A CASE REPORT ON GELASTIC SEIZURES

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ABSTRACT

Gelastic seizure is a rare seizure type, with laughter as the main ictal manifestation. In the presence of a hypothalamic hamartoma, laughing seizures are referred to as gelastic epilepsy which is seen in less than 5% of epilepsies [1]. These seizures begin during infancy with a progressive course and may present with precocious puberty and cognitive decline. In the absence of a hypothalamic hamartoma, gelastic seizures have a later onset and are more seldom encountered. These are seen in less than 1% of all epilepsies and occur as part of a frontal or temporal lobe epilepsy [1]. For gelastic seizures not associated with this lesion, prognosis is good since they are more responsive with AEDs and may be controlled by a single AED.

This is a case report of a 7-year-old male who presented with recurrent attacks of spontaneous, mirthless, and inappropriate laughter associated with hyperkinetic movements. Workup did not show a hypothalamic hamartoma. Interictal EEG showed bilateral frontal lobe discharges in prolonged runs. He was given carbamazepine which provided adequate seizure control. This is the second case reported in this institution from 1992 until present.

INTRODUCTION

Gelastic seizure, coined by Daly and Mulder in 1957, was derived from the Greek word "gelos" which means laughter [1]. Gelastic seizure, classified under focal emotional seizures, is a rare type of seizure that manifests as laughter-like vocalization [2]. According to the PPS ICD registry, there have been 74 out of 4 million reported cases of other epilepsy types including gelastic seizure among others, since 2010. In the Philippines, there were two reported cases both associated with a hypothalamic lesion, one of which was seen in our institution in 1992.

The laughter in gelastic seizures has been described as unnatural, mechanical, mirthless, bubbling, and sometimes mimicking a normal one [3]. Gelastic epilepsy, on the other hand, is often differentiated from gelastic seizure through the presence of an epileptogenic lesion called hypothalamic hamartoma. In the absence of this lesion, seizures are said to arise from frontal and temporal lobes [3]. The onset of seizure is in the first year of life in approximately 85% of cases. Some cases can begin in early to mid-childhood. There is no sex predilection, and most cases are sporadic [2].

CASE REPORT

A 7-year-old right-handed male, who was initially seen at the Telemedicine OPD of our institution, came in with a chief complaint of uncontrollable and inappropriate laughing spells. The history

started six weeks prior to consult, when the patient was observed to exhibit brief episodes of laughter usually occurring three to five times daily, lasting for five to ten seconds. He was reported to be aware during the episodes since he could communicate with his mother while attacks were ongoing. The mother also reported that there were no triggers or events preceding these bouts of laughter and would occur anytime during the day while doing his daily activities. The episodes were initially regarded as attention-seeking behavior since the patient was naturally mischievous as described by the mother.

Five weeks PTC, the sudden outbursts of laughing episodes would now occur more frequently around five to ten times per day and were longer in duration, lasting for ten to twenty seconds. The episodes are now also seen to occur in sleep. The parents were still able to talk to him during these episodes, hence they still attributed it to his naughty behavior, and no consult was done. When asked, the patient verbalized that he cannot control the said outbursts of laughter but is aware that the laughter was happening.

Four weeks prior to consult, the laughing spells were followed by left versive gaze, and head deviation to the left, occurring for ten to twenty times per day with the same duration. The episodes were noted to occur more frequently in wakefulness than in sleep. During this time, the patient started to have complaints of dizziness after each episode but would resolve spontaneously after fifteen to twenty minutes.

Two weeks prior to consult, there was a further increase in the frequency of the episodes, occurring twenty to forty times per day of the same duration. The left versive gaze and head deviation to the left were now accompanied by truncal rotation towards the left, and insuppressible body movements such as rolling on the floor, bipedal kicking, and throwing hand movements. He had preserved consciousness on all the attacks and there was no post laughter confusion or dysphasia. Somatosensory symptoms such as numbness or prickling or tingling sensations were also noted.

The increase in frequency of the episodes and its occurrence even in sleep prompted consult at our institution via telemedicine. During the consult, the patient had approximately 10 brief episodes of sudden outbursts of laughter with hyperkinetic movements which prompted referral to Neurology service for proper evaluation and management. The patient was seen by the Neurology fellow on the same day via video call and was noted to have another two episodes of the same laughing spell and associated body movements. Based on the clinical presentation of the patient, gelastic seizure was considered. The seizure episodes occurred in a stereotypic fashion in the absence of any triggers. He was started on carbamazepine at 10 mg/kg/day and an EEG and cranial MRI were advised. Seizures decreased from 48 to 35 times per day during the one-week medication. Follow-up was done after, and seizures were noted to occur in clusters, with 10 seizure episodes in 1 cluster. Due to this, carbamazepine dose was increased to 15 mg/kg/day with note of

decreasing episodes each day. After another week, the patient attained a seizure-free status.

The patient was born to a 22-year-old, gravida 1 parity 1, with regular pre-natal check-up at a lying-in clinic and regular intake of ferrous sulfate and multivitamins. He had no illness, infection, bleeding, or any feto-maternal complications during the perinatal and post-natal course. He was delivered full term via normal spontaneous delivery at a lying-in clinic assisted by a midwife. The labor lasted for 3 hours without difficulty in delivery. There was no cord coil, meconium-stained amniotic fluid, or premature rupture of membrane. He had good cry and activity at birth, with a birthweight of 3 kilograms. Physical examination was unremarkable with no note of dysmorphism, cyanosis, pallor, jaundice. Newborn screening was normal. Hearing screening was not done. The patient had an unremarkable neonatal course. The developmental history was unremarkable as well. At present, he is a Grade 2 student on modular type of learning and adapted well with this new type of learning modality. However, there was a note of hyperactivity and inattentiveness during his previous school years described as inability to complete tasks and follow instructions.

In the succeeding month, the patient was seen by the Neurology service for follow-up. Seizures were controlled at 15 mg/kg/day. EEG revealed focal epileptiform discharges coming from the right frontal region which appear to evolve and spread to the right frontopolar, frontocentral parietal and the midline frontal and central regions lasting for 32 to 50 seconds in duration seen during sleep. No clinical event was seen. The EEG was consistent with a focal epilepsy coming from the right frontal hemisphere. Carbamazepine assay revealed normal results (22.7 umol/L) (NV16.9-50.8 umol/L). He had good compliance with medications and seizures were controlled. No adverse reactions were noted.

After another month, the patient came in for clearance prior to MRI. He was seen awake and comfortable with stable vital signs. Physical examination was unremarkable. There were no signs of early maturity such as change in body habitus, appearance of axillary, facial, and pubic hair, and deepening of voice. Sexual maturity is appropriate for age (Tanner stage 1). Neurologic examination was unremarkable as well. The patient was kempt at the time of the examination, dressed appropriate for age and sex. He had good eye contact and normoproductive speech. He had euthymic mood and appropriate affect with no disturbance in though content, good insight, judgement, and abstract thinking. The cranial nerves were intact. There were no sensorimotor or cerebellar deficits. Reflexes were 2+ on all extremities and there were no meningeal signs of irritation. The cranial MRI revealed unremarkable results and no hamartomas were seen. Seizures were controlled in the succeeding months, and he was able to do his usual activities.

DISCUSSION

Laughter is a normal physiologic response. It becomes pathologic when it is

inappropriate to the emotional context. In this manner, laughter can be deemed as seizure equivalent and are referred to as gelastic seizures. A seizure is considered as gelastic in the presence of the following criteria: stereotyped recurrence, absence of external precipitants, concomitant manifestations accepted as epileptic, interictal EEG findings, and absence of conditions that can cause pathologic laughter. In our patient, all the mentioned conditions were evident hence a gelastic type of seizure was entertained.

Gelastic seizures are most seen in association with benign malformations arising from the hypothalamus. This lesion is called hypothalamic hamartoma which was first described by Berkovic et al. in 1988, calling it "early-onset gelastic epilepsy, hypothalamic hamartoma, and precocious puberty syndrome." This syndrome frequently causes a severe epileptic encephalopathy resistant to antiepileptic treatment [4]. Seizures originating from hypothalamic hamartoma typically begin in infancy with an average of 10 months at presentation [5]. The clinical course is often progressive and evolves into a more complex seizure disorder. Cognitive regression or behavioral abnormalities such as impulsiveness and aggression may ensue. Precocious puberty is also a significant finding in majority of cases. On imaging studies, T2-weighted MRI scans would show a hypointensity in the presence of a hypothalamic hamartoma, while T1-weighted images would show hyperintensity [5]. EEG findings are associated with an ictal discharge originating from the hamartoma itself. The seizures in the setting of this tumor are intractable by nature but may improve significantly with surgical intervention. In more than 50% of patients, the excision of the lesion has been found to control seizures and improve behavior and cognition [6]. In our patient, the MRI scan did not show hypothalamic hamartoma or any other possible structural lesion. The patient had no pertinent examination that would reveal precocious puberty, and developmental history was also at par with age.

In some cases, such as in our patient, a hypothalamic hamartoma was not seen on workup. Gelastic seizures not associated with this lesion present as part of a frontal or temporal lobe epilepsy. They are said to originate from the anterior lobe, particularly from the basal temporal cortex, the lateral temporal convexity, the cingulate gyrus, and the mesial frontal lobe. [1]. Semiological studies have shown that gelastic seizures arising in the temporal lobe are mirthful in quality whereas those of frontal lobe origin are mirthless [7]. In addition to this, temporal lobe seizures are described to have slower onset and progression. Associated automatisms and post-ictal confusion are also common and are often longer in duration [8]. Frontal lobe seizures, on the other hand, occur in brief episodes with abrupt and explosive onset and rapid progression. The attacks are also associated with hyperkinetic movements, bipedal automatisms, somatosensory symptoms, and loud vocalization [8]. Our patient presented with hyperkinetic movements with interictal EEG findings consistent with a focal epilepsy coming from the right frontal lobe, supporting our diagnosis of a gelastic

seizure associated with frontal lobe epilepsy. A similar case was reported by San Martin et al. in 2002 describing a 35-year-old man who had daily spells of sudden unmotivated laughter attacks which were occasionally complicated by forced head version towards the right. The cranial imaging did not show a structural lesion while EEG results illustrated ictal patterns arising from the left anterior lobe and left frontal lobe implying that there are symptomatogenic areas for ictal laughter present in the frontal and temporal lobes.

The diagnosis of gelastic seizures is made based on the character of the seizure and confirmed by cranial imaging and EEG. Cranial MRI is the imaging of choice and reveals the presence of a lesion on the hypothalamus. Although some epileptogenic lesions in the form of cavernous hemangioma or focal cortical dysplasia have been reported, the exact incidence of the occurrence of these lesions in association with gelastic seizures is not well established [1]. Electroencephalogram (EEG), on the other hand, confirms whether the pathological laughter has an epileptic basis. In the presence of a hypothalamic hamartoma, it is used to evaluate the degree of epileptic progression. However, studies have shown that it has little benefit in distinguishing between patients with and without hypothalamic hamartoma [7].

The management of gelastic seizures, like any other disease, is directed at the underlying condition or syndrome. In confirmed cases of hypothalamic hamartoma, resection usually has good control of seizures. In the absence of this lesion, seizures are commonly benign in course and are typically controlled with one to three anti-epileptic drugs used in focal seizures including Carbamazepine, Lamotrigine, Clobazam, Lacosamide, Levetiracetam, Oxcarbazepine, and Topiramate [12]. There is currently no established report that states the individual efficacy of the mentioned AEDs used in gelastic seizure. In our patient, seizures were controlled using a single AED, namely carbamazepine at 15mg/kg/day.

Thorough investigation using imaging and electrophysiological methods is required to obtain a diagnosis and develop a treatment plan. The main goal of treatment is to liberate the patient from seizures so that he can live a normal social life, and avoid tumor progression, recurrence, and possibly permanent neurological sequelae [9]. In the presence of a hypothalamic hamartoma, prognosis for seizure control and social adaptation is poor unless complete surgical resection is performed. The transcallosal anterior interforniceal technique is currently the most effective surgical approach. Other novel approaches such as endoscopic technique and gamma knife have also been employed with success. Surgical complications are uncommon but may result to third nerve paresis, hemiparesis, appetite stimulation and weight gain, transient hypersomnolence and hyperthermia, and transient endocrine abnormalities such as hypothyroidism and diabetes insipidus. Surgery should be performed as early as possible to minimize long-term cognitive impairment and behavioral disturbances associated with potentially catastrophic condition [11]. According to Zenteno et al.,

in patients who underwent complete resection of hypothalamic hamartoma, 52% to 54% become seizure free and 24% to 35% have more than 90% seizure reduction. On the other hand, for patients without a hypothalamic hamartoma, prognosis is more favorable since seizures follow a benign course and are more responsive with AEDs. Most cases of pure gelastic seizure achieve a seizure free status despite being off from AEDs for an average of 3 to 5 years [13].

SUMMARY

This case presented a 7-year-old male with recurrent attacks of inappropriate and unprovoked laughter with preserved consciousness and no associated autonomic dysfunction. Diagnosis was established with the clinical and EEG findings results typical for gelastic seizure. Cranial MRI failed to demonstrate a lesion denoting that the seizure is part of an anterior lobe epilepsy and not gelastic epilepsy that is associated with a hypothalamic hamartoma. Physical and neurologic examination were unremarkable. Findings of poor prognosis such as intractable seizures, precocious puberty, and cognitive and behavioral impairment were not seen. The patient is currently on carbamazepine at 5.14 mg/kg/day with seizure control for 6 months now.

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