Multimodality Imaging in a Depressed Patient With Violent Behavior and Temporal Lobe Seizures


ABSTRACT

Patients suffering from epilepsy commonly experience behavioral symptoms. Behavioral manifestations are especially prevalent in patients with seizures originating in the limbic system. This case report illustrates how an objective, multimodality work-up can guide the clinician in the diagnosis and the treatment of a patient with a complex presentation.

After the discontinuation of some medications, the patient underwent a multimodality work-up that consisted of MRI, SPECT, and conventional and quantitative EEG (LORETA). In this case, the functional imaging studies showed a convergence of findings across the three modalities: MRI, SPECT and qEEG. Because of these findings, we supported more aggressive treatment of the seizure disorder. Ultimately this treatment resulted in resolution of the aggression and the depression.

In summary, when applied routinely, a comprehensive, systematic, diagnostic approach will minimize treatment false starts and failures, may reduce costs, and also, potentially decrease the severity and the duration of symptoms.

CASE REPORT

After attempting suicide in jail, a 42-year-old Caucasian male with a history of a seizure disorder, depression and aggressive behavior was brought to the hospital ER for clinical evaluation. The patient had been arrested after attacking his wife. Due to his violent behavior, the wife filed an order of protection, and since then, he had been unable to see his family.

Four years prior to the presentation, the patient had a motor vehicle accident (MVA) with subsequent, repeated, depressive episodes (Figure 1A). Initially the depressive episodes were mild. The patient did not report them, nor did he seek treatment. Three years prior to ER visit, the patient suffered a dental abscess, which had penetrated into his brain, specifically the left temporo-parietal area (Figure 1A, a). After neurosurgical removal of the abscess, he began to experience severe depression, including feelings of hopelessness, anhedonia, and passive, suicidal ideation. In addition, two years after the surgery, he reported the onset of uncharacteristic, aggressive behavior (Figure 1C). The patient was treated with venlafaxine SR, 150mg daily (Figure 1A, b), but despite the treatment the depression and aggression progressively worsened. Finally, the behavior culminated in the patient attacking his wife, an event associated with amnesia and attempted suicide.

In addition to his depressive episodes, clinicians believed the patient suffered from generalized tonic-clonic seizures secondary to the abscess (Figure 1B). After removal of his brain abscess and treatment with antiepileptic medication, his tonic-clonic seizures stopped (Figure 1B, a). Clinicians treated the patient with several anti-seizure medications: phenytoin, carbamazepine, valproic acid, levetiracetam, and lamotrigine, but due to side effects, the success with these agents was limited. Finally, gabapentin controlled his seizures at the dose of 1200mg, twice daily and 1500mg, at bedtime. A local hospital performed a long-term (96 hours) EEG and read it as normal (Figure 1B, b). Subsequently, his neurologist concluded that his seizures were under control.

Despite successful seizure control, the patient continued to have episodes of aggressive behavior. He also reported having episodes of amnesia and motor symptoms that included back-arching, muscle-tensing in his extremities, and repetitive movements of his fingers. The patient denied loss of consciousness during these episodes. Since long-term EEG monitoring failed to show evidence of epileptiform activity and his presentation was "atypical," he was diagnosed with pseudoseizures.

Following his presentation in the emergency room, the patient was referred to the Psychiatry Service for fur-
tion Key Institute’s software, LORETA, was used in order to evaluate the level of normality. In addition to the quantitative work-up, we manually chose artifact-free epochs of 1.15 seconds duration (0.30 seconds for frontal brain regions). The Fast Fourier Transform (FFT) was used to assess the absolute and relative power at 0.1 Hz and 70 Hz. The earlobe electrodes were used as the active electrodes, with a nose electrode as the reference. Post-acquisition, linked-ears reference was computed. The awake, eyes closed, EEG was recorded. During the recording, HMPAO ligand (25 mCi) for brain SPECT imaging was administered via an established IV line from the outside of an electrically screened Faraday Chamber. The patient was unaware of when the administration of the ligand injection occurred. The EEG recording continued for an additional 10 minutes following HMPAO administration. The abnormality threshold was set to a 2.5 mm with a standard deviation of 3.5. The images were processed using Hermes software from Hermes Medical Solutions. We normalized the images intensity and spatially co-registered them to the standard atlas. The statistical evaluation was obtained by means of BRASS software comparing the patient to the Hermes normative database using a total count adjustment. The abnormality threshold was set to a 2.5 mm with a standard deviation of 3.5. The MRI studies were completed using standard clinical protocol. T1 and T2 sequences were used, and a board-certified radiologist read the images.

RESULTS

Imaging Results

The visual analysis of the EEG record showed sharp waves with phase reversals in the left posterior temporal region (T5) and in the left parietal (P3) region. The right posterior temporal (T4) region was not as involved (Figure 2). Visual inspection of unprocessed SPECT images revealed a blood-perfusion deficit in the left temporal-parietal-occipital brain region, which closely correlated with the encephalomalacia region seen in the T2-weighted MRI image (Figure 3A). A statistical comparison of the SPECT data between the subject and the normal controls yielded additional information. Besides the perfusion deficit in the left posterior temporal-parietal-occipital region, we found a significant perfusion deficit in the left temporal-lateral and frontal brain regions.

The quantitative EEG (QEEG) analysis of the foreground and background activity demonstrated statistically significant findings in absolute power. The majority of the findings were limited to the left hemisphere (Figure 3B and C).

The quantitative analysis of the background activity demonstrated excess delta and theta absolute power (3 Hz-6 Hz) in the left posterior temporal (T5; Z value = 3.11) and occipital (O1; Z value = 2.34) brain regions. We localized the source of abnormal activity at the peak frequency of 5 Hz in the left temporal brain region using LORETA at z=2.0. (Figure 3B).

The foreground activity analysis revealed specifically increased absolute power in the slow wave range (2Hz-7Hz) in the left posterior hemisphere (T3; Z value= 3.20) (T5; Z value= 4.53) (P3; Z value= 2.43) (O1; Z value=...
LORETA analysis showed topographic distribution (as shown in Figure 3C) of abnormal activity with a peak frequency of 5 Hz at z = 2.0. As indicated by the SPECT images' statistical analysis, the distribution of foreground activity directly correlated with the area of decreased perfusion (Figure 3A and C).

Case Management

Because the QEEG results suggested regional, active and ongoing, dysregulation of brain electrical activity, in addition to gabapentin, the patient was started on topiramate (200mg BID). This combination of antiepileptic medications caused the remission of his aggressive behavior. The patient reported no additional episodes suggestive of partial complex seizures or amnesic episodes. After 5 months from initiation of topiramate, the patient returned home and resumed normal life activities. However, the patient’s depression persisted. We hypothesized that the patient’s depression was also related to persistent alterations in brain electrical activity. Consequently, phenobarbital was added to the patient’s medication regimen. Following the addition of the phenobarbital (90mg BID), within 2 months the depressive symptoms resolved.

The patient did well, and 6 years after his initial presentation, he was doing well with no symptoms of depression or aggression. He is able to drive, and enjoys his professional career as a cartoonist. His symptoms of depression and aggression remain in full remission. The patient continues to be treated with gabapentin, topiramate and phenobarbital.

DISCUSSION

Patients suffering from epilepsy commonly describe behavioral symptoms. The incidence of behavioral manifestations is especially high in seizures originating in the limbic system (temporal and extra-temporal). However, because conventionally recorded EEG tracings poorly record spatial EEG resolution, we often do not detect subtle seizure activity. Therefore, patients may be mislabeled with pseudo seizures, leading to years of suffering and disability.

After completing his QEEG studies, this patient was shown to have temporolimbic epilepsy (TLE). The behaviorally complex presentation in TLE reflects the functional complexity of the temporal lobes and the limbic system, and it is well documented in the literature. The symptom presentation can be temporally related to either the ictal or interictal phases. The treatment recommendations depend on the association of the symptomatology with specific EEG patterns.

In this population, since psychiatric symptoms are associated with TLE and psychotropic medications may reduce the seizure threshold, the use of psychotropic medications must be approached with caution. Among antidepressants, maprotiline, clomipramine and bupropion are associated with the highest risk of inducing seizures. Newer antidepressants, e.g., SSRI and NSRI (venlafaxine), are thought to have a relatively low risk of inducing seizures. However, an individual’s susceptibility to seizures is multifactorial. Their susceptibility is influenced by inherent seizure vulnerability, such as acquired brain injury (in this case: traumatic brain injury (TBI) from MVA, brain surgery and medications). In research on patients with TBI, some reports suggest that when compared with patients not treated with tricyclic antidepressants (TCA), patients treated with TCA have a risk of medication-induced seizures that is 19 times higher.

In this study, the presented patient was treated with venlafaxine. To the best of our knowledge, there have been no reports of venlafaxine-induced seizures except in cases...
of venlafaxine overdose or its use in combination with other epileptogenic medications. In the described case, the patient’s depression was treated with venlafaxine, 150mg daily. Over the treatment course, the severity of his depressive symptoms worsened with the emergence of aggressive behavior. In this subject, we could explain the worsening of behavioral symptoms by a “kindling phenomenon” defined as progressive deregulation of focal neuronal activity. This phenomenon results from repeated sub-threshold stimulations and is followed by the establishment of a “daughter focus.” A daughter focus is defined as progressive deregulation of focal neuronal activity. This phenomenon results from repeated sub-threshold stimulations and is followed by the establishment of a “daughter focus.”

The source of the patient’s persistent and pervasive depression remained unclear. A variety of factors may cause depression, including pathophysiological dysregulation of brain neurotransmitter tracts. The patient’s depression might have benefited from the additional, prescribed, antiepileptic medication, in that there is growing evidence that antiepileptic medications also have mood stabilizing properties. Depression is a multi-faceted condition, as are other psychiatric disorders. The clinical presentation of depression and the response to the medications is highly variable and individual. Based on the current case, polypharmacy targeting neuronal deregulation was needed to fully resolve the symptoms of both aggression and depression.

In the presented case, the functional imaging (SPECT) studies showed left hemispheric brain abnormalities induced by uncontrolled seizures, which presumably led to decreased blood perfusion in that region. Some studies have correlated other injuries to the left hemisphere, e.g., stroke and TBI, with the presence of depression. As in those cases, effective treatment of this patient’s depressive disorder should target the underlying cause of the brain abnormalities and not solely the subjective complaints of depression. In this case, we attribute the successful therapeutic outcome to a synergistic effect of the medications. The patient was treated simultaneously with: gabapentin, topiramate and phenobarbital. We successfully managed the aggressive behavior with gabapentin and topiramate; however, the depression was eliminated only with phenobarbital. Multiple antiseizure medications were used to target more than one mechanism of antiepileptic action, so
we could achieve a more effective stabilization and normalization of neuronal activity.16-18

In the present case, the functional imaging studies showed a convergence of findings across the three modalities, MRI, SPECT and QEEG. These findings point to the left hemisphere as the primary focus of the abnormal findings. We used two different databases (QEEG and SPECT) to provide us with an objective evaluation of this case. These databases demonstrated converging findings and identified existing aberrant activity undetected by standard techniques. These findings motivated the clinician to pursue further pharmacological options.

The clinical presentations of psychiatric patients may be well characterized by behavioral features; however, underlying brain pathophysiology may differ widely among individuals. Therefore, we must individualize the therapeutic hypothesis and treatment. This case report illustrates how an objective, comprehensive and systematic diagnostic approach may increase the treatment efficacy and potentially decrease the percentage of misdiagnosed conditions. When applied routinely, this strategy will minimize treatment false starts and failures, may reduce costs, and also, potentially decrease the severity and the duration of symptoms.

ACKNOWLEDGMENT

This case was one of many clinical cases presented at the symposium entitled “Using neuropsychological, qEEG and SPECT data to direct pharmacological and neurosurgical treatment in refractory psychiatric disorders,” International Neuropsychological Society. Zurich, Switzerland, 2006.

The financial support came from the VA Research Service Merit Grant given to Dr. Lukasz M. Konopka.

REFERENCES