrosis in the parahippocampal gyri, gyrus cinguli, or calcarine cortex that are usual in intracranial hypertension, three of the six patients presented hypoxic brain damage in the basal ganglia, Ammon’s horn, or both. Two of these also had additional hypoxic lesions in arterial boundary zones.

Macroscopic lesions in the corpus callosum of the type described by Strich and Adams, et al., were seen in three of the patients. In two they were hemorrhagic (Fig. 2) and in the third they were necrotic (Table 4). Of the three patients with normal findings on gross examination of the corpus callosum, hemorrhage was visible under the light microscope in one. In all cases these lesions were eccentric. Only one patient had macroscopically visible unilateral necrotic lesions in the superior cerebellar peduncle. Microscopic examination of the corpus callosum revealed anomalies in all cases. Four patients had axonal retraction balls, three had microhemorrhages, and two had foci of necrosis (Table 4).

Different degrees of diffuse axonal lesions were observed in all patients. Axonal retraction balls were present in all cases studied (Fig. 3). These lesions, which are easily seen with simple stains like hematoxylin and

Fig. 1. Pathological findings in Case 2, including macroscopic hemorrhages in the corpus callosum and moderate diffuse axonal injury. The patient survived 4 days after injury. A focus of pressure necrosis was found in the left parahippocampal gyrus. A: Macroscopic appearance of the focus of pressure necrosis. B: Microscopic appearance of the same lesion. H & E, x 40.
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TABLE 4
Corpus callosum (CC) and superior cerebellar peduncle (SCP) lesions

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Survival Time (days)</th>
<th>Macroscopic</th>
<th>Microscopic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CC</td>
<td>SCP</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>11</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>4</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>2</td>
<td>-</td>
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<td>5</td>
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<td>-</td>
</tr>
<tr>
<td>6</td>
<td>63</td>
<td>48</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

* P = axonal retraction balls; H = hemorrhages; M = microglial clusters; N = necrosis. + = mild lesions; ++ = marked lesions; - = negative findings.

eosin, are even more evident using silver staining techniques of the Palmgren type. The brain stem was the site of these lesions in all cases. Four of the patients also presented axonal retraction balls in the corpus callosum, bilateral internal capsule (Fig. 4), and centrum ovale. In two patients axonal retraction balls were found in the subcortical white matter, and in three they were present in the dorsolateral quadrants of the brain stem (Table 4). In only one case (Case 4) was this type of lesion seen in the cerebellar white matter. Axonal

Fig. 2. Characteristic hemorrhagic lesion in the corpus callosum of Case 2. Note the paramedial distribution of the lesion affecting the full thickness of the corpus callosum.

Fig. 3. Case 1. Photomicrographs showing two typical axonal retraction balls, one in the corpus callosum (A) and one in the internal capsule (B). The patient had a left-sided acute subdural hemorrhage and survived 11 days after trauma. Palmgren, x 400.
retraction balls were most evident and more disseminated in patients with prolonged survival (more than 1 week) (Tables 4 and 5). Microglial clusters were seen in three patients (survival time 11, 28, and 48 days); the distribution was similar to that of axonal retraction balls (that is, in the corpus callosum, internal capsule, and brain stem).

Only the patient with a 48-day survival time (Case 6) presented signs of long-tract degeneration (Table 5). This type of degeneration affected the ascending and descending tracts of the brain stem in equal measure.

**Discussion**

Classification of traumatic head injuries on the basis of CT findings as either focal or diffuse lesions, while useful from a clinical point of view, is often a misleading simplification with regard to the true underlying pathology of the brain injury. Cooper, et al., among others, demonstrated that in many cases these two types of lesions may be found together. Diffuse axonal injury is almost always found in patients rendered unconscious at the moment of injury, in whom CT does not demonstrate a space-occupying lesion, and in whom an extraneurological cause for the coma has been ruled out. 3,8,10,13,22,25,26 Patients rendered immediately comatose in whom CT demonstrates a predominantly focal lesion have also been shown to have DAI of varying severity. 3,9,22,23

Acute SDH is found in approximately 10% to 30% of all patients with severe head injury. 3,8,10,13 The mortality rate for different series varies between 50% and 90%. 3,8,11,16,28,29 Many patients with acute SDH are rendered unconscious immediately upon sustaining the injury, 28 and the mortality rate for this group is higher than for patients without coma on impact. 11,20,27,28 Although some authors suggest the possibility of more or less severe associated DAI in these patients, 3,7,9,11,12,18,22 no studies have focused specifically on this feature.

Under ideal laboratory conditions it is possible to separate lesions due to acceleration from those due to impact on the skull; 2,13 however, in real situations the impact and acceleration act together in producing lesions to the brain parenchyma. The rare “pure” acute SDH is the result of insults in which the effects of acceleration dominate those produced by impact. Nevertheless, contact phenomena play a fundamental part in acute SDH associated with cerebral contusion and “pulped” frontal or temporal lobes.

The majority of studies of DAI demonstrate that the entity is seen almost exclusively with dynamic mechanisms, implying high degrees of acceleration and deceleration. 12,13 Gennarelli, et al., 13 provoked DAI in subhuman primates by submitting them to short pulses of rotational acceleration without impact. They also demonstrated that angular acceleration on the coronal (lateral) plane was the most damaging. All of the patients in our series were injured in road traffic accidents, and all were rendered unconscious at the moment of injury. Although some authors such as Pilz 19 demonstrated the presence of diffuse white-matter lesions in patients with lucid intervals, the majority of authors report such lesions only in patients rendered unconscious on impact. 3,5,10,13,22,23,25,26

Increased ICP and the consequent reduction in perfusion pressure is a frequent cause of death in patients with acute SDH. Among others, Seelig, et al., 24 reported that in almost 24% of patients with acute SDH the postoperative ICP rose to uncontrollable levels. They also stated that almost half of their patients who died after evacuation of an acute SDH had uncontrollable ICP. In all of our cases, pathological studies disclosed necrotic foci in one or both parahippocampal gyri. Thus, as in the majority of patients with severe head injuries, adequate control of ICP must be one of the most important goals in patients with acute SDH and DAI.

Although some authors have reported that patients with DAI constantly present macroscopically visible...
lesions in the corpus callosum and superior cerebellar peduncle.\(^\text{5,6}\) others have demonstrated that these specific lesions are found only in the more severe forms of DAI, which usually are related to very high degrees of angular acceleration.\(^\text{11}\) Only three of the six patients in our series had macroscopic lesions in the corpus callosum, and only one patient had them in the dorsolateral quadrant of the rostral brain stem. Although the pathophysiology of these lesions remains controversial, Holbourn’s theory\(^\text{14,15}\) is currently the most widely accepted. According to him, hematic lesions in the corpus callosum, superior cerebellar peduncle, and the hemispheric white matter are the result of shearing forces acting on parenchymal blood vessels. The almost constant finding of such lesions at particular sites would only point to a higher amount of force concentrated at such sites and conditioned by the physical and structural properties of the brain.\(^\text{15}\)

Axonal retraction balls, hypertrophic microglial clusters, and demyelination are all manifestations of the same trauma (that is, axonal injury).\(^\text{3,5}\) Although the first description of axonal retraction balls was made by Ramón y Cajal in 1907,\(^\text{21}\) it was in 1956 that Strich\(^\text{25,26}\) clearly stated that these lesions could be found in patients with severe posttraumatic dementia. Diffuse axonal injury has also been found in minor head injury\(^\text{20}\) and has been reproduced in the laboratory using the Penn-II device.\(^\text{13}\) Axonal retraction balls may be found post mortem within a few hours of injury, but usually they are not easily distinguished until at least 12 to 24 hours have elapsed between the impact and the death of the patient.\(^\text{4,5,7,22,25,26}\)

The coexistence of acute SDH and DAI in patients rendered unconscious on impact may be explained by the fact that the injury mechanism is similar in both lesions. Acute SDH and, more frequently, “pure” SDH are the result of head injury in which the acceleration is of short duration with a high strain load.\(^\text{11}\) Laboratory studies demonstrate that DAI is generally produced by acceleration/deceleration mechanisms of longer duration and with loading of more gradual onset than the loading that produces acute SDH.\(^\text{11,12}\)

The loss of consciousness from the moment of impact and the injury mechanism (traffic accident) are findings suggestive of DAI in patients with acute SDH. When CT discloses hemorrhage in the corpus callosum or small hematic intraparenchymal lesions (single or multiple), an almost certain diagnosis of DAI plus acute SDH can be established. The high morbidity and mortality rates reported for acute SDH in the majority of documented series\(^\text{4,27-29}\) and the therapeutic failure of certain aggressive surgical procedures might in some cases be attributable to a widespread subacute axonal lesion.

In many patients with acute SDH, extracerebral blood clots may be an epiphenomenon that further complicates the course; however, the outcome is decided at the moment of injury and is fundamentally dependent on the severity of the subjacent DAI. Because at the present time and in the majority of patients the presence of DAI and its severity are impossible to establish with certainty, rapid transport from the scene of the accident, quick diagnosis, prompt surgical treatment, and aggressive therapy for intracranial hypertension must continue to be the goals in the management of all patients with acute SDH.

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Address for Dr. Sahuquillo-Barris, Vilalta-Castan and Rubio-García: Department of Neurosurgery, Ciudad Sanitaria Vall de Hebrón, Barcelona, Spain.
Address for Dr. Lamarca-Ciuro: Department of Neuropathology, Hospital Nuestra Señora del Mar, Barcelona, Spain.
Address for Dr. Rodriguez-Pazos: Department of Forensic Pathology, Hospital Clinico, Barcelona, Spain.
Address reprint requests to: Juan Sahuquillo-Barris, M.D., Osona 6, 2°-4°, 08023 Barcelona, Spain.