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CASE REPORT

Beyond the expected of delayed aspirin toxicity in a 2-year-old child: a case report

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ABSTRACT

Background: Salicylate toxicity can manifest with delayed symptoms that complicate prompt diagnosis and intervention. Although delayed peak concentrations after ingestion have been documented, reports of patients remaining asymptomatic for more than 20 hours are uncommon. **Case Presentation:** We present the case of a 2-year-old female who ingested a highly toxic dose of 463 mg/kg of enteric-coated aspirin and remained asymptomatic for the initial 20 hours. Subsequently, she developed severe symptoms of increased respiratory effort and altered mental status, with laboratory findings confirming combined respiratory alkalosis and anion-gap metabolic acidosis. The patient was initially managed through sodium bicarbonate alkalization and was later managed through hemodynamic dialysis due to the persistence of symptoms.

Conclusion: This case report underscores the importance of vigilant monitoring and prompt intervention in patients with salicylate ingestion and the possibility of delayed symptoms following an asymptomatic period.

Keywords: Salicylate toxicity, aspirin toxicity, pediatric, enteric-coated aspirin.

Introduction

Pediatric toxic ingestion is a common presentation at the emergency department. Most of these cases are not lethal and are safely sent home without any further intervention, but a considerable number of cases can progress to serious manifestations even with ingestion of a small amount. For pediatric patients, physicians need to think that one pill can kill phenomena because a safe pharmaceutical adult dose can cause serious harm to a child. Salicylate ingestion is an example of this, where a safe adult dose is toxic for the pediatric population. In the United States, over 27,644 pediatric patients were exposed to salicylates with an associated 0.4% mortality rate in 2018 [1]. In 2020, salicylates accounted for 10% (n = 536) of the total toxic exposures reported in the annual report of the Poisoning Consultations Cases Registry of the Saudi Ministry of Health [2]. With the implementation of safety measures on prescription, salicylate toxicity is less commonly encountered in the pediatric age group, but it can cause major morbidity if missed.

Salicylate toxicity in pediatric patients can present with a range of clinical manifestations ranging between gastrointestinal, respiratory, and neurological symptoms, with other organ involvement as well [3]. The stomach and proximal intestine are the primary sites for salicylate absorption, with peak concentrations at therapeutic doses reached 1-2 hours after ingestion for normal preparations and 4-6 hours for enteric-coated preparations [3]. Overdoses may cause saturation of metabolic and absorption pathways, resulting in longer-lasting effects and delayed peak concentrations [3]. Managing salicylate overdosage involves evaluating serial plasma salicylate concentrations in relation to the time of ingestion as well as assessing the patient's acid-base balance and mental state [4]. Delayed peak concentrations up to 60 hours after ingestion following aspirin overdoses have been documented in the literature [5,6]. However, to our knowledge, there are no prior reports describing patients who remain asymptomatic for > 20 hours after ingestion in our country. We report a case of delayed toxicity following the ingestion of enteric-coated aspirin 100 mg tablets, with no symptoms observed during the first 20 hours of observation. After this prolonged asymptomatic period, the patient developed toxicity, requiring urinary alkalinization and dialysis.

Case Report

A previously healthy, 2-year-old female presented to the emergency department with symptoms of increased respiratory effort and altered mental status, noticed by her mother that morning. The family found an empty bottle

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of aspirin, a prescription medication used by the father for an underlying cardiac condition, at 14:00 the day before the visit. However, the child was asymptomatic, and the family did not suspect ingestion until nearly 20 hours later, when symptoms developed. The bottle, typically containing 90 enteric-coated tablets of 100 mg each, had previously been partially used by the father (30 tablets consumed).

Although ingestion was unwitnessed, calculations based on the remaining quantity and the patient's weight of 12.9 kg suggested a dose of 463 mg/kg, which is highly toxic. The patient remained asymptomatic for the first day and began manifesting symptoms the following morning, including lethargy, tachypnea, fever, and a single episode of non-bilious vomiting upon awakening.

On examination, the patient appeared ill and distressed, with spontaneous breathing in room air and kussmaul respirations. Vital signs included a temperature of 36.5°C, heart rate of 144 beats per minute, respiratory rate of 34 breaths per minute, blood pressure of 109/64 mmHg, and bedside serum glucose of 4.4 mmol/l. Neurological examination revealed responsiveness to auditory stimuli, crying, and a Glasgow Coma Scale score of 15. She had spontaneous movement of all limbs, with no neurological deficits, normal skin color, and bilaterally equal, symmetrical, and reactive pupils. Other system examinations were unremarkable.

Blood gas analysis showed a combination of respiratory alkalosis and high-anion-gap metabolic acidosis (Table 1). Based on clinical presentation and initial laboratory findings, salicylate toxicity was suspected. Initial stabilization included oxygenation, a fluid bolus, and maintenance fluids at 1.5 times the normal rate. Sodium bicarbonate boluses (2 mEq/kg) were administered, followed by a continuous infusion of sodium bicarbonate (150 mEq/l) mixed with dextrose and potassium chloride. Urgent toxicology consultation recommended alkalinization with sodium bicarbonate (1 ml/kg of 8.4% sodium bicarbonate diluted in 500 ml of 5% dextrose) at 2-3 ml/kg/hour to achieve an optimal urine pH of 7.5-8.5. Potassium and glucose levels were closely monitored in the pediatric intensive care unit.

Initial serum salicylate levels measured 5.20 mmol/l (93.6 mg/dl) (Figure 1), indicating lethal toxicity. Despite sodium bicarbonate infusion, clinical and laboratory conditions did not improve. At 23:00, 12 hours after presentation, the patient was started on Continuous Veno-Venous Hemofiltration (CVVH) for 36 hours at 4,000 ml/adjusted surface area, heparin-free, until salicylate levels normalized (<0.36 mmol/l) and blood gas values improved. The salicylate serum level declined to 2.7 mmol/l after 4 hours of dialysis and reached < 0.36 mmol/l after 24 hours from presentation. The patient demonstrated clinical recovery and was observed for 48 hours in the inpatient unit with no recurrence of symptoms or laboratory abnormalities. She was subsequently discharged home safely.

Discussion

Aspirin toxicity remains a significant cause of pediatric poisoning, particularly due to its delayed and unpredictable absorption patterns, which can lead to late-onset clinical deterioration. Salicylate toxicity manifests with a spectrum of symptoms, ranging from early symptoms typically including gastrointestinal disturbances (nausea, vomiting, and abdominal pain) to more severe systemic effects, including hyperventilation with respiratory alkalosis as a hallmark of toxicity with subsequent anion-gap metabolic acidosis [7,8]. Severe intoxication may cause neurological compromise, sepsis-like presentation with hyperthermia, and multiorgan involvement that can be fatal [9,10]. In our patient, the delayed onset of symptoms nearly 20 hours after ingestion posed a diagnostic challenge, which may lead to misdiagnosis or inappropriate initial management, as seen in cases mistakenly attributed to sepsis or diabetic ketoacidosis [6].

The pharmacokinetics of aspirin overdose are complex, with multiple factors contributing to delayed toxicity, including prolonged gastric emptying, pylorospasm, and saturation of hepatic metabolism [11]. A case described by Beauchamp and Hendrickson [5] demonstrated a 17-year-old patient who initially had undetectable serum salicylate levels at 3.9 hours post-ingestion but later developed toxicity at 22 hours [5]. Similarly, Espírito et al. [6] reported a 9-month-old infant with severe metabolic acidosis secondary to salicylate toxicity, initially misdiagnosed as sepsis vs diabetic ketoacidosis and managed acordingly without improvement in anion gap hence suscpcion of ingestion was raised and salicylate level was measured revealed toxic values (76 mg/dl; normal range < 20 mg/dl) through prepration of formula with water containing Aspegic 1,000 mg® (DL-lysine acetylsalicylate 1,000 mg) by her parents [6]. These cases highlight the critical need for repeat salicylate measurements in suspected poisonings, as early levels may be misleadingly low.

It is difficult to reliably interpret the isolated salicylate concentration following an aspirin overdose.

Table 1. *Blood gas level monitoring.*

Timing	pH	pCO2 (mmHg)	HCO3 (mmol/l)	BE (mmol/l)	Lactate (mmol/l)
Initial	7.39	21	13.3	-10.3	0.9
After 2 hours of fluids + sodium bicarbonate bolus	7.33	17	9.5	-14.7	1.1
After 4 hours fluids + sodium bicarbonate infusion	7.45	11	7.8	-13.5	1.4
After 4 hours of dialysis	7.38	21	13	-11	0.9
After 12 hours of dialysis	7.44	35	24.9	-0.1	1.8

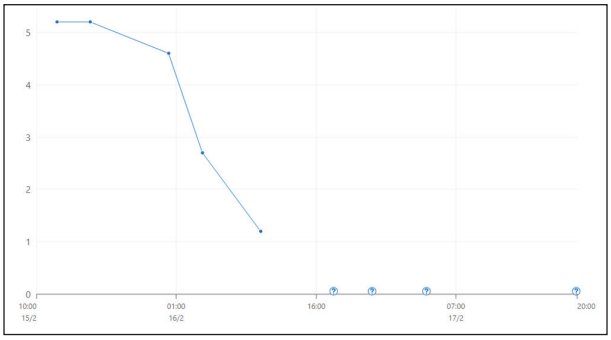

Figure 1. *Level of serum salicylate.*

Concentrations drawn too early in the overdose period may be falsely normal due to incomplete drug absorption. If obtained later, they may be unreliable due to the mobilization of salicylate from the blood compartment [4]. In a retrospective review by Moss et. al. [12], a 3.5% of patients developed serum salicylate> 30 mg/dl almost up to 225 minutes post ingestion, where they had an initially undetectable level [12].

Salicylate toxicity management revolves around prompt recognition and a stepwise approach to enhance elimination and prevent systemic complications. Gastrointestinal decontamination with activated charcoal is recommended if ingestion is recent. Sodium bicarbonate infusion remains a cornerstone of therapy, facilitating both urine and systemic alkalinization, thereby reducing salicylate penetration into the central nervous system and enhancing renal excretion [10,13]. However, bicarbonate therapy necessitates close monitoring of potassium levels, as hypokalemia impairs urinary alkalinization and can exacerbate toxicity. There is no well-validated dose of sodium bicarbonate for intoxication, but initial bolus doses of an 8.4% solution (1-2 mEq/kg) followed by continuous IV infusion of combined solution of 150 mEq/l of sodium bicarbonate in dextrose 5%water with additive potassium chloride at 1.5-2 times maintenance to target urine output of 1.5-2 ml/kg/hour, while aiming for a urine pH of 7.5-8, are recommended [14,15]. Patients with anuric renal failure should be evaluated for renal replacement therapy rather than receiving intravenous sodium bicarbonate.

Extracorporeal removal such as hemodialysis or haemoperfusion, is a life-saving intervention indicated in severe poisoning with high salicylate concentrations [>7.2 mmol/l (100 mg/dl)] or end-organ damage, such as altered mental status, acute kidney injury, respiratory failure, severe acidosis (pH <7.20), or when toxicity persists despite alkalinization [13]. Our patient required CVVH due to progressive deterioration, a modality that has been increasingly utilized when conventional alkalinization proves insufficient. Although hemodialysis remains the preferred extracorporeal modality due to its superior clearance of salicylates, CVVH is a viable alternative in hemodynamically unstable patients or when intermittent dialysis is unavailable. Exchange transfusions are recommended for neonates. Extracorporeal membrane oxygenation might act as a bridge therapy, providing oxygenation and removing carbon dioxide from the blood, thereby supporting the respiratory system and allowing time for the body to recover from the toxic effects of aspirin while applying other treatment measures to enhance aspirin elimination [13].

Conclusion

This case underscores the possibility of delayed aspirin toxicity in pediatric patients and serves as a cautionary tale about the potential risks associated with diagnosing aspirin intoxication. Early consultation with a toxicologist and a systematic escalation of care, including bicarbonate infusion and extracorporeal clearance when necessary, are crucial for optimizing patient outcomes. By recognizing these essential management principles, we can enhance early identification and intervention in cases of pediatric salicylate poisoning, ultimately reducing morbidity and mortality.

Conflict of interest

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Consent for publication

Due permission was obtained from the parents of the patient to publish the case.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee of Riyadh Second Health Cluster and with the OHRP/NIH, USA number IRB00010471. Date: July 2024.

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