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Evaluation of the "non-epileptic" patient in a tertiary center epilepsy clinic

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ABSTRACT

Purpose: The epilepsy clinic at the Montreal Neurological Institute receives a high volume of referrals. Despite most patients assessed in the clinic eventually being diagnosed with epilepsy, other disorders causing alteration of consciousness or paroxystic symptoms that could be misdiagnosed as seizures are seen frequently. The incidence and clinical characteristics of such patients have not yet been determined. We aimed to determine the proportion and clinical characteristics of patients referred to our epilepsy clinic who had a final diagnosis other than epilepsy.

Methods: We performed a retrospective chart analysis of consecutive patient referrals to the epilepsy clinic from January 2013 to January 2015, inclusively.

Results: Four hundred four patient referrals were evaluated, 106 (or 26%) had a final diagnosis other than epilepsy. Referrals came primarily from general practitioners and nonneurology specialists. Although most patients had a normal routine electroencephalography (EEG) prior to the clinic visit, sleep-deprived EEG and cardiac investigations were rarely performed. Patients received a final diagnosis other than epilepsy after 1 to 2 visits in 92% of cases and with minimal paraclinical investigations. Prolonged video-EEG recording was required in 27% of patients. The most common diagnoses were syncope (33%), psychiatric symptoms (20%), followed by migraine (10%), and psychogenic nonepileptic seizures (9%).

Conclusions: A significant proportion of patients seen in our tertiary care epilepsy clinic is in fact, not patients with epilepsy. Enhanced knowledge of these differential diagnosis and important anamnesis components to rule out seizures will help improve guidelines for referral to Epilepsy clinic and cost-effectively optimize the use of paraclinical investigations.

1. Introduction

Transient alterations in consciousness and paroxysmal neurological symptoms pose a diagnostic challenge to many physicians. Patients presenting with such symptoms are often misdiagnosed with seizures and referred to epilepsy centers. Moreover, previous studies have shown that 20–30% of patients with treatment-refractory seizures in epilepsy centers were, in fact, misdiagnosed [1]. In England, 92,000 patients were misdiagnosed with epilepsy in 2002, and another study found that 74,000 people were being treated unnecessarily with antiepileptic medication, [2,3]. In the United Kingdom, studies estimate that costs of epilepsy misdiagnosis could reach up to 138 million British pounds [3]. In the United States, the annual cost of nonepileptic spells misdiagnosed as seizures is estimated between 650 million and 4 billion dollars [4].

An inappropriate diagnosis of epilepsy generates a large financial burden to society and the health care system, but it also results in patients being unnecessarily exposed to treatment with central nervous system active medication and facing driving, leisure, and employment restrictions [2,3]. Meanwhile, failure to identify the diagnosis responsible for the symptoms can pose serious health consequences to these patients.

Numerous reasons for misdiagnosis of epilepsy have been reported in the literature [5]. Failure to recognize epilepsy as a spectrum of heterogeneous disorders and the assumption that missing a diagnosis of epilepsy is associated with greater risks than leaving other differential conditions undiagnosed increases the proportion of wrong diagnosis [5]. Another commonly reported reason is the over interpretation of electroencephalography (EEG) findings [5]. One-third of patients misdiagnosed as having epilepsy had previous EEGs interpreted as having epileptiform abnormalities [1].

A body of literature was published to help guide the diagnosis of patients presenting with transient neurological disturbances or loss of consciousness [6–11]. Whether this literature has improved physicians'

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abilities to recognize what symptoms are consistent with seizures is still unclear. When suspecting seizures, what investigations do clinicians use to either confirm or rule out an epileptic disorder? Furthermore, which factors prompt referral to an epilepsy clinic?

To address these questions, we studied the patient population newly referred to the epilepsy clinic of the Montreal Neurological Institute and Hospital. The first objective of this study was to identify the proportion of patients referred to our tertiary care epilepsy center who ultimately did not have epilepsy. Secondly, we aimed at describing the clinical characteristics of these patients and the investigations performed prior to and after evaluation in the epilepsy clinic. We were specifically interested in determining the length of time required to rule out epilepsy in these patients and which investigations, if any, were required to do so.

2. Methods

We conducted a retrospective review of all consecutive patient referrals to the Epilepsy clinic of the Montreal Neurologic Institute and Hospital from January 2013 to January 2015 inclusively. Patients were identified using the electronic chart and visit scheduling system of the hospital. Patients were included in our study if, after an evaluation in the epilepsy clinic, the epileptologist concluded that the symptoms were caused by a diagnosis other than epilepsy or seizure. This study was approved by the Research Ethics Board of the Montreal Neurological Institute and McGill University. After the initial chart review, patients were contacted by telephone to clarify the chart data, if needed, as well as missing follow up information.

3. Results

A total of 442 patients were referred to the Epilepsy clinic between January 2013 and January 2015. Initially, 38 charts had to be excluded due to lack of information available at the time of review. From 404 charts fully reviewed for this study, 106 (26%) patients had a final diagnosis other than seizure or epilepsy. The characteristics of these patients are detailed in the next sections.

3.1. Demographics and clinical characteristics

Patients were between 10 and 82 years old (see Fig. 1). Forty-two (40%) were men, and 64 (60%) were women. Seventeen patients (16%) had a positive family history of epilepsy, 6 patients (6%) of migraine, and 7 (7%) of syncope. Medical comorbidities were present in 76 (72%) of patients; of these, 25 had vascular risk factors such as hypertension and dyslipidemia. Nine patients (8%) had a history of migraine headaches. Previously identified intracranial lesions, which could be considered epileptogenic, were present in 12 patients (11%): intracranial or subdural hemorrhages (N = 3), space occupying lesions (N = 7), and previous Cerebrovascular accident (CVA) (N = 2). Eleven patients (10%) had a history of traumatic brain injury (TBI). None had previous epilepsy surgery.

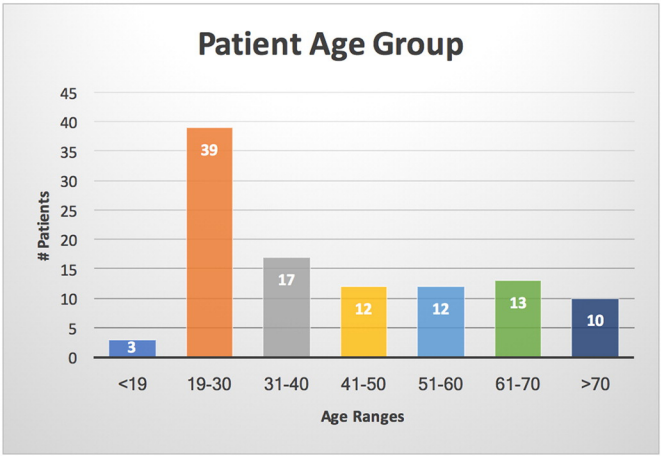

Fig. 1. Distribution of patients by age group (patient count not percentage).

Psychiatric comorbidities (Fig. 2) were present in 38 patients (36%) of patients, and depression was the most common type of illness (N = 13 or 12%).

3.2. Referral information

Most patients were referred by general practitioners (N = 34 or 32%) (see Fig. 3). Other sources of referral originated from consultant neurologists in the institution's emergency room (N = 21 or 19%) and specialists outside the field of neurology (N = 26 or 24%). Multiple reasons were stated for referral to the epilepsy clinic (detailed in Table 1). Common symptoms prompting referral included loss of consciousness (N = 26 or 25%) and transient neurological symptoms (N = 55 or 52%), which were suspected to be seizures by the referring physician (see Table 2 for details).

Patients waited on average 83 days for an evaluation in the clinic, with a time interval ranging from 4 to 393 days. The delay between first symptom and evaluation in the clinic was variable (range: 70 days to 45 years). Out of 106 patients, 46 (43%) patients manifested symptoms that began during the year preceding the evaluation in the epilepsy clinic. We suspected that the patients with longstanding symptoms had previous investigations; however, we could not find evidence of this in their chart.

3.3. Investigations prior to clinic visit

Routine EEG during wakefulness had been performed prior to referral to the epilepsy clinic in 64 (60%) patients. These EEGs were recorded on average 20 days after the event (range: 1–114 days) and were normal in 43 (72%) patients. Nonspecific slowing of background activity was reported in 9 (15%). Sleep EEG with sleep deprivation was performed in 16 (15%) of patients, and 12 out of 16 (75%) studies were reported as normal. Epileptiform abnormalities were reported in 5 patients (8%) on either routine or sleep EEG. Six patients (5%) had undergone previous prolonged video-EEG recordings. These recordings were normal in 4 patients (67%). More specifically, no epileptiform activity was associated with clinical spells, thus leading to a diagnosis of PNES in 2 of these patients.

Magnetic resonance imaging (MRI) of the brain was performed in 37 patients (35%), and of those, 19 (51%) were normal. Imaging abnormalities included malformation of cortical development (periventricular heterotopia and focal cortical dysplasia, N = 2), previous CVAs (N = 2), intracranial space occupying lesion (N = 4), and demyelinating lesions (N = 2), postsurgical changes (N = 2) and asymmetry in the insular region (N = 1). Results of the MRI were not available in 5 patients.

Cardiac investigations were performed in 16 patients (36%), 10 (62%) of which were referred for loss of consciousness. The type of investigation varied among patients, however, the most common test of cardiac function performed was a Holter monitoring (N = 5 or 31%). Cardiac investigations were normal in all these patients.

3.4. Antiepileptic drug therapy prior to clinic visit

Twenty-four patients (22%) were started on antiepileptic therapy prior to evaluation in our clinic. Of these, 18 were treated with monotherapy: Levetiracetam (N = 8), Carbamazepine (N = 4), Valproic Acid (N = 2), Phenytoin (N = 1), Topiramate (N = 1), and Lamotrigine (N = 1). Six patients were on polytherapy, including varied combination of these drugs.