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Case Report

Case report of non-convulsive status epilepticus

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Non-convulsive status epilepticus (NCSE), like the easily recognized convulsive status epilepticus, is a condition requiring prompt treatment. However it is often unrecognized as the cause of mental status impairment or coma. Herein we describe a case in which treatment of a patient was delayed due to the lack of recognition of NCSE. A brief review of NCSE follows, including its presentation, diagnosis, and treatment. Clinicians should be aware of NCSE and include it in the differential diagnosis when treating a patient with unexplained mental status change.

Key words: Non-convulsive status epilepticus, mental status, coma.

INTRODUCTION

Status epilepticus (SE) with generalized convulsions is an easily recognized medical emergency well known to requiring prompt treatment to prevent morbidity and mortality. However, in the absence of obvious convulsions, SE may not be recognized. Non-convulsive status epilepticus (NCSE) is often unrecognized as the cause of mental status change or coma, and thus treatment is delayed (Meierkord and Holtkamp, 2007). NCSE can have various presentations that can be related to mental status (confusion, unresponsiveness, psychosis, coma), motor symptoms (unusual position of limbs or head, myoclonias, twitches), and/or automatisms (verbal, mimicry) (Chang and Shlomo, 2011). Lacking the typical tonic-clonic movements of SE, the diagnosis is often missed. The outcomes of patients experiencing NCSE range from benign to fatal, related to the cause. Therefore it is of critical importance that NCSE be recognized and managed in a timely manner (Meierkord and Holtkamp, 2007). Here we describe such a case in a woman with no previously known seizure history and in whom the diagnosis was delayed over 18 h. Following the case presentation, a brief review of NCSE is provided.

CASE PRESENTATION

KSB is a 43 year old female brought to the emergency department (ED) by ambulance after her mother discovered her at her home unable to respond to simple commands, though awake. There were no signs of trauma. Emergency responders noted she was able to make eye contact when addressed, but was not responsive in any other way. Upon arrival in the ED, her fingerstick glucose was found to be <69 mg/dL, so dextrose was given intravenously, with no effect. A fluid bolus of 1 L of normal saline was also given. Initial vital signs were: T-97; BP-154/93; P-63; RR-14; oxygen saturation 99% on room air. Physical examination was unremarkable save the mental status changes. CT scan of the brain was normal. The patient was admitted to the ICU for monitoring.

The past medical history (provided by her mother) was remarkable for anorexia nervosa, hepatitis C, anxiety, attention deficit disorder of adulthood, gastroesophageal reflux disease, and "hepatic encephalopathy." She had undergone an appendectomy in the past. Current medications included: hydroxyzine, 25 mg four times a day, clonazepam 2 mg four times a day, buproprion SR, 300 mg each morning, 150 mg at night, metoclopramide 10 mg before meals and at bedtime, eszopiclone, 3 mg at bedtime, fluoxetine 20 mg daily, ranitidine 150 mg twice daily, docusate 100 mg twice daily, baclofen 10 mg three times a day as needed, lactulose in uncertain dose, hydrocodone three times a day as needed, and amphetamine and dextroamphetamine in uncertain dose. There was no contributory family history. Social history revealed the patient was unemployed, living with her mother and daughter, with a previous history of multiple drug abuse (no recent history), occasional binge drinking,

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and smoking ½ packs per day for over 20 years.

Her exam in the ICU revealed a nonresponsive female. While awake and alert, eye contact was infrequent and there was no response to verbal cues. Neurologic examination was limited due to unresponsiveness. Pupils were 5 mm and reactive. Ocular vestibular reflexes were intact and deep tendon reflexes were normal. The laboratory examination included a normal complete blood count and urinalysis. There were no detectable salicylates or acetaminophen. Her chemistries were normal other than sodium of 131 mmol/L, a chloride of 96 mmol/L, and a glucose of 226 mg/dL after the glucose infusion. Her ammonia level was 22 umol/L (normal 16 to 60). Her urine drug screen was positive for benzodiazepines, but negative for barbiturates, amphetamines, cannabinoids, cocaine, opiates, and phencyclidine. Her alcohol level was 8 mg/dL.

A neurological consultation documented myoclonic twitching movements of the torso and upper extremities. At that time the diagnosis of non-convulsive status epilepticus was considered. Intravenous lorazepam was given with a rapid improvement in the patient's mental status. After giving her usual dose of clonazepam, the patient's mental status was normal. A few hours later she insisted on leaving the hospital. The patient failed to keep her appointment for an EEG.

DISCUSSION

NCSE is a heterogeneous clinical disorder broadly defined as prolonged seizure activity in the absence of major motor signs. As such, the incidence is difficult to assess. It is estimated at 2 to 8 per 100,000 per year with a marked age association—in geriatric population's estimates of 55 to 86 per 10,000 per year have been reported (Meierkord and Holtkamp, 2007). It may comprise up to 1/3 of all patients with SE (Walker, 2007). Of note is that 58% of NCSE diagnoses occurred in people with no previous history of a seizure disorder (Chang and Shlomo, 2011). In comatose patients, 8% without clinical signs of seizure activity were found with EEG to be in NCSE (Towne et al., 2000).

The clinical presentation of NCSE is typically understated. In a retrospective review of 23 patients with NCSE presenting to the emergency department with altered mental status, only 13 were diagnosed in less than 24 h (Kaplan, 1996). The three major clues to the diagnosis of NCSE include an abrupt onset, fluctuating mental status, and subtle clinical signs such as eye fluttering and various automatisms (involuntary, autonomic movements that occur with an alteration in consciousness, including those that are gestural (for example, picking movement with the fingers) or oroalimentary, for example, lip smacking or stuttering) (Chang and Shlomo, 2011; Towne et al., 2000; Kaplan, 1996; Kaplan and Stagg, 2011). Mental status changes can be on a spectrum from slow mentation and responses to confusion or psychosis to complete unresponsiveness (Wells et al., 1992). While there are no universally agreed upon diagnostic criteria (Meierkord and Holtkamp, 2007), and no pathognomonic EEG changes in NCSE, persistent abnormalities without convulsive activity are the "gold standard" of diagnosis (Chang and Shlomo, 2011). For those patients with an unexplained changes in behavior or mental status, with features highly suggestive of NCSE such as eye movement abnormalities, aphasia with a history of absence seizures, or with risk factors for seizures such as stroke, neoplasia, dementia, history of demyelinating syndromes (that is, multiple sclerosis), or previous neurosurgery, an EEG is clearly indicated (Meierkord and Holtkamp, 2007; Wells et al., 1992; Primavera et al., 1996; Hussain et al., 2003). A therapeutic trial of a benzodiazepine may be diagnostic if an EEG is not available, but may confuse further diagnostic evaluation due to sedation.

NCSE may be subdivided into clinical forms; however, there is no general agreement on the various types. One straightforward categorization suggests three types:

1. Absence—characterized by sudden onset of unresponsiveness with fluctuating lethargy, disorientation, or slow speech, and subtle clinical signs such as automatisms.
2. Complex partial—associated with impaired consciousness, a cessation of verbal and motor activities, and may have an aura prior. (Aphasic NCSE is a sub-type of complex partial NSCE, in which the sole manifestation of SE is aphasia, with reports of SE lasting up to 21 days before a diagnosis was discovered (Wells et al., 1992).
3. Subtle generalized—a natural progression of untreated or insufficiently treated generalized tonic-clonic SE in which motor phenomena are exhausted with motor activity greatly diminished. Patients are usually stuporous/comatose (Chang and Shlomo, 2011).

NCSE can occur *de novo* or develop after a convulsive event. It should be included in the differential diagnosis of any patient with new-onset altered behavior of undetermined cause. It should be especially considered in patients who fail to awaken after a generalized seizure (Chang and Shlomo, 2011). Some of the other diagnoses that can mimic NCSE are listed in Table 1 (Meierkord and Holtkamp, 2007). There are many potential etiologies including metabolic causes, neoplasms, infections, drugs, and toxins. Table 2 lists some reported causes (Maganti et al., 2008).

The clinical consequences of NCSE vary according to the cause and the time to recognition and treatment. In patients with pre-existing epilepsy, the prognosis is better than if the cause is related to an acute neurological or systemic disorder (Meierkord and Holtkamp, 2007).

Table 1. Disorders mimicking non-convulsive status epilepticus.

Metabolic encephalopathy
Migraine aura
Post-traumatic amnesia
Prolonged postictal confusion
Psychiatric disorders
Substance intoxication or withdrawal
Transient global amnesia
Transient ischemic attack

*From Meierkord and Holtkamp (2011).

Table 2. Conditions associated with non-convulsive status epilepticus.

Hypoxic encephalopathy
Stroke
Metabolic disorders
Hypoglycemia
Hyperglycemia
Hypocalcaemia
Hyponatremia
Hepatic encephalopathy
Uremia
Hypertensive encephalopathy
Hashimoto's encephalopathy
Acute porphyria
Alcohol withdrawal
MELAS**
Serotonin syndrome
Neuroleptic malignant syndrome
Malignancy
Primary or metastatic brain tumors
Paraneoplastic syndromes
Infections
Meningitis/encephalitis (bacterial, viral, fungal)
Sepsis
Drugs
Antibiotics (cephalosporins, imipenem, meropenem, isoniazid, gatifloxin, ofloxin)
Psychotropic drugs (olanzapine, clozaril, lithium, tricyclics)
Immunosuppressants (cyclosporine, tacrolimus)
Chemotherapeutic agents (ifosfamide)
Illicit drugs (cocaine, amphetamines, heroin, phencyclidine)
Toxins
Carbon monoxide

*Adapted from Maganti et al. (2008); **Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke.

Animal studies indicate the potential for neuronal damage exists; however available human data indicate most clinical forms of NCSE are benign in terms of morbidity and mortality. Subtle generalized seizures which are more often due to an underlying systemic cause, such as post-hypoxic or septic encephalopathies are associated

with a high mortality rate, (Holtkamp and Meierkord, 2011) especially in elderly, critically ill individuals (>50%) (Meierkord and Holtkamp, 2007).

Treatment of NCSE is directed by the cause. Most absence and complex partial NCSE can be treated with usual doses of intravenous benzodiazepines, reversal of any underlying cause, and possible adjustment of previous anti-epileptic medications. Occasionally resistance to those treatments requires intravenous fosphenytoin or valproic acid. Because outcomes are generally positive in these patients, it is uncommon to use intravenous anesthetics, though they may be used if the NCSE cannot be terminated with the aforementioned medications (Meierkord and Holtkamp, 2007). According to Hopp et al. (2011) response to benzodiazepines is very predictive of a good ultimate outcome, with 100% of those responding surviving as opposed to 55% survival in the non-responders (Hopp et al., 2011).

Subtle generalized NCSE is much more complex to treat since these patients are often critically ill, and involves treatment of the underlying causes. Intravenous administration of benzodiazepines, fosphenytoin, or phenobarbital was successful in less than a quarter of the patients in a randomized trial of 134 patients (Treiman et al., 1998). In such patients, aggressive treatment with intravenous anesthetics (midazolam, propofol, thiopental, or pentobarbital) may be considered.

CONCLUSION

Recognition of NCSE is critical in the care of patients. Without the usual convulsive manifestations of SE, the diagnosis can easily be missed, as was the case for the first 18 h in the aforementioned case. It is important to keep NCSE in the differential diagnosis of patients with acute behavioral or mental status change or coma, so appropriate management can be initiated.

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