

## Case report Ενδιαφέρουσα περίπτωση

### **Pharmacoresistant partial-onset epilepsy misdiagnosed as panic disorder: A case report**

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**T**he clinical differentiation between simple partial epileptic seizures of temporal lobe origin and panic attacks is often difficult on clinical grounds alone, because both conditions are characterized by common symptomatology which includes the feeling of fear, autonomic system dysfunction, disorientation and alternation of the level of consciousness when these conditions evolve clinically. The symptoms stem from common pathophysiologic and anatomic substrates of these two conditions, localized in the limbic system, especially the amygdala. We present the case of a young woman who had a febrile seizure in childhood and subsequent episodes of fear accompanied by tremor and possible alteration of consciousness followed by headache. These spells were diagnosed as panic attacks during her teenage years and she was given Clobazam in order to suppress them. The patient responded well for several years without attacks but her symptoms reappeared following discontinuation of her medication in order to conceive. At that time a detailed history was taken from her spouse and further clinical evaluation raised the suspicion of seizures especially due to the fact that her spells were characterized by alteration of consciousness; she was therefore referred for additional investigations which included admission to a monitoring unit for epilepsy. Long-term video-EEG recording revealed the presence of simple partial seizures with secondary generalization confirming the clinical impression. She was subsequently treated with antiepileptic medications; however the patient's condition worsened to the point where she became pharmacoresistant having failed several antiepileptic drug trials in monotherapy or combination. An MRI scan of the brain revealed the presence of right-sided mesial temporal sclerosis, a known consequence of febrile seizures. Her seizures were nocturnal tonic-clonic and gradually worsened to the point of occurring during most nights. She was therefore referred for a presurgical evaluation which confirmed that the epileptic focus was associated with the area of mesial temporal sclerosis. The epileptic focus was successfully removed from the right anterior temporal lobe and since then she remained free of seizures whereas, in addition, the presumed symptoms of panic

attacks also resolved. This case indicates the occasional difficulty in diagnosing simple partial seizures and how it may be confused with psychiatric conditions. Therefore, the treating physician, especially the psychiatrist, should remain vigilant when treating cases of panic attacks, especially when they present with either atypical symptomatology, such as the case described, or when they do not respond to appropriately chosen treatment; such cases may warrant referral for further investigation.

**Key words:** Epilepsy, panic attacks, video-EEG, pharmacoresistant.

## Introduction

Partial seizures may present with psychiatric symptomatology, often delaying a correct diagnosis and appropriate therapy by several years.<sup>1</sup> On the other hand, the distinction between simple partial seizures and anxiety disorders, especially panic attacks, may be difficult to achieve on clinical grounds alone.<sup>2</sup>

We present the case of a 33 year old right-handed woman who was diagnosed with panic disorder and was so treated for several years prior to establishing that she had partial-onset epilepsy.

## Case report

In elementary school she had paroxysmal episodes of fear associated with shivering and flushing sensations lasting 2–3 minutes. There was questionable alteration of consciousness. Initial frequency of the episodes was every several months. These events occurred throughout secondary school and were associated with a post-event headache. At age 19 she had an episode of depression treated successfully with Clomipramine and Clobazam. Since the age of 22 she remained on Clobazam monotherapy for the presumed diagnosis of panic attacks, as described above. Attempts to withdraw Clobazam, in order to conceive, resulted in re-emergence of her symptoms. A brief trial of Lamotrigine for its mood elevating effects was ineffective. Detailed description of the patient's events, by her spouse, revealed the presence of orofacial automatisms and decreased responsiveness which the patient was unaware of.

Her past medical history was remarkable for one episode of febrile convulsions at the age of 2 years.

Upon presentation, she was on Clobazam 10 mg bid and denied drug allergies. Family history was significant for a seizure in the patient's paternal grandfather during childhood. Also, a cousin had febrile convulsions. The patient was a civic employee and denied alcohol or tobacco abuse. Physical and neurological examinations were normal except for mild left hand atrophy. Routine electroencephalograms (EEG's) were normal. Brain magnetic resonance imaging (MRI) scan was reported normal.

The patient's family history, the brief duration of her spells, the episode of a febrile seizure, the suggestion of alteration of consciousness, and the suppression of the events by Clobazam, raised the suspicion for simple partial seizures and she was admitted for long-term video-EEG monitoring. During hyperventilation, she reported an event about to occur and, thereafter, she engaged in lip smacking, and became unresponsive for about 3 minutes. Concomitant EEG revealed diffuse slowing with persistent faster frequency activity and sharply contoured components over the right frontotemporal derivations. This activity was of higher amplitude over the right sphenoidal electrode. Interictally rare epileptiform spikes were seen over the right sphenoidal electrode which recorded from the right medial temporal lobe area.

Reinterpretation of her MRI scan revealed subtle right hippocampal asymmetry consistent with mesial temporal sclerosis.

She was subsequently treated with antiepileptic (AED) medications which included Levetiracetam, Lamotrigine, Carbamazepine and Clobazam in various combinations and in monotherapy. Unfortunately she did not respond to treatment and her events became progressively more frequent and intense to the point where she would have nocturnal generalised tonic-clonic seizures.

Readmission to the monitoring unit recorded two seizures consisting of vocalisation followed by oral

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automatisms, tonic posturing and head deviation to the left, progressing to a generalised tonic-clonic seizure. EEG was again associated with a build-up of epileptiform spikes over the right sphenoidal electrode, followed by gradual involvement of all derivations, predominantly the right frontotemporal area.

As the patient became pharmaco-resistant, the possibility of a surgical resection was discussed and she underwent further investigations which included neuropsychological assessment revealing a significant difference between her verbal and performance intelligence at the  $p < 0.05$  level. Short and long term memory was unimpaired. A Wada test revealed unilateral localization of memory and language functions over the left hemisphere. Repeat MRI scan with improved resolution revealed unequivocal right mesial temporal sclerosis.

At the age of 29 years, she underwent a right anterior hippocampectomy under intraoperative monitoring and resolution of the epileptiform activity on the EEG during surgery. She remained seizure-free thereafter on Lamotrigine monotherapy. Her presumed psychiatric symptoms resolved.

## Discussion

This case illustrates the difficulty clinicians often face in distinguishing panic attacks from simple partial seizures.<sup>3</sup> Our patient probably began having simple partial seizures in elementary school and was treated subsequently for presumed depression and panic attacks; the correct diagnosis of partial-onset epilepsy with secondary generalisation was not confirmed until she was 24 years old, about fifteen years after the onset of epilepsy. Such delay has been reported elsewhere as well.<sup>2,4-6</sup>

The case also illustrates the value of a detailed history and physical examination in cases where the presumptive diagnosis fails to respond to appropriately chosen therapies. Suggestive features in our case included the presence of febrile convulsions in childhood, and in family members, a known risk factor for epilepsy.<sup>7</sup> Moreover, subtle asymmetries on physical examination and information provided by the spouse raised the suspicion of epilepsy which led to a re-interpretation of the MRI scan and admission for video-EEG monitoring.

Temporal lobe epilepsy and panic attacks share clinical and probable pathophysiological mechanisms<sup>8</sup> including fear sensation, tachycardia, blood pressure fluctuations and diaphoresis, depersonalization and derealisation, symptoms which may occur both ictally as well as interictally.<sup>5</sup> Anatomically the shared symptomatology stems from the amygdala where limbic symptomatology is expressed and, in addition, electrical stimulation of the area, resembling focal epileptic discharges, commonly elicits panic-like symptoms.<sup>1,4,8-10</sup> Feeling detachment from the environment, and *déjà vu* phenomena, commonly occur among both groups of patients.<sup>9,11</sup>

The diagnosis of both seizures and panic disorder is often a clinical one based on the constellation of symptoms.<sup>12,13</sup> When a patient presents with atypical symptomatology for either disorder, and fails to respond to adequate treatment, a consideration of an alternative diagnosis is in order.

The reverse situation could also be true as up to 30% of patients considered to have pharmaco-resistant epilepsy turn out to have psychogenic seizures upon further investigations. To complicate matters further, there are patients who exhibit both epileptic as well as non-epileptic seizures.<sup>14</sup> It is therefore critical to consider alternative diagnoses when history and response to treatment do not corroborate.

A normal EEG does not exclude the diagnosis of epilepsy<sup>15</sup> and the best method to assess a patient accurately is by long-term video-EEG monitoring which may clarify the differential diagnosis.<sup>6</sup> Moreover, epileptic seizures may be misdiagnosed if they manifest with psychiatric symptoms,<sup>16</sup> or when seizures occur in patients with no psychiatric illness. In a study of six patients with epilepsy that presented with prominent psychiatric symptoms, and of which only two had pre-existing psychiatric illnesses, three were initially diagnosed with panic attacks, two with psychosis and one with schizophrenia. Of these, five patients had temporal lobe epilepsy, whereas a sixth patient had absence status epilepticus.<sup>16</sup> The value of imaging, especially MRI, is also demonstrated in the above study; patient imaging revealed a dysembryoblastic neuroepithelial tumor in one patient, a cavernous hemangioma in another, post-traumatic changes and bilateral mesial temporal sclerosis in

another, and was normal in two patients with temporal lobe epilepsy. Our case had mesial temporal sclerosis revealed by MRI scanning.

Video-EEG telemetry is therefore instrumental in establishing the diagnosis in difficult cases. This was demonstrated recently in a case of traumatic epidural hematoma following which episodes characterized by anxiety, fear, whole body tingling and associated autonomic symptoms lasting up to two minutes appeared. Consciousness and speech during the spells were preserved prompting the diagnosis of panic attacks.<sup>6</sup> An initial EEG was normal and, even though MRI scan of the brain showed focal encephalomalacia, she was followed for a subsequent period of 8 years without a definite diagnosis until video-EEG was performed and a right temporal epileptic discharge was captured.

Most cases of epilepsy will respond to appropriately chosen AED medication,<sup>17</sup> even though, as in our case, some patients may prove intractable to treatment and require a surgical intervention.<sup>18</sup> The same is true regarding cases with panic attacks. It is therefore imperative for the treating physician, especially the psychiatrist who will most often follow patients with panic attacks and other psychopathology, to remain vigilant regarding the differential diagnosis in cases where the history, clinical description, or response to therapy are atypical. The issue assumes added importance in the case of epilepsy because these patients run the risk of progressing to convulsive seizures and have increased risk for additional morbidity and mortality including sudden unexpected death.<sup>19</sup> On the other hand, prompt recognition and treatment of a seizure disorder will diminish adverse outcomes and enhance quality of life.<sup>20</sup>

## Εστιακές φαρμακοανθεκτικές κρίσεις επιληψίας διαγνωσθείσες ως κρίσεις πανικού: Περίπτωση ασθενούς

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Ο κλινικός διαχωρισμός των κρίσεων πανικού από τις απλές εστιακές κρίσεις επιληψίας καθίσταται συχνά δύσκολος καθόσον και οι δύο παθήσεις χαρακτηρίζονται από κοινή συμπτωματολογία η οποία περιλαμβάνει την αίσθηση φόβου, διαταραχές του αυτόνομου νευρικού συστήματος, αποπροσανατολισμό και αλλοίωση του επίπεδου συνείδησης, εφόσον και οι δύο παθήσεις εξελιχθούν κλινικά. Η συμπτωματολογία πηγάζει από κοινό παθοφυσιολογικό και ανατομικό υπόστρωμα για τις δύο παθήσεις, το οποίο εντοπίζεται στο δρεπανοειδές σύστημα, κυρίως στην αμυγδαλή. Παρουσιάζεται περιστατικό γυναίκας η οποία είχε επεισόδιο πυρετικών σπασμών στην παιδική ηλικία και μετέπειτα ανέφερε επεισόδια φόβου συνοδευόμενου από τρόμο και πιθανή αλλοίωση της συνείδησης, τα οποία ακολουθούσε κεφαλαλγία. Τα επεισόδια αυτά διεγνώσθησαν ως κρίσεις πανικού κατά την εφηβική περίοδο και της χορηγήθηκε φαρμακευτική αγωγή με κλοβαζάμη. Η ασθενής απάντησε με πλήρη έλεγχο χωρίς περαιτέρω κρίσεις αλλά τα επεισόδια επανεμφάνιστηκαν μετά τη διακοπή της αγωγής με σκοπό να εγκυμονήσει. Κατά την περίοδο αυτή διενεργήθηκε επαναξιολόγηση της κλινικής εικόνας και του ιστορικού κατά την οποία ο σύζυγός της ανέφερε ότι οι κρίσεις χαρακτηρίζονταν από σαφή αλλοίωση της συνείδησης εγείροντας την υποψία επιληπτικών επεισοδίων. Ως εκ τούτου παραπέμφθηκε για πρόσθετη διερεύνηση η οποία περιέλαβε εισαγωγή σε μονάδα καταγραφής κρίσεων. Η παρατεταμένη οπτικο-ηλεκτροεγκεφαλογραφική αξιολόγηση ανέδειξε την παρουσία απλών εστιακών κρίσεων

επιληψίας με δευτεροπαθή γενίκευση επιβεβαιώνοντας την κλινική εντύπωση, και χορηγήθηκαν αντιεπιληπτικά φάρμακα. Παρά τη θεραπεία η επιληψία επιδεινώθηκε και κατέστη φαρμακοανθεκτική, και η ασθενής δεν απαντούσε στα αντιεπιληπτικά φάρμακα που χορηγήθηκαν σε μονοθεραπεία και σε συνδυασμό. Διενεργήθηκε μαγνητική τομογραφία του εγκεφάλου η οποία ανέδειξε την παρουσία μέσης κροταφικής σκλήρυνσης στον δεξιό λοβό, η οποία αποτελεί αναγνωρισμένη επιπλοκή των πυρετικών σπασμών. Οι επιληπτικές κρίσεις εξελίχθηκαν σταδιακά σε τονικοκλονικές και εμφανίζονταν σχεδόν κάθε βράδυ με αποτέλεσμα να προχωρήσει σε περαιτέρω προεγχειρητικό έλεγχο ο οποίος επιβεβαίωσε ότι η επιληπτική εστία εντοπιζόταν στην περιοχή της μέσης κροταφικής σκλήρυνσης. Διενεργήθηκε επομένως αφαίρεση της αναγνωρισθείσας εστίας από τον πρόσθιο κροταφικό λοβό και έκτοτε η ασθενής παρέμεινε ελεύθερη κρίσεων, τα δε θεωρούμενα συμπτώματα πανικού εξέλειπαν. Το περιστατικό αναδεικνύει τη δυσκολία που ενίοτε προκύπτει στη διάγνωση της απλής εστιακής επιληψίας, η οποία χαρακτηρίζει την ασθενή, και η οποία χρειάστηκε εξειδικευμένη αξιολόγηση για τελική διάγνωση και θεραπεία, ενώ μπορεί αρχικά να εκληφθεί σαν ψυχιατρική νόσος. Ο θεράπων ιατρός, κυρίως ο ψυχίατρος ο οποίος πρωτίστως χειρίζεται τα περιστατικά αυτά, δέον όπως ευρίσκεται σε εγρήγορση σε περιπτώσεις υποτιθέμενων κρίσεων πανικού που είτε παρουσιάζονται με άτυπη συμπτωματολογία, όπως η περίπτωση που περιγράφεται είτε δεν απαντούν στην ενδεικνυόμενη θεραπεία. Τα περιστατικά αυτά χρήζουν περαιτέρω αξιολόγησης.

**Λέξεις ευρετηρίου:** Επιληψία, κρίσεις πανικού, βίντεο-ΗΕΓ, φαρμακοανθεκτική επιληψία.

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