Dangerous Assumptions of Psychosis: A Near-Missed Case of Chronic Aspirin Toxicity

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Abstract: We report a case of a 59 year-old female with a history of bipolar I disorder with psychotic symptoms who presented to the Emergency Department (ED) with cough and request for medication refill. During the course of her stay, the patient was noted to have an altered mental status (AMS). Specifically, the patient was not only confused and disoriented but frankly delusional with a disorganized thought process. Her review of systems was notable for a non-productive cough and her physical exam was unrevealing. Her initial lab results were unremarkable except for a mild leukocytosis. She was initially diagnosed with pneumonia and started on antibiotics. The Emergency Department medically cleared the patient for psychiatric evaluation. A psychiatric consultation was placed for suspected mania secondary to psychiatric illness given her medication non-compliance. During the psychiatric evaluation, she became more confused and combative - her behavior was concerning more for delirium than mania. Consequently, the psychiatry team requested additional ingestion labs including aspirin and acetaminophens levels and requested the ED entertain possible medical explanations for the patient’s condition. Seven hours after initial evaluation and during “discovery rounds” and transfer of patient care to the overnight team, her salicylate level was shown to be elevated to 75.7 mg/d and her venous blood gases showed significant mixed respiratory alkalosis and metabolic acidosis, causing further concern for salicylate toxicity. The overnight team obtained collateral information that revealed that the patient chronically ingested “BC Powder”, an over-the-counter (OTC) medication containing aspirin and caffeine. Of note, there are several different formulations of BC powder with different dosages of aspirin. As her delirium worsened, the patient was intubated for airway protection and a hemodialysis catheter was placed. She was given a bolus of sodium bicarbonate, followed by a steady infusion of sodium bicarbonate for urinary and serum alkalinization. Afterward, she received emergent hemodialysis. Herrefractory acidosis resolved, she was extubated and her mental status returned to baseline. She was discharged on day four of admission. In conclusion, polypharmacy must always be considered as a cause of AMS. All recent medications should be recorded, including OTC formulations and herbal supplements. Additionally, delirium secondary to chronic salicylate overdose can be difficult to discern from psychosis, especially since it is an uncommon manifestation of a common medication. Therefore, toxic ingestions should be ruled out prior to a diagnosis of psychosis secondary to a psychiatric condition, regardless of the past medical history.

Keywords: Salicylate poisoning, aspirin toxicity, mental illness, psychosis, chronic aspirin use, delirium, BC powder, Goody Powder.

INTRODUCTION
Salicylic acid and its derivatives are found in many pharmaceuticals as well as in non-medicinal products. They are used therapeutically as anti-inflammatory agents and analgesics. Salicylates may also be used as fragrances. Common formulations of salicylate-containing products include: sodium salicylate, methyl salicylate, acetylsalicylic acid (ASA), magnesium salicylate, and bismuth subsalicylate. While these formulations may be applied via different routes, including topically, they are all metabolized in the body to salicylic acid and can cause salicylate toxicity [1-3]. One popular OTC medication is ‘BC Powder’, which has several variations with significant quantities of salicylic acid. In 2014, the American Association of Poison Control Centers’ National Poison Data System
CASE REPORT

A 59 year-old female with a history of bipolar I disorder with psychotic features, poor compliance with medication, and polysubstance use disorder presented to the Ben Taub General Hospital Emergency Department with the chief complaint of "pneumonia" and a request for medication refill. She brought with her a discharge summary dated for the same day from a nearby medical center which included chest imaging results of a possible pneumonia, a diagnosis of acute bronchitis, and a prescription for levofloxacin and albuterol.

At presentation, she was verbal, but confused. She reported mostly inconsistent information with elements of non-bizarre delusions. However, she confirmed to the resident physician that she had a nonproductive cough for two months and that she had not been taking her prescribed psychiatric medications for an extended period of time. Review of the electronic medical records revealed eight to ten prior hospital visits for mental health concerns. Review of systems was otherwise negative.

On initial evaluation, her vitals were as follows: temperature 97.8°F, heart rate 88 beats/min, blood pressure 112/57 mm Hg, 18 breaths/min, and 96% saturation on room air. She was alert and oriented, neither toxic appearing nor acutely distressed. The rest of the physical exam was entirely unremarkable. Laboratory results were notable only for leukocytosis (WBC 14.2) and the presence of benzodiazepines on urine drug screen. The point-of-care basic metabolic panel and the rest of her tests were within normal limits. She was diagnosed with pneumonia and no further workup was done. Her altered mentation was attributed to her bipolar disorder. As a result, she was medically cleared for discharge to the ED Psychiatry team.

While the patient remained in the ED, she became increasingly confused and agitated, eventually requiring nonviolent restraints. In the psychiatric evaluation, she continued to give an inconsistent story regarding the history of her illness. However, she endorsed having depressed mood, racing thoughts, and decreased energy level, changes in appetite, poor concentration, and insomnia. On exam, she had disorganized thought, poor attention, emotional liability, slurring of words, psychomotor depression, and delusions. Collateral information was then obtained from her daughters, which revealed that the patient had been coughing and wheezing for the past eight weeks with progressively worsening confusion. The daughter verified that this acute state of agitation and disorganized behavior over the past few hours was abnormal and coincided with the patient’s recent state of illness. Given the chronicity of her medical illness and her acutely progressive change in mentation, the psychiatric consultant believed that her condition was more consistent with delirium secondary to a general medical condition than with mania. As a result, the ED was requested to reevaluate the patient for possible causes of delirium.

The patient was signed out to the evening team at 1900, seven hours had elapsed since the initial medical examination and three hours had elapsed since the psychiatric team’s examination was concerning for delirium. By the time the patient was being transferred to the evening team, the additional laboratory work requested by psychiatry had resulted and revealed an elevated serum salicylate level of 75.7 mg/dL (therapeutic range 15-30 mg/dL) as well as a venous blood gases showed a significant mixed acid-base disturbance consisting of a respiratory alkalosis and a concomitant metabolic acidosis: pH 7.54, pCO2 20.5, HCO3 17.5. These lab results were gravely concerning for aspirin toxicity and overdose.

Upon further questioning, the patient’s daughter adamantly denied the possibility of a suicide attempt via aspirin overdose by the patient. She added that for several weeks, the patient had been using an unspecified dose of “BC Powder”. The patient reportedly used the powder regularly to remedy any ailments, including her recent cough. As a result of this new information, she was diagnosed with chronic salicylate intoxication. Her treatment included aggressive fluid resuscitation with Lactated Ringer’s, sodium bicarbonate bolus followed by a steady infusion for urine and serum alkalinization and emergent hemodialysis. Other electrolytes were repleted as necessary.

She was then admitted to the MICU at a nearby affiliated hospital. Her serum salicylate level decreased to 7.0 mg/dL following dialysis. Her mental status recovered to baseline over subsequent days. Additionally, repeated chest x-ray during the admission was suggestive of aspiration pneumonia for which she received empiric antibiotics. However, blood cultures were negative and the patient lacked any other signs of sepsis. Accordingly, it was not deemed contributory to her AMS. She was ultimately discharged in good medical condition after four days of admission without any agitation, delusions, or confusion.

DISCUSSION

Salicylates are found in numerous over-the-counter medications, with many different formulations amongst the products. These are often used on a daily basis as long-term treatment for a number of chronic medical conditions. The concentration of ASA in ‘BC...
Powder’ ranges from 845 mg to 1000 mg per dose, which is significantly higher than the dose found in many other products [6]. Severity of acute salicylate ingestions can be initially assessed by ascertaining the amount of salicylate ingested [5]. Salicylates typically have a therapeutic serum level of 10 to 30 mg/dL with symptoms of intoxication commonly occurring at or above the upper limit of that range [7, 8]. Some evidence shows that serum salicylate levels taken 6 hours after acute ingestion can roughly correlate with degree of toxicity [5, 7]. While serum levels drawn before 6 hours may confirm acute salicylate toxicity, they reflect the absorption-distribution phase of salicylate pharmacokinetics and may not show the peak levels that correlate with symptoms [5]. In order to confirm peak values, repeat salicylate levels should be drawn until serum concentrations trend downward [7].

Enteric-coated (EC) salicylates have delayed absorption into the body, which can cause a significantly slower rise in serum level and presentation of symptoms [9]. Wortzman et al [10] reported a case where serum levels in an asymptomatic 22-year-old man did not peak until 24 hours after his EC salicylate overdose. Additionally, chronic overdose of salicylates can cause severe toxicity at significantly lower serum levels, due to the accumulation of the compound in the body [5, 11].

At therapeutic doses, salicylic acid is metabolized and eliminated from the body within 2 to 3 hours. However, at high therapeutic doses and in overdose, salicylate metabolism changes to zero-order kinetics and can cause intoxication at lower serum levels as absorption and elimination are prolonged [5]. In this case, it was unclear how much BC Powder the patient had been taking, only that she had been using it daily for at least several weeks. Over time, the prolonged absorption and elimination compounded the amount of salicylates in her system, causing her to become more intoxicated than would be expected with the suggested daily dose.

The serum salicylate levels should be interpreted in context of the patient’s clinical status. Mild salicylate toxicity can produce classic presenting symptoms such as tinnitus, nausea, vomiting, and hyperventilation within hours of ingestion. Moderate toxicity will produce these symptoms, as well as hyperpyrexia, sweating, loss of coordination, and restlessness. Severe toxicity will include signs and symptoms of hypotension, significant mixed respiratory alkalosis and metabolic acidosis, renal failure, hallucinations, and coma [7]. Additionally, acute salicylate ingestion may cause a coagulopathy notable in lab results, separate from ASA’s normal antiplatelet effects [12]. Both acute and chronic intoxication may present with less obvious symptoms including noncardiogenic pulmonary edema, hypoglycemia, neuroglycopenia, hypoglycorrhachia, and liver failure [13, 14]. Another important and alarming symptom of chronic salicylate intoxication is altered mentation, which makes it difficult to obtain a reliable history from the patient. This AMS can overlap with or mimic that of mental illness in that the only presenting symptoms may be confusion and irritability. Consequently, timely diagnosis and treatment may be delayed by this obscured clinical picture [5]. A thorough history and physical are necessary to distinguish between true psychosis and delirium.

Another factor contributing to the difficulty of diagnosing chronic salicylate toxicity is age. Elderly patients are vulnerable to unintentional intoxication due to their chronic use of ASA for multiple medical reasons [15]. Toxicity can easily be overlooked if the warning signs are not acutely apparent or the patient has other confounding diagnosis and medical history (such as bipolar I and a history of psychosis). Even when there are acute signs and symptoms, they are not specific to salicylate intoxication and are difficult to differentiate from other concurrent medical conditions. Retrospective research has shown that a significant portion of adult salicylate intoxications remain undiagnosed up to 72 hours after presentation, even when ‘classic’ acid-base disturbances, hyperventilation, and neurologic symptoms were present. This delay in diagnosis was predominantly seen in elderly patients who did not volunteer a history of salicylate ingestion but unintentionally took too much ASA to treat a separate medical illness. These patients with delayed diagnosis had a mortality rate up to twenty-five percent, several times the rate seen with patients immediately diagnosed upon presentation to the ED [15]. Therefore, blood gases and salicylate levels should be immediately obtained if intoxication remains on the differential.

Treatment is based on the acuity of intoxication and the patient’s clinical status. In toxic ingestions, serum and urine alkalinization with fluids such as sodium bicarbonate are utilized as first-line treatment for moderate-to-severe salicylate intoxication [16]. Evidence has shown that urine alkalinization significantly increases elimination of salicylic acid and promotes transfer of the compound from the central nervous system [16]. If necessary, fluid resuscitation should be accomplished using Lactated Ringer’s solution rather than normal saline. Use of normal saline can result in hyperchloremic metabolic acidosis, which could worsen salicylate toxicity in a patient [17, 18].

Single-dose activated charcoal (SDAC) can also be utilized for gastric decontamination and reduction of salicylate absorption in acute ingestions [19]. While current evidence suggests that SDAC is most effective within one hour of ingestion, the prolonged absorption of ASA may lengthen this timeframe [20]. Notable contraindications to charcoal include a compromised or unprotected airway,
substances with high aspiration potential, significant bowel pathology, and ingestion of corrosives [20].

Hemodialysis should also be considered with moderately elevated serum salicylate levels if the patient shows signs of CNS dysfunction (e.g. delirium, seizures, and coma), renal failure, pulmonary edema, or refractory acid-base imbalance [21]. Additionally, a serum salicylate level above 100 mg/dL is another commonly utilized indication for emergent hemodialysis [21]. Hemodialysis should also be considered in chronic salicylate users who are both symptomatic and with a serum salicylate level above 60 mg/dL, as was the indication for this patient [22].

In this case, the diagnosis and treatment of severe chronic salicylate intoxication was significantly delayed as a result of the patient’s inability to provide an adequate history of her presenting illnesses, her confounding psychiatric and medical history, her atypical symptomatology, and the lack of notable initial lab results. Nonetheless, the oversight could have been avoided with a more inclusive differential diagnosis and less anchoring to the notion that the patient’s symptoms were caused by her underlying psychiatric illness. This case highlights the importance of maintaining a high index of suspicion for substance intoxication in mentally altered patients particularly those with a previous psychiatric diagnosis. Delayed diagnoses or worse, complete misdiagnoses of salicylate toxicity for psychiatric conditions directly impact patient care and can lead to significant morbidity and mortality. Sometimes “crazy” is not just crazy. Although caffeine, the other main component of BC Powder, can also have toxic effects, such as hypokalemia, sympathomimetic toxicity, and hyperglycemia, the patient in this case did not exhibit any of these signs or symptoms, thus making concomitant caffeine intoxication unlikely [23, 24].

CONCLUSION

Unintentional salicylate intoxication is a fairly common occurrence due to the ubiquity of salicylate use for numerous medical conditions. Chronic salicylate ingestion may warrant more aggressive management compared to acute ingestion. It is critical to aptly distinguish the less overt yet serious symptoms of chronic intoxication as well as to maintain a high index of suspicion for elderly patients and those with mental illness. Delirium caused by chronic salicylate overdose can be difficult to discern from psychosis secondary to a psychiatric condition. Additionally, polypharmacy should always be considered in an elderly patient with AMS. Therefore, substance toxicity should be ruled out in all patients presenting to the ED with altered mental status prior to a consideration of a psychiatric diagnosis, regardless of their past psychiatric history. In light of this, one should explicitly clarify a patient’s over-the-counter medication use, as well as vitamins and supplements, in addition to their prescription medications.

REFERENCES