Severe cerebellar atrophy following salicylate poisoning and respiratory insufficiency: A case report

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INTRODUCTION

Over-the-counter (OTC) drugs have sometimes been used for suicide attempt and it was reported that among OTC drugs used in adults the most common was acetaminophen in emergency hospitals in Canada [1]. Other OTC analgesics in their cases included acetylsalicylates, ibuprofen and others, and deaths were observed in case of acetaminophen and acetylsalicylate intoxications [1]. Respiratory insufficiency could occur in acetylsalicylate intoxications by way of central nervous system involvements, metabolic disorders or vomiting-induced suffocation [1]. Severe respiratory insufficiency will cause miscellaneous neurological manifestations because of secondary hypoxic-ischemic encephalopathy (HIE). In these cases the cerebellum is one of the vulnerable sites [2, 3]. However, exclusive severe cerebellar atrophy associated with remarkable cerebellar symptoms after respiratory insufficiency has not been reported probably because patients with HIE usually show extensive brain lesions as a whole.

We experienced a patient who exhibited exclusively marked cerebellar dysfunction and atrophy on magnetic resonance imaging three years after salicylate poisoning and respiratory insufficiency. Cerebellar atrophy was considered to be induced in these unique clinical situations, although its definite pathophysiology remained unknown.

CASE PRESENTATION

The patient was a middle-aged female homemaker who had been doing her housework well. She went shopping, drove her car and took walks regularly every day. No motor or sensory troubles had been observed. At 42 years of age she attempted suicide in the face of unsolvable family problems by taking an overdose of Bufferin®, which she had bought over the counter. A single Bufferin® tablet contains 330 mg acetyl salicylate (aspirin) and 150 mg of diazepam. She had sometimes taken this drug for headaches. This time she crushed the tablets and drank them with water; the total amount was unclear. Before noon she was found by her husband in a state of agonizing abdominal pain with frequent vomiting and was immediately transported to emergency hospital. After arrival she was drowsy and vomited several times; a blood examination showed dehydration. Following intravenous infusions of isotonic fluids, she became alert and her vital signs were normal; she responded correctly to the staff members’ questions and orders. The blood concentration of salicylate was not examined. On the evening of that day, because she looked well, she was transferred to a psychiatric hospital and was admitted due to fears about the possibility of a repeated suicide attempt. She was calm in the psychiatric ward. She was given intravenous infusions of isotonic fluids due to anorexia, along with mirtazapine (15 mg, peroral), olanzapine (2.5 mg, peroral) and brotizolam (0.25 mg, peroral). During the night, she vomited several times, and in the early morning of the next day she was obtunded, with fever (37.6°C) and dyspnea (SpO₂ 90%) and was given 5 L/min of oxygen via nasal cannula, and was
then transferred again to the former emergency hospital in the morning.

In the hospital, she was comatose, showing high fever (>40°C), hypoxemia and decreased blood pressure, indicating a shock state. Therefore, an emergent endotracheal intubation was performed and her respiration was controlled by respirator. X-ray findings showed neither pulmonary edema nor pneumonia. Her high fever persisted for several days in spite of continuous intravenous infusion of antibiotics, and acute rhabdomyolysis of unknown cause also occurred. Accordingly continuous hemodiafiltration was performed for five days, with a infusion of a large amount of intravenous fluid. On the seventh hospital day, extubation was attempted. However, as the patient remained hypoxic and comatose, O2 supply from respirator via an endotracheal tube was necessary up to the 13th hospital day. During this time, she received nasogastric tube feeding without major trouble. After extubation on the 14th hospital day, she required additional non-invasive positive pressure ventilation for a week due to edematous stenosis of the upper respiratory tract, and on the 20th hospital day her normal respiration and consciousness recovered and oral feeding was started. She said later that her memory fully recovered at around the 20th hospital day. Then rehabilitation for walking was initiated.

When she was readmitted to the former psychiatric hospital on the 27th hospital day at the emergency hospital, her mental state was stable, although she showed inarticulate speech and could only walk with the aid of a walker. Her electrocardiography and chest X-ray findings were normal, her serum levels of markers reflecting the liver and kidney functions were normal, and her electrolyte levels were normal. Complete blood cell counts were within normal limits. Forty days after her suicide attempt using Bufferin®, she was transferred to another rehabilitation hospital. According to the inpatient medical record there, she was alert and cooperative without obvious dementia. Her speech was slurred, but comprehensible. She showed staggering gait, requiring a walker in the room. Because her hand movement was clumsy, she ate meals with a spoon, rather than chopsticks. After three months of rehabilitation, she returned home with some improvement of her motor functions and spent her days at home uneventfully with aid from her family members. She walked with walker in her room, and used a wheelchair by herself outside her home.

Three years later, at 45 years of age, she visited the neurology department of our hospital in order to obtain an official physical disability certificate, and underwent a neurological examination. She was alert and her cognitive level, as evaluated by the revised Hasegawa Dementia Scale (HDS-R) [4], was 30 (full score: 30). The HDS-R is a verbal cognitive test that is known to be as useful as the mini-mental state examination (MMSE) [4]. Other tests covering the speech (aphasia), visuospatial and praxic functions were all normal. A moderate degree of dysarthria, definitely scanning and explosive, was observed, suggesting cerebellar dysfunction. Nystagmus was not present. The tendon reflexes of her limbs were normal without positive toe extensor signs. Muscle tonus was normal. She exhibited dysmetric clumsiness in coordination tests of all limbs, though she could drink water with one hand. She could walk only with human aid or a walker, and showed a staggering and wide-based gait with step width of approximately 30 cm. Sensory test results were normal. These findings implied exclusively cerebellar dysfunctions without obvious other nervous system abnormalities.

Brain magnetic resonance imaging (MRI) of the brain on the same day showed remarkable cerebellar atrophy involving vermis and cerebellar cortex, more marked in the vermis, associated with slight bifrontal atrophy on T1-weighted and fluid attenuated inversion recovery (FLAIR) images, without obvious lesions on diffusion-weighted or T2* images. Scattered small high-intensity lesions in the white matter and basal ganglia regions of the cerebral hemispheres were seen on FLAIR images (Fig. 1). Voxel-based morphometry based on T1-weighted imaging, introduced by Matsuda et al. [5], was performed to show the sites of focal brain atrophy (Fig. 2). This software program for the analysis of MRI, which exhibits sites and degrees of focal brain atrophy based on comparison with averaged brain images of healthy controls [5]. In this map, the sites of the brain atrophy were indicated with blue (mild), green, and yellow to red (severe) according to the severity of atrophy. This patient exhibited atrophy of the cerebellum, which was most marked on vermis (red), followed by the cerebellar cortex (yellow to blue). Outside the cerebellum, scattered small focal atrophy was also shown in the frontotemporal lobes and basal ganglion regions (Fig. 2).
The functional neurologic deficits of this patient have remained unchanged during a year of follow-up, and she has been spending her daily life at home.

DISCUSSION

This patient had not suffered from the brain disorders, including spinocerebellar degeneration, before she attempted suicide with Bufferin®. First, it must be discussed whether a large amount of aspirin could introduce respiratory insufficiency, followed by cerebellar destruction. It has been reported that an acute dose of salicylate that exceeds 150 mg/kg or a total of 6.5 g may induce toxicity, including hematemesis, tachyplea, hyperpnea, dyspnea, tinnitus, deafness, lethargy, and seizures [1]. Severe toxicity is expected at doses of 300-500 mg/kg, although the dose-dependent toxicity is not clear [1]. With regard to brain lesions associated with salicylate poisoning, the lesions specific to it have not been documented. Exceptionally, it was reported that damage to the peripheral acoustic nerves and auditory cortex could occur [6]. In another case with previous cerebral infarction, left hemiparesis recurred following chronic salicylate ingestion, without fresh cerebral infarction on MRI [7].

Our patient suffered from frequent vomiting soon after taking an overdose of Bufferin®. She was then transferred to an emergency hospital and because her consciousness recovered without outstanding physical or neurological troubles, she was admitted to a psychiatric hospital for further observation. That night, frequent vomiting recurred and the next morning she presented a shock state and was readmitted to the former emergency hospital. Thereafter, respiratory insufficiency persisted for approximately 20 days, needing endotracheal intubation and an aid of respirator, also associated with impaired consciousness and rhabdomyolysis of unknown cause. At that point it was considered that salicylate toxicity caused frequent vomiting on the first day, followed by severe respiratory insufficiency due to possible suffocation. This trouble probably induced hypoxic-ischemic encephalopathy (HIE), with subsequent extensive cerebellar lesions which were observed in this patient, although salicylate poisoning itself might have played some role in pathogenesis of brain lesions.

The severe cerebellar atrophy on MRI as a sequela of HIE seems to be rare. In the literature, severe HIE in older children and adults was reported to extensively affect the gray matter structures (the basal ganglia, thalami, and cerebral cortex, especially of sensorimotor and visual cortices), the cerebellum and hippocampi [2, 3]. Therefore, sequelae of HIE are usually expressed as severe incapacity in activities of daily living, rather than by outstanding focal clinical manifestations [8]. It has been reported that the cerebellum is more vulnerable to hypoxic-ischemic events in post-natal and older patients than it is in perinatal period, because Purkinje cells become mature in the post-natal period [2, 3]. Regarding neonatal HIE, a report stated that cerebellar vermal atrophy occurred after HIE in up to 46% of patients [9].

However, exclusive extensive cerebellar lesions on MRI have not been described in post-natal and older patients as sequel of HIE [2, 3]. As an exception, a 36-year-old woman showed typical Lance-Adams syndrome associated with right cerebellar infarcts and a concomitant decrease in blood perfusion in the same site three months after cardiac arrest [10].

It must be mentioned that voxel-based morphometry introduced by Matsuda et al. [5] can reveal focal atrophy of the brain. Significant atrophy of hippocampus and entorhinal cortex was demonstrated in 116 patients with Alzheimer’s disease, based on comparison to 40 age-matched healthy controls [5], and this software program is now widely used in the clinical setting in Japan. Subsequently, using this software program, focal brain atrophy has been observed outside of the medial temporal areas. For example, a white matter volume reduction was demonstrated in patients with corticobasal syndrome (CBS) and Richardson’s syndrome, with a significantly greater volume reduction of the white matter in CBS [11]. In Gerstmann-Strassler-Scheinker syndrome with P102L mutation, atrophy of thalamus was shown with this method [12]. In our case, other than severe diffuse atrophy of the cerebellum, only scattered and small lesions were observed in the cerebral white matter and basal ganglia regions.

In conclusion, this was a rare case that showed severe cerebellar atrophy that occurred probably after HIE following a suicide attempt with salicylate, although the role of salicylate poisoning and the unique
distribution of the brain lesions remained unclear.

AUTHOR CONTRIBUTIONS

MM: executed the neurologic study and drafted the manuscript. TT: conducted the study as a primary care physician. TN: conducted the study as a psychiatrist.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest in association with the present study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

Written informed consent was obtained from the patient’s family to publish this case report and any accompanying images.

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REFERENCES


FIGURE REGENDS

Fig. 1
Magnetic resonance imaging (MRI) of the brain at 45 years of age, three years after salicylate poisoning. (A) Sagittal T1-weighted image of cerebellum and brain stem, showing diffuse cerebellar atrophy, including in the vermis and cerebellar lobes. (B) Coronal FLAIR image showing remarkable cerebellar cortical atrophy. (C) Axial FLAIR image of the brain, showing marked dilatation of the fourth ventricle. (D) Axial FLAIR image showing small high intensity lesions in the white matter. (E) Axial FLAIR image showing mild bifrontal atrophy. (F) Coronal FLAIR image showing small high intensity lesions in the white matter and basal ganglia regions.

Fig. 2
Voxel-based morphometry of the axial planes based on T1-weighted imaging [5]. The foci of brain atrophy are shown from blue (mild) to red (severe) in order according to the degree of atrophy. The vermis is the main site of atrophy (red), followed by the cerebellar lobes (yellow to blue). Other than the cerebellum, disseminated small atrophic lesions (blue) were observed in the white matter and basal ganglia regions of the cerebral hemispheres.

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