

Exacerbation of Pre-existing Epilepsy by Mild Head Injury: a Five Patient Series

P.C. Tai, D.W. Gross

ABSTRACT: *Objective:* While the risk of developing seizures following a mild head injury has been reported and is thought to be low, the effect of mild head injury on patients with a pre-existing seizure disorder has not been reported. We present a series of cases where a strong temporal relationship between mild head injury and worsening of seizure frequency was observed. *Methods:* Five cases were identified and reviewed in detail. Information was derived from clinic and hospital charts with attention to the degree of injury, pre- and postinjury seizure patterns and frequency. *Results:* One patient has primary generalized epilepsy and four have localization related epilepsy. Prior to the head injury, three of the patients were seizure free (range: two to 24 years). The patients suffered from mild head injuries with no or transient loss of consciousness and no focal neurological deficits. In all cases, the patients experienced a worsening of seizure control within days of the injury. In one case, the patient's seizure pattern returned to baseline one year after the accident, while in the remaining four cases, the patients continue to have medically refractory seizures. *Conclusions:* A close temporal relationship between mild head injury and a worsening of seizure control was observed in five patients with epilepsy. Although further study is required, this observation suggests that a head injury that would be considered benign in the general population can have serious consequences such as recurrence of seizures and medical intractability in patients with epilepsy.

RÉSUMÉ: *Exacerbation par un traumatisme crânien léger d'une épilepsie préexistante: série de cinq patients.* *Objectif:* La littérature fait état du risque de présenter des crises d'épilepsie suite à un traumatisme crânien léger, ce risque étant considéré comme faible. Cependant, l'effet d'un traumatisme crânien léger chez des patients ayant une épilepsie préexistante n'a jamais été rapporté. Nous présentons une série de cas chez lesquels une relation temporelle entre un traumatisme crânien léger et une augmentation de la fréquence des crises a été observée. *Méthodes:* Nous avons identifié cinq cas dont nous avons révisé les dossiers cliniques et hospitaliers en détail, particulièrement en ce qui a trait à la sévérité du traumatisme ainsi qu'à la nature et à la fréquence des crises avant et après le traumatisme. *Résultats:* Un patient avait une épilepsie généralisée primaire et quatre avaient une épilepsie focale. Avant le traumatisme crânien, le temps écoulé depuis la dernière crise variait de 2 à 24 ans chez trois des patients. Les patients ont subi un traumatisme crânien léger sans perte de conscience ou avec perte de conscience passagère, sans déficit neurologique focal. Dans tous les cas, les patients ont présenté une détérioration du contrôle des crises dans les jours suivant le traumatisme. Dans un cas, le problème est rentré dans l'ordre un an après l'accident. Dans les quatre autres cas, les patients présentent toujours des crises réfractaires au traitement médical. *Conclusion:* Nous avons observé une relation étroite entre un traumatisme crânien léger et une détérioration du contrôle des crises chez cinq patients épileptiques. Cette observation suggère qu'un traumatisme crânien, qui serait considéré comme bénin dans la population en général, peut avoir des conséquences sérieuses chez des épileptiques, telles une récurrence des crises et une résistance au traitement médical.

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Over the last several decades, the risk of developing post-traumatic epilepsy (PTE) after military and civilian head injury of varying severity has been demonstrated and partially quantitated.¹⁻³ Risk factors for developing PTE have been identified and relative risk for PTE depending on the severity of the injury has been determined.² Based on the association between head injuries and the development of seizure disorder, one might expect head injury to have a negative impact on seizures in patients with a pre-existing seizure disorder.

To date, there has been no discussion in the literature of the impact of head injury on patients with pre-existing epilepsy. We present five patients with pre-existing epilepsy in whom mild

From the Division of Neurology, University of Alberta, Edmonton, Alberta, Canada.
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Reprint requests to: Donald Gross, 2E3.19 Walter Mackenzie Center, University of Alberta, Edmonton, Alberta T6G 2B7 Canada.

head trauma was observed to cause a significant increase in seizure frequency. The types of head injuries our patients sustained would not generally be associated with a significantly increased risk of developing epilepsy in nonepileptic patients.

METHODS

Five patients from the University of Alberta Epilepsy Clinic were identified where there was a history of worsening of seizure control after mild or trivial head injury (Table 1). Available charts, both clinic and in-hospital, were retrospectively reviewed in order to determine severity of injury, pre- and postaccident seizure frequency, temporal association of increased seizures to the accident, and investigations performed. Severity of head injury was classified as mild, moderate or severe based on criteria defined in earlier studies on civilian head injury and epilepsy by Annegers et al² (Table 2). This classification system did not distinguish between degrees of mild head injury, as done after concussion but was chosen to permit comparison with prior estimates of incidence of post-traumatic epilepsy in nonepileptic patients.

Patient 1:

This 27-year-old right-handed woman was diagnosed with epilepsy at the age of 12 years. She had a history of fetal distress requiring cesarean section, but there was no history of febrile seizures, central nervous system infection, significant head injury or early developmental delay. She had one aunt with a history of epilepsy. The patient had impaired school performance and failed grade two which, retrospectively, may have resulted from unrecognized absence seizures. She experienced her first generalized tonic-clonic convulsion (GTC) at the age of 12 years. The generalized seizure lasted one or two minutes and was not preceded by an aura. An EEG demonstrated a three Hz spike and wave pattern, and she was diagnosed with primary generalized epilepsy for which she was treated with valproic acid. On valproic acid she became seizure free and was able to obtain her driver's license. An attempt at discontinuing medication at age 17 resulted in a recurrence of seizures, which led to her being restarted on valproic acid, after which she became seizure free.

At the age of 20, the patient was the unrestrained passenger in a motor vehicle accident where her vehicle struck a parked car at about 50kph. Her head struck the windshield forcefully enough to break the glass and she lost consciousness for about ten seconds. Her Glasgow Coma Scale was 15/15 at emergency room assessment and she was discharged home. The following day she returned to the emergency room with the complaint of 10 to 12 brief lapses of consciousness that were interpreted as absence seizures. A few months later she had a GTC in association with alcohol use and stress. She had one more GTC seizure shortly after becoming pregnant. Following the second seizure the patient remained seizure free for two years and was able to re-obtain her driver's permit.

At age 22, the patient was again the unbelted passenger in a car in a side-on collision at about 80kph. She is documented to have had no loss of consciousness at admission to hospital, although later she indicated that her first memories after the accident were of the emergency room. She was admitted for four days, due to rib fractures and abdominal injuries. Computerized tomography scan of the head was normal. Within days of the accident, she began having absence spells two to three times a day. Due to uncontrolled seizures, she lost her job. A year later, she was still having seizures four to five times a week while on valproic acid. In

a three day admission for EEG telemetry monitoring at the time, with no changes to medications and therapeutic drug levels, she had seven clinical absence seizures with associated 3 Hz spike and slow wave complexes. Since that point in time, she has continued to have daily absence seizures which have been refractory to trials of multiple medications. She has however had no further GTC. Due to ongoing seizures, the patient has been unable to re-obtain her driver's permit.

DISCUSSION

The development of seizures after head injury is well-documented in the literature. Incidence of epilepsy in wartime penetrating brain injury is thought to be between 30%⁴ and 50%,¹ whereas in civilian settings, badly injured patients with prolonged loss of consciousness, prolonged amnesia, subdural hematomas and brain contusion have a 16.7% incidence of seizures over 30 years.² Civilian head injuries when stratified, as by Annegers et al, into severe, moderate, or mild (as described in Table 2) have a risk of post-traumatic seizures in five years of 10%, 1.2% and 0.7% respectively.² Mild and moderate head injury patients have a risk of seizures only about 1.5 times and 2.9 times that of the general population, compared to a 17.0 times increased risk in severe head injury.²

The impact of head injury on patients with pre-existing seizure disorder has not been documented. Four of five of our patients suffered from mild head injuries based on the classification of Annegers et al.² In fact, not all patients had documented craniocerebral impact but are assumed to have had some degree of deceleration injury related to their motor vehicle accidents. We have classified the second head injury experienced by patient one as mild to moderate based on an uncertain duration of amnesia (possibly greater than 30 minutes).² Although the degree of head injuries in all five cases would be expected to be associated with a low risk of post-traumatic epilepsy, all five patients had dramatic worsening of their pre-existing seizure disorder immediately following their head injury with three of five patients going from being seizure free for extended periods (two to greater than 20 years) to medical intractability.

In the case of patient 3, with Sturge-Weber Syndrome, it is possible to postulate on how a trivial head injury could result in the recurrence of seizures. Such patients already have cerebral vascular abnormalities and underlying cortex is often chronically hypoxic due to abnormal venous drainage.⁵ They can spontaneously deteriorate with stroke or transient ischemic attack-like episodes.⁶ We hypothesize that this patient's underlying pathology might have made him more susceptible to minor head injury. It is, however, harder in the other patients to explain why mild head trauma associated only with a marginally increased risk of epilepsy in healthy individuals would precipitate a marked worsening of seizure control. Seizures which occur in relation to trivial head injury and an underlying structural abnormality have been reported before.⁷ Epileptics, therefore, may similarly be at increased risk of seizures due to an underlying susceptible neurochemical makeup and a hyperexcitable cortex. Mild head injury may be sufficient to tip the balance in favour of seizures at a higher rate than observed in normal individuals. Whereas in nonepileptic individuals it may be necessary for the head trauma to be severe enough to set up an epileptogenic focus in order to manifest as a seizure disorder, epileptics already have

Table 1: Head injury and changes in seizure patterns per patient

Patient Age, gender	Epilepsy type	Age of epilepsy onset	Pre-accident status	Nature of accident	Severity of head injury	Temporal relationship of recurrent epilepsy to accident	Post-accident epilepsy status	Medications
#1 27 female	Primary generalized epilepsy	12 years old at diagnosis (probable unrecognized absences before)	Seizure free for three years	Age 20 – MVA @50kph with parked car. Head broke windshield. Brief LOC	Mild	Onset within the next day	10-12 absence seizures the next day	valproic acid <i>Previous medications:</i> ethosuximide, phenytoin, carbamazepine, clobazam
			Seizure free for two years. Able to hold a driver's permit	Age 22 – MVA @80kph. No LOC, amnesic of the accident, confused in the ambulance	Mild to moderate	Onset within the next day	2-3 absence seizures daily (documented by video-EEG, therapeutic levels). Unable to hold a job or driver's permit due to seizures	
#2 26 female	Localization related epilepsy (R. frontal)	13 years old	1-2 seizures/month. Able to hold a job	Age 24 – MVA – belted passenger. No LOC	Mild	Onset within days (documented by GP who saw pt 3-4 days after accident)	Frequent daily seizures (documented by video-EEG while on medications)	carbamazepine, gabapentin. <i>Previous medications:</i> topiramate, clobazam
#3 28 male	Localization related epilepsy (Sturge-Weber syndrome)	5 months old	Seizure free for 20 years	Shelf fell on head at age 24. No LOC	Mild	Within 30 minutes of accident	Seizures initially infrequent, now medically refractory, recurrent partial status	Valproic acid, phenytoin, carbamazepine, phenobarbital. <i>Previous medications:</i> topiramate, lamotrigine, clobazam, valproic acid
#4 39 female	Localization related epilepsy (R. Frontal)	5 years old	well controlled	Fell on ice, hit head. No LOC.	Mild	Within 2 weeks.	Transient in complex partial seizures	carbamazepine, levetiracetam <i>Previous medications:</i> topiramate, valproic acid, phenytoin, clobazam
			(frequency not well documented). Nocturnal seizures only, able to hold driver's permit	Age 37 – Rear-ended in MVA. No LOC	Mild	Increased for one year after the accident, then return to baseline.	frequency and severity of convulsions, with generalized tonic-clonic seizures as well.	
#5 41 female	Localization related epilepsy (temporal lobe epilepsy)	Seizures from birth until age 5	Seizure free for five years	Cyclist hit by a car at age 10, no LOC, wrist injuries	Mild	Onset within 1 week	Seizures every month or two	valproic acid <i>Previous medications:</i> carbamazepine, phenytoin, phenobarbital

LOC = Loss of consciousness. MVA = Motor vehicle accident. pt = patient. GP = general practitioner

Table 2: Head Injury Severity classification

Mild	Post traumatic amnesia or loss of consciousness less than 30 minutes
Moderate	Post traumatic amnesia or loss of consciousness between 30 minutes and 24 hours, OR skull fracture
Severe	Post traumatic amnesia or loss of consciousness lasting greater than 24 hours, OR brain contusion OR intracranial hemorrhage

After Annegers et al.²

such circuitry in place and may need only tip the system in favour of diminished inhibition or increased excitation.

Head injury has been described to be associated with the development of non-epileptic events.⁸ In patients three, four and five, no reason was seen in the course of care to investigate or treat their events as being anything other than seizures, whereas in patients one and two, epileptic events were documented during in-patient video-EEG monitoring. Stress also may provoke seizures in epilepsy⁹ and the stress associated with head injury or a motor vehicle accident could potentially have been a trigger. However these patients have had prolonged periods with seizures, in many cases after years of seizure freedom, making the likelihood low that their change would be solely due to stress.

Patients one, two and three were involved in litigation following their injuries. However, although observational biases might be suspected to arise in situations where litigation was pending or there was stress and post-traumatic hypervigilance, this would not have been the case in patients one, three and five, who had prolonged seizure free periods beforehand. Patient two also demonstrated a clear change uncomplicated by observational factors, going from well-functioning in society previously with seizures every few weeks, to being demonstrated in hospital on usual medications to be seizing frequently each day. From chart review it is unclear the degree to which these issues were a factor in patient four.

Seizure types were the same before and after trauma in all except patient five, in whom we were unable to ascertain if this was the case since her initial seizures as an infant occurred over 40 years ago.

In a large population of patients with epilepsy, it is expected that remissions and relapses would occur spontaneously. It is therefore possible to hypothesize that the recurrence of seizures or exacerbation of seizures in association with minor head injury could have occurred by chance alone. However, the temporal relationship between trauma and seizure exacerbation in all five subjects was striking and, in our opinion, strongly supportive of a direct relationship between the minor head injuries and exacerbation of seizure disorder. As this observation has important clinical implications regarding counseling patients with epilepsy regarding participation in activities with high risk of minor head injury (such as contact sports), further prospective studies are necessary in order to quantify the risk of exacerbation of a pre-existing seizure disorder associated with minor head injury.

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