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Case report

Adult-onset seizures in a patient with Down syndrome and portosystemic shunt

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Abstract

Objective: The prevalence of epilepsy in patients with Down syndrome (DS) is 5–13%, which is higher than the prevalence in the general population. Transient hyperammonemia is often observed following seizure, but it typically resolves within a day. Here, we describe the case a 37-year-old woman who had DS and a history of adult-onset epilepsy and was admitted to our hospital with recurrent seizures. After admission, her ammonia levels fluctuated without any apparent cause, and dynamic computed tomography revealed a portosystemic shunt. The findings suggest that her seizures possibly precipitated from hyperammonemia secondary to a portosystemic shunt, and we reviewed the relevant literature. *Methods:* We conducted PubMed, Web of Science, and EMBASE searches without language restrictions for articles published between 1970 and February 2013. *Results:* In addition to the present case, 7 cases were ultimately included in this review. Four patients were newborns, 2 patients were 1 month old, and 1 patient was 3 years old. No adult cases were described until now. *Conclusion:* Adult patients with DS diagnosed with epilepsy are not routinely assessed for portosystemic venous shunts. Measuring ammonia levels in patients with DS the day after admission would help detect portosystemic shunts, even if the patients have been previously diagnosed with epilepsy. *Practice Implications*: If ammonia levels fluctuate without any apparent cause after seizure, dynamic computed tomography should be performed, especially for patients with DS, whether or not they have been previously diagnosed with epilepsy.

Keywords: Down syndrome; Seizure; Epilepsy; Portosystemic shunt; Hyperammonemia

1. Introduction

The prevalence of epilepsy in patients with Down syndrome (DS) is 5–13%, which is higher than that in the general population [1]. A bimodal distribution of seizure onset has been described in DS: the first peak is during early childhood, and the second occurs during middle age [1]. The prevalence of epilepsy in individuals with DS increases with age; it is 46% in subjects over 50 years old [2]. Unusual electroclinical patterns and epileptic syndromes have been described in adult patients with DS; these include focal epilepsies, reflex seizures (auditory stimulus), and myoclonic epilepsy associated with dementia, which is defined as "Late-Onset Myoclonic Epilepsy in DS" [1].

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The prevalence of epilepsy in adults with DS is high [3], but a subset of such patients may actually have symptomatic seizures due to hyperammonemia that mimic epilepsy [4]. Transient hyperammonemia is often observed following epileptic seizure but typically resolves within a day [5]. Possibly, the prevalence of hyperammonemia in patients with DS may be underestimated once a patient is diagnosed with epilepsy. However, because chronic hyperammonemia can cause encephalopathy [6], it is important to identify the underlying cause if ammonia levels remain high for several days after a seizure. Our recent experience in treating an adult patient with DS and recurrent seizures possibly precipitating from hyperammonemia secondary to a portosystemic shunt prompted a literature review and formed the basis of this report.

2. Patient and methods

2.1. Patient

A 37-year-old Japanese woman with DS was admitted due to seizures. She experienced her first seizure at age 30 and was treated with oral valproic acid (VPA 100 mg) at another country hospital. Two months before admission, she exhibited seizure and hematemesis. At that time, blood tests revealed hyperammonemia (223 μg/dl) and low VPA levels (1.6 μg/ml), and upper gastrointestinal endoscope revealed duodenal ulceration. Because the seizure was presumed to be due to hyperammonemia following duodenal ulceration, electroencephalography was not performed. Blood levels of ammonia gradually decreased following parenteral nutrition therapy. At discharge from that hospital, her blood levels of ammonia and VPA were 30 μg/dl and 6.3 μg/ml, respectively.

Upon admission to our hospital, her body temperature was 36.6 °C; heart rate, 88 bpm; blood pressure, 103/81 mmHg; respiratory rate, 22/min; and oxygen saturation, 99%. Her Glasgow Coma Scale score was E1V1M5. She experienced tonic seizures and was administered diazepam followed by phenytoin. The seizures subsequently subsided, and her consciousness level gradually improved. VPA was discontinued.

Physical examination revealed marked oral cavity dryness. Signs of meningeal irritation were absent. Blood tests revealed normocytic anemia (Hb level, 6.8 g/dl), slightly elevated blood urea nitrogen (43.9 mg/dl), hypoalbuminemia (Alb level, 2.9 g/dl), hyperammonemia (361 μg/dl), and low VPA levels (4.4 μg/ml). Arterial blood gas analysis was normal. Head computed tomography (CT), magnetic resonance imaging, and magnetic resonance angiography showed severe cerebral and cerebellar atrophy, which are consistent DS features [3]. Electroencephalography and endoscopic examination of the upper digestive tract revealed no abnormalities.

On day 4, there was no recurrence of convulsions, and the electroencephalogram was normal. However, blood ammonia levels repeatedly fluctuated without any apparent cause. An amino acid fractionation test showed normal levels of citrulline, arginine, and ornithine. However, the Fischer ratio was low (1.02; standard values, 2.43–4.40), and plasma levels of biliary acid were high (35.2 μmol/l; standard values, <10 μmol/l). Abdominal dynamic CT revealed a shunt between the right branch of the portal vein and the inferior vena cava, as well as marked atrophy of the right lobe of the liver (Fig. 1). Recurrent convulsions were determined to occur due to hyperammonemia resulting from the portosystemic shunt. We reduced her protein intake, and ammonia levels gradually decreased. Her family refused surgery, and she was discharged with instructions to eat a protein-restricted diet. Her blood levels of ammonia and VPA at the time of discharge were 67 μg/dl and 37.7 μg/ml, respectively. Six months after admission, the patient remained seizure free.

2.2. Methods

In February 2013, we conducted PubMed, Web of Science, and EMBASE searches without language restrictions for articles published between 1970 and February 2013. We used the search terms “Down syndrome” or “mental retardation” or “cognitive impairment” in combination with the words “seizure,” “epilepsy,” “convulsion,” “portosystemic shunt,” and “hyperammonemia.” Titles and abstracts were examined to determine whether they could be included. Reference lists of included articles were also examined to identify additional papers for inclusion. Three reviewers (RI, KN, and NM) performed independent screenings. All relevant case reports and series were included, and references of retrieved publications were screened for relevant literature. We imposed the following criteria for exclusion in the review: (1) other shunt diagnosis (e.g., arterioportal shunt), (2) incomplete or inconclusive diagnosis, (3) incomplete medical history, or (4) meeting abstracts.

3. Results

Our database search identified 77 relevant studies. Among these, 71 were excluded, and 6 studies of 7 cases were included [6–11]. Clinical findings, including other venous system defects, types of intrahepatic portosystemic venous shunts, and treatments, are summarized in Table 1.

Most patients were newborns or 1-month-old males; however, 1 patient was a female, and another was 3 years old. Two patients died before portosystemic venous shunt treatment [7,8]. Congenital portosystemic shunts were classified as extrahepatic (Abernethy Types