Traumatic intracranial hemorrhage in patients with seizures: Descriptive characteristics

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Abstract

We reviewed the records of all patients with recurrent seizures and severe head injury-induced traumatic intracranial hemorrhage (TIH) between 1989 and 2003 in three Israeli medical centers. We identified 52 cases (44 males, mean age = 43 ± 19 years, range = 8–84; 8 females; mean age = 74 ± 12 years, range = 48–85). Twenty-seven (52%) had additional known risk factors for TIH, e.g., older age, alcohol abuse, and anticoagulant use. All five children and adolescents had mental retardation. Approximately one-half of patients with seizures and TIH have additional risk factors for TIH. Non-mentally retarded children and adolescents with seizures are probably at low risk of developing TIH. Women less than 70 years old with seizures are much less prone to TIH than men. In young “otherwise healthy” patients with epilepsy, suboptimal treatment seems to be an important factor in the occurrence of TIH.

Keywords: Traumatic intracranial hemorrhage; Seizure; Epilepsy

1. Introduction

Physical trauma in epilepsy leads to two types of negative consequences: direct, in terms of sequelae of the injury itself, and indirect, as expressed by anticipation of its occurrence. The physician often faces the dilemma of needing to prevent overprotection and isolation of the patient, on the one hand, and to recommend measures to prevent trauma on the other. Different patients apparently have different degrees of risk for injury and, therefore, require different degrees of protection. Buck et al. [1] defined risk factors for trauma in patients with seizures: they listed degree of severity and frequency of seizures as being predictors of all types of injury, and adverse effects related to medications as predictors of injury occurring while bathing or swimming. The study by Neufeld et al. [2] added the parameter of younger age at seizure onset as a significant predictor of trauma.

The head is the most common site of seizure-related injury [2–5]. In a population of multihandicapped patients with therapy-resistant epilepsy, 74% of all seizure-related injuries were localized to the head and face [3]. Moreover, 55% of all lifetime injuries in epilepsy patients were localized to the head [2]. Neufeld et al. [4] reported that the proportion of traumas affecting the head relative to all other sites is much higher in patients with seizures (66%) compared with controls (25%).
Despite the relative frequency of head injury, traumatic intracranial hemorrhage (TIH) is rare. Russell-Jones and Shorvon [6] reported 2 cases of TIH among 766 seizure-related head injuries (0.26%), and Buck et al. [1] reported 1.4%.

There are few reports on the characteristics of patients with seizures who have a TIH. One-half of 20 such patients described by Zwimpfer et al. [7] showed evidence of alcoholic intoxication, and 12 (60%) had subdural, 5 (25%) had epidural, and 3 (15%) had intracerebral hemorrhages; 16 of them (80%) were men.

The current study presents a relatively large series of patients who have had seizures and TIHs, with the aim of defining the characteristics of these patients.

2. Methods

We reviewed the hospital records of all cases of TIH diagnosed by computed tomography (CT) scans in patients with recurrent seizures during a 15-year period (1989–2003) in three major medical centers in Israel: Soroka (Beer-Sheva: south), Tel-Aviv–Sourasky (central), and Rambam (Haifa: north). The patients were identified by cross-checking the ICD-9-CM codes for epilepsy or seizure with the codes for all types of TIH (epidural, subdural, subarachnoid, traumatic intracerebral) (see Table 1). Excluded were patients whose trauma was associated with first-ever seizure or clearly related to causes other than seizure. The data analysis included demographic information, seizure history, history of other neurological or mental disease, antiepileptic medications, use of anticoagulants, substance abuse, trauma setting, reason for admission to medical care, and type of TIH. Because of concern over the inaccuracy of the definition, brain contusion, brain laceration, and other types of traumatic intracerebral (parenchymic) hemorrhage were all considered together under the single category traumatic intracerebral hemorrhage.

3. Results

We identified 52 cases of recurrent seizures and TIH (age range = 8–85, mean = 50 ± 21), including 44 males (age range = 8–84; mean = 43 ± 19) and 8 females (age range = 48–85, mean = 74 ± 12). There were 19 from the Soroka, 6 from the Tel-Aviv-Sourasky, and 27 from the Rambam medical centers. A trauma–seizure connection was documented for 18 patients (35%), whereas such a connection was not documented, but not excluded, for the remaining 34 patients (Table 2).

3.1. Type of TIH

The types of TIH in the study group were epidural, subdural, subarachnoid, and traumatic intracerebral (Tables 2 and 3). Twenty-five of 52 patients (48%) had more than one type of TIH. There was only one death during hospitalization, that of an 85-year-old woman with a subdural hematoma.

3.2. History of alcohol abuse

Thirteen of 52 patients (25%), all male, had a history of alcohol abuse (Table 2). Three patients had been treated with antiepileptic drugs (AEDs) before they experienced the TIH: two received phenytoin 300 mg daily and one received vigabatrin 1000 mg daily. There was a documented connection between a trauma event and a seizure in three of the alcohol abusers.
3.3. Mental handicap

Fourteen of 52 patients (27%) had different mental handicaps. Eleven (mean age = 25 ± 14 years, range = 8–47) were mentally retarded, one 27-year-old patient had poorly controllable schizophrenia, and two patients had dementia (an 84-year-old man and an 80-year-old woman, who was the only female in this subgroup). The reason for admission of the two patients with dementia to the emergency room was head trauma due to a fall, but the relationship between the fall and seizures was not mentioned in the medical records. One of these two patients had been taking two AEDs, and the other, one AED. Among the 12 other, younger mentally handicapped patients, 6 (50%) had fallen, and an association with seizure was documented. Six of these 12 patients had been taking more than one AED prior to the TIH, three were on monotherapy, and for two, the treatment was unknown. One 8-year-old patient had received no AEDs whatsoever.

3.4. Oral anticoagulation treatment

Three patients were taking oral anticoagulants. One was an 11-year-old boy who had homocystinuria, mental retardation, and epilepsy. Warfarin was prescribed due to a history of pulmonary embolism (neither INR nor PT were mentioned). The patient was treated with phenytoin (dosage not given). His brain CT scan demonstrated a number of traumatic intracerebral hemorrhages. The second patient, a 48-year-old woman with poststroke epilepsy, ischemic heart disease, and peripheral vascular disease, was being treated with acenocoumarol (INR = 4.3). She was taking topiramate 200 mg daily. Her brain CT scan disclosed frontal falx subdural hematoma. The third patient, a 72-year-old women treated with warfarin (INR = 1.92), suffered from chronic atrial fibrillation and had a history of recurrent ischemic stroke. For her poststroke epilepsy, she took phenytoin 300 mg daily. The CT scan disclosed acute and chronic subdural hematomas and a traumatic intracerebral hemorrhage. All these patients had fallen and had suffered head trauma, but there was no documentation relating the fall to a seizure.

3.5. Children and adolescents

Five patients were in the first two decades of life (age range = 8–16), all male and all mentally retarded. A trauma–seizure connection had been documented for three of them.

3.6. Older patients

There were 16 patients aged 60–85, seven females and nine males. Two of the males (62 and 63 years old) had a history of alcohol abuse. One 80-year-old woman and one 84-year-old man had dementia. All 16 patients had fallen, but precise information relating the falls to seizures was lacking.

3.7. Younger patients (<60) without mental handicap or alcohol abuse

This group comprised 12 patients, 1 female and 11 males. Nine of them (75%) fell because of a seizure; for three others who fell (Table 4, cases 4, 9, and 10), an association with seizures was not clear. Two patients (Table 4, cases 5 and 12) had more than one TIH. Eight patients (67%) were undertreated or not being treated with AEDs (Table 4, cases 1–4, 6, 8, 10, and 11).

3.8. Recurrent TIHs

Two of the 52 patients had recurrent TIHs. One patient (Table 4, case 5), a 37-year-old man diagnosed as having epilepsy with frequent seizures and taking sodium valproate 600 mg daily, suffered a head trauma from a fall due to seizure 2 days before admission to the emergency room. The brain CT scan at that time disclosed an epidural hematoma and a traumatic intracerebral hemorrhage. Nine years later, he was found in a confusional state with signs of head trauma. A brain CT scan demonstrated a left epidural hematoma and a left traumatic intracerebral hemorrhage. The other patient (Table 4, case 12) was a 58-year-old man with epilepsy who had been seizure-free for the last 10 years. His treatment consisted of three AEDs (phenytoin 300 mg daily, phenobarbital 200 mg daily, and clonazepam 1 mg daily). One week before admission to the emergency room, he had fallen due to a seizure and had sustained a head trauma and suffered from headache and general functional decline as a result. A subarachnoid hemorrhage and brain contusions were diagnosed on a brain CT scan. Progressive cognitive impairment was noted following this episode. Approximately 1 year later, the patient again fell and sustained a head trauma due to seizure. At that time, he was taking phenytoin 300 mg daily and phenobarbital 100 mg daily. An epidural hematoma and a traumatic intracerebral hemorrhage were detected on the brain CT scan. Two months after the second event, the patient again traumatized his head due to a fall, but whether the fall was related to a seizure was not mentioned this time. The antiepileptic treatment was the same as before the second event. The brain CT scan now disclosed a subdural hematoma.

4. Discussion

In Israel, the vast majority of patients with TIHs are transferred to hospitals that have neurosurgical departments. There are six such hospitals in Israel, three of which participated in the current study, and so we assume that approximately one-half of all recorded cases of TIH in patients with recurrent seizures nationwide during the 15-year study period are represented herein. As such, a population of approximately 2.5–3 million people (half of the Israeli population) in which there were 52 cases during 15 years yields an incidence of 1.2–1.4 cases yearly per 1 million general population.
There were 8 females among the 52-patient study group. The incidence of head trauma is recognized as being higher in men than in women in the general population [8], partially explained by the more frequent involvement of men in dangerous activities. It is doubtful that this explanation is applicable to the population of epilepsy patients for whom trauma due to seizures plays an important role. Zwimpfer and colleagues [7] reported a male:female ratio of 15:5 among 20 patients with TIH due to seizures. When we broke down the ages of the women in our current study, it emerged that seven of them were in the eighth and ninth decades of life, leaving only one woman among our 45 study patients younger than 70. Even after excluding the 13 patients with a history of alcohol abuse (all males), the male:female ratio would be 31:1. Given that the prevalence of epilepsy is similar in men and women [9], this means that women younger than 70 with epilepsy may be much less prone to TIH than men.

According to our findings, TIH in patients with seizures is, apparently, rarely lethal. Only one of our 52 study patients died in hospital. It must, however, be noted that only patients who arrived at one of the three participating hospitals were included in the study, and so possible prehospital mortality was not considered.

The most common type of TIH was intracerebral (29 cases, 56%), followed by subdural (24, 46%), subarachnoid (16, 31%), and epidural (12, 23%). Alcohol abuse by itself (independent of seizures) is a risk factor for head injury [10]. In 10 of our 13 alcoholic patients, the trauma could not be clearly related to seizure, partly due to the difficulty in taking a history in patients with alcohol intoxication or withdrawal. We could not, therefore, estimate the significance of seizures as a cause of TIH in the alcoholic population.

The group designated as being mentally handicapped comprised patients with mental retardation, dementia, and schizophrenia. We identified two patients with dementia: they both were in their ninth decade of life, and a relation between seizures and trauma was not documented in their medical charts. One 58-year-old patient (Table 4, case 12), who suffered from recurrent TIHs, developed cognitive impairment over a period of 2 years. Because only three cases were identified, we can only state our impression that dementia probably does not play a major role in the occurrence of TIH in patients with seizures. Six of the 12 young mentally handicapped patients were being treated with more than one drug. We cannot exclude intractability of epilepsy as an important factor in the occurrence of TIH among young mentally handicapped patients; on the other hand, only one patient in this group was undertreated.

The situation for the group of 12 patients who were younger (<60) and free of mental handicap and alcohol abuse was considerably different. Eight of them (67%) were undertreated or not being treated and, therefore, cannot be defined as having intractable epilepsy because the definition requires recurrent seizures despite adequate antiepileptic therapy. Thus, in young, “otherwise healthy” patients with epilepsy, undertreatment seems to be an important factor in the occurrence of TIH.

### Table 4

Patients <60 without mental handicap or alcohol abuse who had a traumatic intracranial hemorrhage

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Antiepileptic drug*</th>
<th>Frequency of seizures</th>
<th>No. of TIHs</th>
<th>TIH type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>M</td>
<td>VPA 600 mg/day; no regular treatment</td>
<td>No information.</td>
<td>1</td>
<td>Subarachnoid</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>M</td>
<td>CBZ, unknown dosage; plasma level 5.2 µg/ml</td>
<td>1/month</td>
<td>1</td>
<td>Traumatic intracerebral</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>M</td>
<td>CBZ 400 mg/day and VPA 800 mg/day</td>
<td>3 admissions in 2 years for seizures that led to trauma</td>
<td>1</td>
<td>Traumatic intracerebral</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>M</td>
<td>No antiepileptic treatment</td>
<td>No information</td>
<td>1</td>
<td>Epidural and traumatic intracerebral</td>
</tr>
<tr>
<td>5b</td>
<td>37</td>
<td>M</td>
<td>VPA 600 mg/day</td>
<td>Unknown</td>
<td>2</td>
<td>Epidural and traumatic intracerebral</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>M</td>
<td>Irregular treatment with VPA (plasma level &lt;10 µg/ml) and CBZ (plasma level 4.5 µg/ml)</td>
<td>1/month</td>
<td>1</td>
<td>Traumatic intracerebral</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>M</td>
<td>OXC 750 mg/day</td>
<td>Last seizure 1 year ago</td>
<td>1</td>
<td>Epidural and traumatic intracerebral</td>
</tr>
<tr>
<td>8</td>
<td>43</td>
<td>M</td>
<td>CBZ 600 mg/day; plasma level 5.7 µg/ml</td>
<td>Several per month</td>
<td>1</td>
<td>Subdural, subarachnoid, and traumatic intracerebral</td>
</tr>
<tr>
<td>9</td>
<td>48</td>
<td>F</td>
<td>TPM 200 mg/day</td>
<td>Unknown</td>
<td>1</td>
<td>Subdural</td>
</tr>
<tr>
<td>10</td>
<td>52</td>
<td>M</td>
<td>CBZ dosage unknown; plasma level 4.0 µg/ml</td>
<td>Unknown</td>
<td>1</td>
<td>Subdural, subarachnoid, and traumatic intracerebral</td>
</tr>
<tr>
<td>11</td>
<td>57</td>
<td>M</td>
<td>No antiepileptic treatment</td>
<td>Unknown</td>
<td>1</td>
<td>Subdural, subarachnoid, and traumatic intracerebral</td>
</tr>
<tr>
<td>12b</td>
<td>58</td>
<td>M</td>
<td>PHT 300 mg/day, Pb 200 mg/day, CLZ 0.5 mg/day</td>
<td>10 years without seizures</td>
<td>3</td>
<td>Subarachnoid and traumatic intracerebral</td>
</tr>
</tbody>
</table>

* VPA, sodium valproate; CBZ, carbamazepine; OXC, oxcarbazepine; TPM, topiramate; PHT, phenytoin; Pb, phenobarbital; CLZ, clonazepam.

b These patients had recurrent TIH; the data in this table reflect only the first TIH event.
All five children and adolescents in our study were mentally retarded. Taking into account that the estimated population of 2.5–3 million children did not yield a single case of a nonretarded child or adolescent with epilepsy complicated by TIH during a 15-year period, we suggest that such patients are probably at very low risk of TIH.

None of the 16 patients who were ≥60 years had a documented history of fall due to seizure. Insofar as older people are prone to falls unassociated with the occurrence of seizures, it would be very difficult to define the role of seizures as a cause of TIH in this subgroup of patients.

What is the role of other risk factors for TIH among patients with seizures? The risk factors for subdural hematoma have been best defined and include age >65, alcohol abuse, and anticoagulation [11,12]. In our study, 12 patients were ≥70, 13 had a history of alcohol abuse, and 3 were being treated with oral anticoagulants—one of whom was also over 70 years of age—for a total of 27 patients (52%). This suggests that approximately one-half of patients with recurrent seizures and TIHs have additional risk factors for TIH.

Only three of our patients were being treated with oral anticoagulants, and there was no clear relation between their TIHs and seizure occurrence. We cannot conclude anything about the safety of anticoagulation in patients with seizures because of the extremely small number of such patients in this study, and so, for patients with seizures, the answer to the question “to give or not to give” an anticoagulant when there is an option awaits definition by additional studies.

Another question that arises is whether TIH in a patient with seizures increases the risk for additional TIHs in the same patient. As only two patients had recurrent TIHs, our sample is too small to answer to this question.

5. Summary

- Approximately one-half of patients with recurrent seizures and TIHs have additional risk factors for TIH.
- TIH in patients with recurrent seizures is apparently rarely lethal.
- Women younger than 70 with recurrent seizures are less prone to TIH than men.
- Children and adolescents who have recurrent seizures but are not mentally retarded are probably at low risk for TIH.
- Suboptimal treatment may be an important factor in the occurrence of TIH in patients with recurrent seizures who are younger than 60, have no history of alcohol abuse, and are not mentally handicapped.

6. Study limitations

Because of its retrospective nature, all the information on the 52 study patients was obtained from their medical charts, and therefore, the accuracy of the data is completely dependent on the accuracy of the physicians’ reports. In many cases, it was impossible to define the exact type of seizure or epilepsy syndrome and to conclude how the head trauma related to seizure occurrence. As the data on patients with alcoholism were insufficient to differentiate between epilepsy and withdrawal seizures, all patients with alcohol abuse and recurrent seizures were included in this study. Lastly, our study does not define the risk factors for TIH in a population of patients with seizures, but rather presents selected descriptive characteristics of patients with seizures complicated by TIH.

Acknowledgment

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References