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Case Report
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Acute on Chronic Salicylate Toxicity: Multi-Organ Repercussions

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Abstract

This 38-year-old female presented to the Psychiatric Emergency Center with gradual onset pallor, agitation, jaundice, concentration impairment, disorientation, auditory and visual hallucinations that worsened over the last three days. Labs were significant for profound macrocytic anemia with a mean corpuscular volume of 135.8 fL and an initial salicylate level of 20.1 mg/dL. Her medical history was significant for back pain. She had been regularly taking over-the-counter salicylate products for 20 years to manage pain. She was medically admitted for delirium. Her mentation returned to baseline after stopping salicylate products, administration of intravenous fluids, and a one-time administration of cyanocobalamin 1000 mcg intramuscularly. This 3-day admission for delirium compounded other unusual and extreme symptom presentations over the past five years. She had other admissions for a severe high grade pyloric stenosis requiring surgical intervention, nausea and vomiting with weight loss of over 30 pounds in three months, delirium, severe constipation with new onset hypothyroidism, colitis, microcytic anemia, and acute hypoxemic respiratory failure due to acute noncardiogenic pulmonary edema. Outside of the acute-care setting, she saw primary care, psychiatric, pain management, gastroenterology, and gynecology providers. However, chronic salicylate use went unrecognized. In addition to neuropsychiatric symptoms, chronic salicylate use can cause a variety of medical problems including thyroid dysfunction, gastrointestinal problems, and respiratory complications. Normal salicylate levels do not rule out chronic salicylate toxicity. Providers should consider acute on chronic salicylate toxicity, regardless of the salicylate level, in patients with altered mental status and in patients with conspicuous medical symptoms.

Keywords: Salicylates; Toxicity; Acute on chronic; Neuropsychiatric symptoms; Delirium; Acute on Chronic Salicylate Toxicity; Multi-Organ Repercussions

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Case Presentation

This 38-year-old female presented to the Psychiatric Emergency Center with gradual onset of pallor, agitation, jaundice, concentration impairment, disorientation, auditory hallucinations, and visual hallucinations that worsened over the last three days. She had a history of unusual and extreme symptom presentations over the past five years.

Medical History

At age 33, she was hospitalized for 23 days after losing 30 pounds and vomiting 4 to 5 times per week over a three-month period. Upon admission, she had a severe high-grade pyloric stenosis and chronic atrophic gastritis. The pyloric stenosis and chronic atrophic gastritis were diagnosed by esophagogastroduodenoscopy; the gastric mucosa biopsy was negative for *Helicobacter pylori*; no ulceration was present. A gastrointestinal surgeon performed an antrectomy with Billroth I reconstruction and vagotomy, cholecystectomy, and pyloric sphincterotomy. Chronic atrophic gastritis and the pyloric stenosis were correctly attributed to chronic salicylate use. She reported that she had been taking 4 or more Excedrin (acetaminophen, aspirin, and caffeine) tablets daily for the last 15 years and BC powder (aspirin and caffeine) in unknown quantities for the last 3 years. Prior to discharge, the nausea and vomiting resolved; she advanced to a regular diet. She was advised to stop taking over-the-counter salicylates however, continued to do so.

One year later, she was hospitalized for 5 days for nausea, vomiting, intermittent confusion, visual hallucinations, fatigue, and severe constipation for a period of one month. The workup was remarkable for microcytic anemia with hemoglobin 8.9 g/dL and hematocrit 33%, previously undetected hypothyroidism with Thyroid Stimulating Hormone (TSH) of 124.58, and imaging that revealed thickening of the right colon that was suspicious for colitis. She had no prior history of

hallucinations due to a psychiatric condition. She was treated with intravenous levothyroxine. She was not given salicylates during the admission. Her nausea and vomiting were attributed to chronic salicylate use. There was no suspicion that salicylates caused new onset hypothyroidism, constipation, and delirium. Her fatigue, constipation, gastric distress, and changes in mentation resolved and she was discharged. She was advised to stop taking over-the-counter salicylates however, continued to do so.

At age 35, she was seen by pain management for back pain that began at age 15. Magnetic Resonance Imaging (MRI) revealed degenerative lumbar disc changes, especially at L1/L2, L3/4, and L5/S1, that were thought to be the cause of her pain. She did not disclose that she uses over-the-counter salicylates at any point during her treatment. She stopped going to pain management appointments citing "what I do works better."

At age 36, she was hospitalized for 4 days for gradual onset confusion, auditory and visual hallucinations, delusions, lethargy, and multiple falls in the past week. A family member reported that she regularly took BC powder four times a day in unknown quantities. The initial salicylate level was 51 mg/dL; a repeat salicylate level at 3 h was 44 mg/dL. She was treated with sodium bicarbonate intravenously for acute salicylate toxicity. She was treated with oxygen by nasal cannula and furosemide for acute hypoxemic respiratory failure due to acute noncardiogenic pulmonary edema due to acute on chronic salicylate toxicity. She received 2 units of Packed Red Blood Cells (PRBCs) for severe microcytic anemia with hemoglobin 6.5 g/dL and hematocrit 22.7%. Her mentation returned to baseline, and she was discharged. She was advised to stop taking over-the-counter salicylates however, continued to do so.

At age 37, she was sent to the ER from an outpatient psychiatry clinic for new onset confusion and auditory hallucinations. She received 3 units of PRBCs for normocytic anemia with hemoglobin 5.5 g/dL and hematocrit 18.8%. Levothyroxine was restarted for TSH of 10.5. Menorrhagia was suspected as the cause of her anemia, and she was referred to outpatient gynecology. There was no documentation addressing her use of salicylates. Her mentation returned to baseline, and she was discharged.

The Diagnosis

Stat labs were drawn and she was transferred from the Psychiatric Emergency Center to the medical ER. She was medically admitted for delirium. A Complete Blood Count (CBC) showed profound macrocytic anemia with a mean corpuscular volume of 135.8 fL. The initial salicylate level was 20.1 mg/dL with four and eight hours repeat levels 13.1 mg/dL and 9.8 mg/dL respectively. Other pertinent laboratory work included a normal Computed Tomography (CT) of the head, negative drug and alcohol screening, unremarkable ammonia level, vitamin B12 76 pg/mL, and Methylmalonic Acid 1.85 umol/L. After three days of management with intravenous fluids, a one-time administration of cyanocobalamin 1000 mcg intramuscularly, and stopping salicylates, her mentation returned to baseline. She discharged after 3 days with a diagnosis of acute on chronic salicylate toxicity. She was advised to stop taking over the-counter salicylates.

Discussion

Acute salicylate intoxication with tinnitus, vertigo, nausea, vomiting, and hyperpnea is readily recognized, especially if the history of ingestion can be obtained [1]. Chronic salicylate toxicity is more likely to go undetected due to overreliance on drug levels, lack of clear history of excess ingestion, and atypical presentations mimicking other illnesses [2]. The plasma levels associated with chronic toxicity are generally lower than in acute intoxication presentations and are often within therapeutic range [2]. Chronic toxicity can even occur at therapeutic doses [2]. According to the NEJM (2020), "when the baseline tissue burden of the drug is high and pathways for salicylate elimination are nearly or fully saturated, additional intake of the drug may lead to substantial accumulation of free salicylate and extension of the normal half-life of 2 h to 4 h to as long as 20 h" [3]. In this patient, the signs and symptoms of chronic salicylate toxicity were mistaken for other illnesses, until complications were so severe, they required hospitalization. Despite visits with primary care, psychiatric, pain management, gastroenterology, and gynecology providers between ages 33 and 38, chronic salicylate toxicity went undetected. Many disease processes were treated without attributing the processes directly to chronic salicylate toxicity.

Hypothyroidism

The patient was diagnosed with primary hypothyroidism without acknowledgement that salicylate administration depresses thyroid function. Chronic salicylate poisoning likely caused or significantly contributed to hypothyroidism in this patient. Due to inconsistent engagement with the healthcare system, it is unclear to what extent. The proposed mechanism by which salicylates depress thyroid function is multifactorial and obscure. Salicylate administration increases oxygen consumption, increases the basal metabolic rate, and reduces the protein bound iodine concentration [4]. The protein bound iodine reduction can be explained by a decrease in production, increase in peripheral degradation of thyroxine, or both [1]. Austen, Maroney, and Wolff (1958) demonstrated that an increase in oxygen consumption due to routine administration of salicylates directly correlates with a decrease in protein-bound iodine concentrations and thyroxine. Subsequent studies during which salicylate-treated patients were given exogenous thyrotropin showed increased uptake of iodine, an increase in the serum protein bound concentration, and accelerated release of iodine from the thyroid gland [5]. This same experiment showed that salicylates do not appear to concentrate in the pituitary gland, hypothalamus, or thyroid/adrenal glands. Therefore, salicylates inhibit thyrotropic stimulation at the pituitary or higher-level centers [5].

Gastrointestinal Dysfunction

The patient's microcytic, normocytic, and macrocytic anemias can be attributed to the chronic overuse of salicylates. She was transfused several times without clinicians identifying chronic salicylate toxicity as causal. Salicylates *in vivo* alter iron uptake as well as cause acute or chronic blood loss due to gastrointestinal tract erosion [6]. Chronic salicylate poisoning initially presented as severe high-grade pyloric stenosis and chronic atrophic gastritis in this patient. Over time, a microcytic anemia caused by acute blood loss, chronic blood loss, and iron malabsorption shifted to a normocytic anemia then a macrocytic anemia. The mechanism by which salicylates causes macrocytic anemia is likely destruction of the gastric mucosa which in turn reduces secretion of intrinsic factor or hypochlorhydria leading to development of vitamin B12 deficiency [7]. The patient's colitis was also likely caused by chronic salicylate use. Salicylates disrupt the epithelial barrier which affects the interaction between the gut biome and immune cells in the gastrointestinal lining [8].

Respiratory Complications

As a result of chronic salicylate toxicity, the patient developed acute hypoxemic respiratory failure due to acute noncardiogenic pulmonary edema. Salicylates have a direct effect on the respiratory center of the medulla [2]. Salicylates stimulate the respiratory center causing an increase in the respiratory rate and subsequently, respiratory alkalosis [2]. Acute and chronic salicylate toxicity causes pulmonary edema by increasing capillary permeability of the lungs which leads to leaking of fluid into pulmonary tissues [9].

The Take Away

Chronic salicylate use can cause many general medical and neuro-psychiatric signs and symptoms. While salicylate levels can confirm the diagnosis of acute salicylate intoxication, salicylate levels do not rule out chronic salicylate toxicity. Providers should consider chronic salicylate toxicity in patients with altered mental status and a myriad of disease processes including hypothyroidism, metabolic acidosis, respiratory alkalosis, anemia, and gastric distress. Clinicians should be especially suspicious in patients with medical conditions with unusual presentations outside norm for age.

References

1. Yip L, Dart RC, Gabow PA. Concepts and controversies in salicylate toxicity. Emerg Med Clin North Am. 1994;12(2):351-64.
2. Clegg DJ. Salicylate toxicity. N Engl J Med. 2020;382(26):2544-55.
3. Wong OF, Fung HT, Lam TSK. Case report of aspirin overdose: Bezoar formation and controversies of multiple-dose activated charcoal in salicylate poisoning. Hong Kong J Emerg Med. 2010;17(3):276-80.
4. Austen FK, Meroney WH, Wolff J. Salicylates and thyroid function. I. depression of thyroid function. J Clin Invest. 1958;37(8):1131-43.
5. Wolff J, Austen FK. Salicylates and thyroid function. II. the effect on the thyroid-pituitary interrelation. J Clin Invest. 1958;37(8):1144-52.
6. Merchant MA, Modi DN. Acute and chronic effects of aspirin on hematological parameters and hepatic ferritin expression in mice. Indian J Pharmacol. 2004;36(4):226-30.
7. van Oijen MGH, Laheij RJF, Peters WHM, Jansen JBMJ, Verheugt FWA. Association of aspirin use with vitamin B12 deficiency (results of the Bach Study). Am J Cardiol. 2004;94(7):975-7.
8. Hesdorffer CS, Longo DL. Drug-induced megaloblastic anemia. N Engl J Med. 2015;373(17):1649-58.
9. Haddad LM, Winchester JF, Shannon MW, Borron SW, Burns M. Haddad and Winchester's clinical management of poisoning and drug overdose (4th Ed). Saunders/Elsevier. 2007.