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A Case of Salicylate Toxicity Presenting with Acute Focal Neurologic Deficit in a 61-Year-Old Woman with a History of Stroke

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 61-year-old
Final Diagnosis: Salicylate toxicity
Symptoms: Hemiparesis
Medication: Aspirin/Acetylsalicylic Acid
Clinical Procedure: —
Specialty: Toxicology

Objective: Unknown ethiology

Background: Over-the-counter medications that contain aspirin are widely used, and patients generally regard them as safe. However, the side effects of salicylate toxicity can be severe, and delay in the diagnosis may increase the risk of mortality. Neurologic symptoms are a common presenting feature of salicylate toxicity in the elderly, and their recognition may allow earlier diagnosis. This report is of a case of a 61-year-old woman who presented with acute focal neurologic deficit associated with salicylate toxicity and who had a previous history of stroke.

Case Report: A 61-year-old woman presented to the Emergency Department after awakening with left-sided weakness. She had a history of ischemic stroke with an associated seizure disorder. The patient denied recent seizure, and brain magnetic resonance imaging (MRI) showed no evidence of an acute stroke. Following her arrival, she became acutely confused and complained of tinnitus, shortness of breath, and blurred vision. On direct questioning, she gave a history of excessive use of salicylate for the previous two to three weeks. Her initial serum salicylate level was significantly increased at 78.1 mg/dl (upper therapeutic limit, 19.9 mg/dl). She recovered completely following treatment with oral activated charcoal, intravenous sodium bicarbonate, and potassium replacement.

Conclusions: This case demonstrates that physicians should consider salicylate toxicity as a possible cause of exacerbation of neurological deficit in elderly patients.

MeSH Keywords: Acid-Base Imbalance • Neurotoxicity Syndromes • Salicylates

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Background

Over-the-counter medications that contain aspirin are widely used for the treatment of conditions such as osteoarthritis and headaches and as prophylaxis to prevent thromboembolism [1]. However, patients often forget to report the use of these medications or omit them form the medication history due to presumed harmlessness [1]. Despite these beliefs, salicylates are not without risk. Salicylate overdose can cause metabolic acidosis, respiratory alkalosis, pulmonary edema, platelet dysfunction, hypokalemia, and acute kidney injury [2–4]. Mortality from salicylate toxicity remains a significant clinical concern [5]. Also, the use of non-prescribed salicylates that are obtained over-the-counter and without the knowledge of healthcare professionals may be more common, and the risks of salicylate toxicity may be even greater in elderly patients [6].

This report is of a case of a 61-year-old woman who presented with acute focal neurologic deficit associated with salicylate toxicity and who had a previous history of stroke.

Case Report

A 61-year-old woman awoke in the morning with left-sided hemiparesis but was able to contact emergency medical services. On arrival by ambulance at the Emergency Department, the patient reported that her left upper and lower extremities were equally affected. She felt that her strength had been normal when she went to bed at about 10:00 p.m. the previous evening. She denied numbness or tingling in her extremities, headache, changes in vision, or difficulty speaking. On further questioning, she described that she had been unwell for the previous two weeks, with symptoms that included persistent chest pressure that was not associated with exertion and did not change with deep inspiration. She stated that aspirin relieved the discomfort. Until the onset of her left-sided weakness, her only other symptoms were anxiety and generalized malaise.

The patient had a past medical history of essential hypertension and generalized anxiety disorder. She also had a previous history of ischemic stroke due to occlusion of the right middle cerebral artery (MCA). Following her stroke, she developed a seizure disorder, but her only residual neurologic deficits were mild left upper and lower extremity dystonia. Her seizure disorder was well controlled on diazepam and phenobarbital with out a seizure in many years. However, she had not taken either of her seizure medications for one week prior to this Emergency Department visit due to her acute illness. She was not taking prescribed antiplatelet or anticoagulant medications.

Table 1. Initial laboratory results of a 61-year-old woman with a history of stroke and acute neurologic deficit due to salicylate toxicity.

	Value	Normal range
Basic metabolic panel		
Sodium (mEq/L)	138	136–145
Potassium (mEq/L)	2.7	3.5–5.1
Chloride (mEq/L)	106	98–107
Bicarbonate (mEq/L)	12	22–32
BUN (mg/dl)	8	6–20
Creatinine (mg/dl)	0.71	0.44–1.03
Calcium (mg/dl)	8.5	8.6–10.4
Glucose (mg/dl)	115	70–139

While in the Emergency Department, the patient began to show inappropriate behaviors that included tangential speech and fits of laughter. She also described a situation from approximately one week earlier in which she thought that masked angels had saved her after she lost consciousness in public. The patient perseverated on this story and returned to it regardless of the examiner's line of questioning. Further history taking was challenging, but the patient was able to describe the onset of blurred vision, shortness of breath, and tinnitus.

The initial neurologic examination was notable for slow movement and hyperreflexia in the left upper and lower extremities without objective weakness or sensory deficits. Cranial nerve examination showed bilateral horizontal nystagmus. Her vital signs included a temperature of 36.5°C, blood pressure of 102/83, heart rate of 92 bpm, respiratory rate of 20/min, oxygenated hemoglobin (SpO_2) of 97%. The lungs were clear on auscultation, but a Kussmaul breathing pattern was noted. Cardiac examination revealed a regular heart rate and rhythm without murmurs. Palpation of the chest wall did not reproduce the discomfort that the patient had described when she gave the history of her recent symptoms.

The initial laboratory results are shown in Table 1. Her electrocardiogram (ECG) showed no abnormalities, and her chest X-ray was normal. The concern for recurrent stroke or transient ischemic attack (TIA) prompted brain magnetic resonance imaging (MRI), which showed changes from her previous stroke, without evidence of acute cerebral infarction (Figure 1). The patient's calculated serum anion gap was increased at 20 (anion gap=sodium–chloride–bicarbonate). The wide anion gap metabolic acidosis was further evaluated with urinalysis and measurement of serum osmolality, lactic acid, and venous blood gas. Urinalysis did not show significantly increased levels of ketones. Table 2 shows the results of her further laboratory tests.

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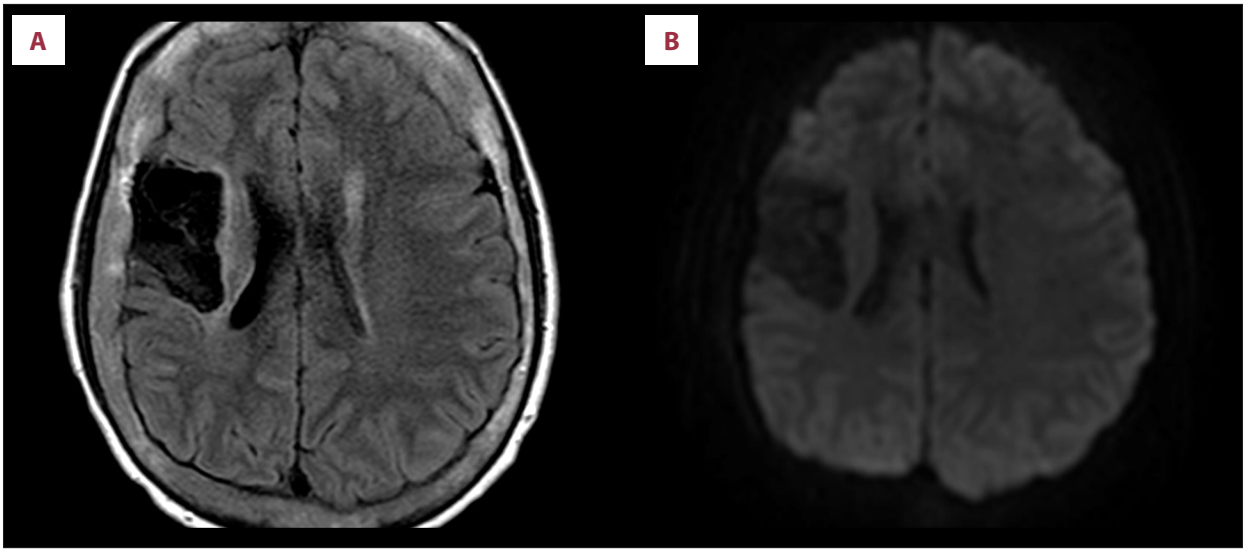

Figure 1. Brain magnetic resonance imaging (MRI) of a 61-year-old woman with a history of stroke and acute neurologic deficit due to salicylate toxicity. Axial T2 fluid-attenuated inversion recovery (FLAIR) MRI (**A**) and diffusion-weighted MRI (**B**) demonstrate a chronic cerebral infarct in the territory of the right middle cerebral artery. The findings show liquefactive volume loss and encephalomalacia on FLAIR imaging without hyperintensity on diffusion-weighted imaging. There is no evidence of cerebral edema.

Table 2. Further laboratory results of a 61-year-old woman with a history of stroke and acute neurologic deficit due to salicylate toxicity.

	Value	Normal range
Osmolality	295	275–295
Lactic acid	0.9	0.5–2.0
Venous blood gases		
pH	7.46	7.33–7.43
pCO_2 (mmHg)	21	38–50
pO_2 (mmHg)	32	30–50
Bicarbonate (mmol/L)	15	22–30

The finding of alkalosis on blood gas testing was unexpected. Based on blood gas analysis, a diagnosis was made of a mixed acid-base disorder with a wide anion gap metabolic acidosis and respiratory alkalosis. Given the typical acid-base findings, her tinnitus, and Kussmaul breathing pattern, salicylate toxicity was considered as a possible diagnosis. On further questioning, the patient admitted to taking two 325 mg aspirin tablets approximately every 2 hours while awake during the previous three weeks, due to chest discomfort. Her initial serum salicylate level was significantly increased at 78.1 mg/dl (upper therapeutic limit, 19.9 mg/dl).

When the diagnosis of salicylate toxicity was made, the local poison control service and the nephrology service were consulted. Although chronic salicylate ingestion was likely to have been present, some degree of acute toxicity was also suspected, given the evolution of symptoms in the Emergency Department. She was immediately treated with oral activated charcoal, intravenous administration of crystalloid with dextrose, potassium, and sodium bicarbonate. Activated charcoal was given to prevent the absorption of recently ingested salicylate into the systemic circulation. Because the patient was alert and cooperative, this was considered a low-risk intervention [7]. Intravenous dextrose was administered, as utilization of glucose by the central nervous system (CNS) is increased during salicylate toxicity, and serum glucose concentrations may not reflect those in the CNS [8,9]. Damage to the CNS via neuroglycopenia can occur at normal serum glucose concentrations, making dextrose supplementation a standard treatment for salicylate toxicity [8].

The cornerstone of management was intravenous sodium bicarbonate, which was given as a 1,000 ml bolus followed by a continuous infusion. Bicarbonate containing crystalloid has been shown to enhance urinary excretion of salicylate through alkalinization of the urine. Maintaining a urinary pH of 7.5–8.0 increases urinary excretion of salicylates greater than tenfold [8]. Urinary alkalinization is the recommended treatment for patients with severe salicylate toxicity and intact renal function. Hemodialysis was considered but deemed unnecessary in this case. Indications for hemodialysis include severe neurologic manifestations such as coma, hallucinations, or seizures, in conjunction with renal impairment or inability to tolerate bicarbonate infusion [10]. Although this patient showed a focal neurologic deficit, delirium, and possibly hallucinations,

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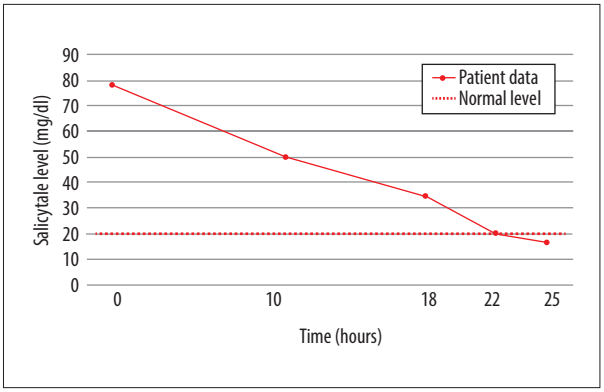

Figure 2. Salicylate levels measured at five points over 25 hours of a 61-year-old woman with a history in stroke and acute neurologic deficit due to salicylate toxicity. The initial serum salicylate level was significantly increased at 78.1 mg/dl (upper therapeutic limit, 19.9 mg/dl), indicating salicylate toxicity. Serum salicylate levels are shown to decrease following treatment that included intravenous sodium bicarbonate, which began at hour 7.

her neurologic manifestations were not considered to be severe, and her renal function was normal (Table 1).

Her serum salicylate levels gradually decreased over five serial measurements, falling to within the therapeutic range at 16.5 mg/dl by 25 hours after the initial measurement (Figure 2). The patient's metabolic acidosis, respiratory alkalosis, delirium, and hemiparesis improved significantly and resolved completely by 48 hours after her initial presentation. Her chest pain, which was believed to be caused by anxiety, also resolved.

Discussion

Despite the availability of alternative analgesics and recent evidence against primary prophylaxis with aspirin to prevent thrombosis [11,12], salicylate use remains widespread. The use of salicylate-containing products may be especially common among elderly patients. In 2005, a survey found that 48.5% of individuals over the age of 65 years reported using aspirin at least every other day [13]. Also, salicylate overdose, whether accidental or intentional, is not an uncommon reason for presentation to the Emergency Department. Salicylate toxicity is frequently reported to poison control centers [14]. It is important to recognize and treat salicylate toxicity as soon as possible because it can be fatal. For example, in the 2017 Annual Report of the American Association of Poison Control, salicylates were responsible for 30 fatalities and represented 1.3% of all medication-related deaths [5].

Delay in the diagnosis of severe salicylate toxicity has been associated with a risk of mortality as high as 15–25% [3,15]. Therefore, early diagnosis is important. In this case, the diagnosis might have been made earlier if salicylate toxicity was suspected from the initial clinical presentation or medication history, as the serum salicylate level was not measured until seven hours after her presentation to the Emergency Department. Previous reports have shown that failure to recognize the presenting symptoms of salicylate toxicity can contribute to a delay in diagnosis [15,16]. Also, chronic salicylate toxicity has previously been reported to occur more commonly in elderly patients and often presents atypically [1]. Furthermore, depending on the timing of ingestion, salicylate toxicity may present without an increased anion gap or even with a normal initial serum salicylate level [14,15]. One of the factors that can delay the diagnosis is a failure to recognize the neurologic manifestations of salicylate toxicity. Delirium is a common presenting feature, and chronic ingestion can masquerade as other neurological conditions such as stroke or movement disorders [1,4,15].

In this case, the neurologic presentation resulted in consideration of several diagnoses other than salicylate toxicity. Stroke or transient ischemic attack (TIA) were the most concerning initial possibilities, given her age and medical history. MRI of the brain was obtained early in her clinical evaluation and showed evidence of previous cerebral infarction without signs of acute infarction. Some of her presenting features suggested the possibility of postictal paresis, also known as Todd's paresis, including the patient's recent non-adherence to antiepileptic medication. However, postictal paresis would be unlikely without a history of prolonged seizures or status epilepticus [17]. The patient denied any recent seizure activity.

Given this patient's history of previous ischemic stroke and her recent illness, the most likely diagnosis is thought to be a toxic or metabolic disturbance resulting in an exacerbation of existing neurologic deficit. Exacerbation of existing neurologic deficit is well recognized as a manifestation of both infection and hypoglycemia but has not previously been associated with salicylate toxicity. This case also illustrates that atypical neurologic symptoms may precede both delirium and tinnitus in the course of salicylate toxicity.

Conclusions

This report was of a case of a 61-year-old woman with a history of neurologic disease who presented with acute focal neurologic deficit associated with salicylate toxicity. The case highlighted that due to her age and medical history, an initial diagnosis of a further stroke was made until this diagnosis was excluded by cerebral MRI. Salicylate toxicity was confirmed by serum toxicology. However, the delay in diagnosis was a concern, considering the potentially fatal nature

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of salicylate toxicity and the importance of early treatment. Therefore, physicians should maintain a high index of suspicion for salicylate toxicity in patients who present with acute neurologic symptoms, and medication history should include direct questioning for salicylate use.

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Conflict of interest

None.

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