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Case Series

Post-Traumatic, Drug-Resistant Epilepsy: Case Series and Review of literature

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Abstract

Post-head traumatic epilepsy or Post-traumatic epilepsy(PTE) is a devastating complication after a traumatic head injury. Initial 6-8 months after a head injury, PTE is commonly found and chances increase till the 10th year from head injury episode. Most of the cases do well with medical therapy but few develop drug-resistant epilepsy and require surgical intervention. 18 Cases were identified from 2014 until 2018. These drug-resistant PTE individuals were taken in this case series. Gender 15 (83.33%) were male, the mean age of the first episode of PTE was 24.4 years, the mean age of PTE surgery intervention was 31.2 years and the mean period from brain injury to seizure onset was 3.7 years. Most of the individuals presented with only focal onset seizure, with 12 cases (66.66%) without unconsciousness, and the other 6 cases (33.33%) reported focal to bilateral tonic–clonic seizures. 7 patients provided a history of more than 2-4 seizures in a month (38.88%). MRI findings before epileptic surgery were identified in the majority of patients (15 patients, 83.33%). On pathological identification, we found Temporal sclerosis (10 patients); FOCAL neurodegeneration (1 patient), encephalomalacia (3 patients); focal cortical dysplasia (2 patients), and focal gliotic lesion (2 patients). On EEG recording, more than 50% of PTE cases were identified with temporal lobe epilepsy (10 patients, 55.5%). 14 patients out of a total of 18 patients after surgery become seizure-free after a 1-year follow-up (EC 1, 77.77%). Around 50% of cases are identified with mesial temporal epilepsy. The surgical outcome of patients was satisfactory, only 4 patients didn't show improvement after epilepsy surgery but seizures were in control with antiepileptic medications.

Key words: Seizers, Epilepsy, Traumatic brain injury, Post-traumatic epilepsy, Temporal lobe epilepsy

INTRODUCTION

Every day people suffer from head injuries. In a vehicle accident, trip or fall from height, sports injury, etc, the severity of head injury varies from mild head injury to concussion to coma or death. Traumatic Head/Brain Injury (TBI) can be fatal or can produce complications or neurological deficits in head injury survivors, which includes Post-traumatic epilepsy (PTE), headache, etc, and also affects the quality of life with complications.

Unfortunately, due to the high-density population and so much traffic on roads, India has the highest number of head injuries in the world. Every year, more than 100,000 deaths with more than 10,00,000 suffering from a neurological deficit or post-traumatic head injury-related complications.[1]

Any injury to the brain skull or head resulting from external force, acceleration-deceleration forces, blow to the skull, concussion, bullet or blast injuries, any penetrating injury to the head, etc known as Traumatic head injury. Seizures and epilepsy are the two most common complications in post-traumatic brain/head injury survivors.[2]

Among all cases of acquired epilepsy, Post-traumatic epilepsy (PTE) shares 20% as early PTE or late PTE complication of TBI. Usually, PTE is found as drug-resistant epilepsy.

PTE is commonly present in cases of very severe head injury and gross neuronal damage.[3]

Poor Neurological functional outcomes are found in patients of PTE with physical deficiency, cognitive impairment, etc.[2]

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Worldwide, most of the cases of PTE belong to developing countries like India, Africa, Indonesia etc.

Here, we report a case series of drug-resistant PTE individuals, who were selected and eligible for surgical intervention from 2014 to 2018 in India.

METHODS

We are publishing a retrospective study at a single medical center with hospital approval.

Drug-resistant or drug-intractable PTE patients were selected from the admission database between 2014 to 2018.

Only PTE individuals [With informed consent] who had a history of traumatic head injury, were selected for this case series.

Post-operative records are managed with age, sex, demography, and radiology like CT/MRI reports, and electroencephalogram reports. Engel classification [EC 1-4] is also used to recognize the surgical outcome up to 1-year minimum.

CASE EXAMPLE

Case 1

A 31-year-old male came into the emergency room with a complaint of drug-intractable PTE with a history of road traffic accident [RTA] associated with bilateral subarachnoid hemorrhage and contusions. after 2 years of RTA with head injury, focal seizure started which started from uncontrolled irregular movements left leg to hand and followed by complete consciousness.

We started drug therapy with phenytoin sodium for the first sitting. But after 18 days, the patient visited with the same complaints in OPD and later we added another valproic acid. But he didn't get free from seizure disorder.

We found bilateral frontotemporal encephalomalacia and right temporal sclerosis (MTS). Also on EEG, epileptic discharges were recorded.

The patient and his relative's counseling was done for surgical intervention and operated for right amygdalohippocampectomy. Postoperative 1-year follow-up, the patient became seizure-free.

CASE DESCRIPTION

18 drug-resistant PTE individuals were taken in this case series. Gender 15 (83.33%) were male, the mean age of the first episode of PTE was 24.4 years, the mean age of PTE surgery intervention was 31.2 years, and the mean period from brain injury to seizure onset was 3.7 years.

Most of the individuals presented with only focal onset seizure, with 12 cases (66.66%) without unconsciousness, and the other 6 cases (33.33%) reported focal to bilateral tonic–clonic seizures.

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On pathological identification, we found Temporal sclerosis (10 patients); FOCAL neurodegeneration (1 patient), encephalomalacia (3 patients); focal cortical dysplasia (2 patients), and focal gliotic lesion (2 patients).

On EEG recording, more than 50% of PTE cases were identified with temporal lobe epilepsy (10 patients, 55.5%). 14 patients out of a total of 18 patients after surgery become seizure-free after a 1-year follow-up (EC 1, 77.77%).

DISCUSSION

Generally, Epilepsy has two types: Congenital and acquired. 20% of acquired epilepsy is shared by PTE as with fast world and high-speed vehicles, increasing this to approximately 16% in 30 years surprisingly.[4] Closed Head injuries like contusion, SAH, and brain hematoma, the risk of developing PTE is up to 30%.[5] For any intracranial bleeding, hemoglobin degradation products increase the chance of neuronal toxicity-induced epilepsy.[6] Post-traumatic head injury epilepsy is categorized under 3 types: Immediate (seizure appears within 24 hours after head injury), Early (seizure appears within first 7 days of head injury), and late (seizure appears within first 7 days of head injury).[5] Post-TBI Immediate or early seizures usually appear as generalized tonic–clonic type, on the other side delayed or late seizures appears as focal type.[7]

As per the ILAE (International league against epilepsy), an independent/isolated delayed unprovoked seizure or seizures associated with a known Traumatic brain injury complete the criteria for seizure/epilepsy.[8]

Kazis D *et al*. mentioned PTE-related classical risk factors like gender, sex, post-traumatic amnesia, alcohol abuse history, focal neurological symptoms or signs, and history of post-seizure consciousness status after TBI. CT brain or MRI imaging findings in traumatic brain injuries like

diffuse axonal injury, skull bone fracture, focal or multiple contusions, hemorrhage, intracranial mass effect midline shift, etc enhance the chance of PTE.[3]

Post-traumatic encephalomalacia of the brain is one of the often causes of PTE. A study by Vangberg *et al.* revealed that multiple dendrites found in the FLAIR hyperintense area that surrounds encephalomalacia, which proves higher neural density in that area, and this fact correlated with the production of repetitive excitatory impulse, which produced finally epileptic attack. The larger the area of encephalomalacia or the larger the hyperintense lesion the chances of PTE will be more.[9] But again, not all the cases or lesions of encephalomalacia or TBI-related FLAIR hyperintense areas are associated with epilepsy or PTE. EEG plays an important role in finding out the exact site of PTE or epilepsy and helps to get proper localization of the epileptic focus site.

After brain injuries, restructure of lost neuronal areas or reformation of cells started by the brain which produces variations in neural network and architecture of neurons, which is very common in and around hippocampus or neocortex or both. Post-traumatic brain injury initiates the release of various neurotransmitters, free radicals, calcium-mediated factors, neoangiogenesis, cell mitochondrial dysfunctioning, and cell-mediated inflammatory reactions, these all are directly or indirectly responsible for seizures.[2]

Concept pathology behind PTE association with traumatic brain injury includes neuronal damage; specially c-aminobutyric acidergic interneurons, defected axonal architecture with sprouting of axons, reactive neo - synaptogenesis, molecular re-organization of GABA receptor or Glutamate receptor and all these are mentioned in various literatures.[10] A neurotoxic guanidino compound which is produced due to reactive oxygen, works as an epileptogenic agent. This initiates the release of aspartic acid, an excitatory amino acid, and also reduces the release of GABA, an inhibitory amino acid. This imbalance of neurotransmitters is the main cause of seizures.[6]

After brain injury, multiple pathogenesis starts which produce inflammatory mediators, free radicals chemicals, etc, start triggering various neuronal circuits and produce seizures. Mainly this pathogenesis is found in the hippocampus which often produces thalamocortical and limbic seizures.[10] Various researchers noted that the most common PTE are temporal lobe and frontal lobe-associated epilepsy. Due to the impact-prone location of the temporal and frontal region, thin skull bone at the temporal region, and fall forward (frontal trauma) due to accelerated direction or gravity, both regions are commonly associated with PTE. Starting of seizure impulse from one lobe and spreading to the neighboring lobe is quite common in frontal neocortical epilepsy to the hippocampus.[11]

For a long time, multiple publications proved that temporal lobe epilepsy is the primary and most common cause of PTE. Sclerotic changes and cell loss in the hippocampus and neocortical region are often found in post-operative resected specimens' histopathological reports.[12] Temporal lobe Epilepsy and MTLE (Mesial temporal lobe epilepsy) are the main contributors to PTE, which is continuously getting recognized in previous studies also. Various studies noted more than 70-80 % of PTE cases are associated with temporal lobe epilepsy, especially with MTS.[13]

PTE patients with mesial temporal lobe epilepsy (MTLE) after surgery present 80% to 90% seizure-free outcomes, proving that drug-resistant PTE due to MTLE is always a good target case for surgical resection. Other than MTLE, patients with perfect localization and encephalomalacia also present with post-operative seizure-free outcomes.[14]

Most of the cases are associated with unifocal PTE but it is necessary to exclude multifocal type PTE always because PTE can be because of unifocal lesions or multifocal. It is mandatory to do proper localization of PTE, and whenever needed should use invasive monitoring with ideal precautions.[15]

In our study we did not include cases of drug-sensitive epilepsy, also this case series is a small-size study with a retrospective type that can not prove any significant comparison and is associated with bias due to lacking various untouched aspects of the topic. The need of the hour is a multicentric study on this topic, which includes both drug-sensitive and drug-resistant cases of PTE.

CONCLUSION

Our case series and review of literature provided clinical aspects of PTE in a single medical center in India. In this, we found that MTLE and encephalomalacia are the main causes of PTE. CT, MRI, and electroencephalogram reports are remarkable for localized epileptic focus in the brain.

Most of the PTE individuals presented with temporal lobe epilepsy and encephalomalacia had wonderful outcomes after surgical intervention. Neurosurgeons should be alert and smart to determine the cause of PTE and should rule out multifocal PTE. A multicentric study needs of hour to get a more significant precise and definitive study outcome.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of Interest

There are no conflicts of interest.

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