

CASE STUDY: SALICYLATE TOXICITY

One in a series of case studies developed to stimulate enhancement of problem-solving techniques for physicians and nurses when challenged by patients who present with unusual or complex clinical syndromes.

These case studies are intended primarily for the medical, nursing and paramedical staff of Santa Rosa Memorial Hospital one of our sponsor hospitals.

HISTORY

A 48-year-old male is brought to the Emergency Department by his mother, with the complaint from the mother of the patient not acting like himself. Most history is obtained from the mother as the patient is a poor historian. She states for the last three days he has not been acting like himself. He has a history of Huntington's Chorea and a psychiatric disorder and for those reasons is usually hard to talk to, but these last three days he has been worse. She relates the onset of these symptoms to his taking a long walk on a very hot day. Since then she has noticed that he seems flushed and "is having trouble breathing." She thought this was all related to his walk, but the symptoms have become worse with the passage of time. She is describing him as becoming more confused and "not making sense" when he talks. The mother is able to tell us that he has had a recent change in his meds, having been taken off of amitriptyline and Buspar and put on Serzone, an antidepressant. He reportedly took only two doses of the Serzone and has had none since (this was three days ago) because it made him feel bad. The patient himself has no complaints, "I feel fine, there is nothing wrong." The mother reports the patient has otherwise been eating, drinking, and without other symptoms.

PHYSICAL EXAMINATION

Blood pressure: 106/65, respirations: 24, pulse: 90, no fever.

Generally, a well-developed male with mild facial erythema and diaphoresis who does not otherwise appear ill.

Head and neck show pupils 4mm and reactive, moist membranes.

Neck is supple.

Respiratory: Increased rate but lungs are clear. No stridor.

Heart: normal.

Abdomen: soft, bowel sounds normal.

Extremities: He does have occasional choreiform movements of the arms consistent with his history.

Neurologic: He is awake and oriented to person and place. He is mildly confused regarding time and date. He answers very simple questions and responds with well-formed words but does not form sentences. There are no focal findings.

Preliminary tests: accucheck sugar at 98 and a pulse ox of 98%.

How would you proceed from here?

Send the patient home with his mother and tell him to take his Serzone?

Refer the patient to his psychiatrist?

Order further tests? Which ones?

Make sure you formulate a plan before you go on...

COURSE IN THE EMERGENCY DEPARTMENT

More tests were ordered which demonstrated a WBC of 13.8 with 19 bands. Chemistries: sodium of 142, potassium of 3.7, chloride of 100, bicarbonate of 14, and glucose of 120. Urinalysis is normal, as are the chest x-ray and ECG.

An ABG is then ordered which demonstrates a pH of 7.3, pCO₂ of 19.7, pO₂ of 79.2, and bicarbonate of 12.

What is your interpretation of these tests? What calculation would be helpful?

The bicarbonate of 14 was key; it led the physician to order the arterial blood gases. The blood gas results demonstrate a partially compensated metabolic acidosis.

When confronted with such a situation it is of considerable value to calculate the anion gap.

What is the anion gap? How is it calculated? How can it help us to form a diagnosis? Make sure you consider these questions before you proceed.

The anion gap is the difference between the commonly measured positive and negative ions in the serum, namely sodium (a cation) and chloride and

bicarbonate (anions). The calculation is sodium – (chloride + bicarbonate) = anion gap. The normal difference is 10-15 mEq/L reflecting unmeasured anions in the serum. When the anion gap is greater than 15, investigation as to what pathological condition has resulted in the production of a greater amount of unmeasured anions is in order. Calculation of the anion gap in this case is sodium 142- (chloride 100 + bicarbonate 14) or $142 - (100 + 14) = 28$ mEq/L. So investigation is imperative.

A common mnemonic to help consider the causes of increased anion gap is SLUMPED:

- S- Salicylate, seizure
- L- Lactic acid
- U- Uremia
- M- Methanol
- P- Paraldehyde
- E- Ethanol (alcohol), ethylene glycol
- D- Diabetic ketoacidosis.

What other questions should you ask his mother? Are more tests indicated?

The patient's mother states the patient has a history of excessive alcohol use, but not in the recent past. He has never had a seizure. When asked about other medications or ingestions she responds, "he takes aspirin all the time for headaches. He takes them by the handful."

An aspirin level is ordered and comes back 107 mg/dL, which is very high. The patient is admitted. His course is stormy and complicated by pulmonary edema requiring endotracheal intubation and ventilation. With proper treatment he returns to near his normal baseline function by the time of discharge.

DISCUSSION

Salicylate toxicity takes two forms: chronic and acute. Each has similar metabolic effects but the timing and severity of the symptoms and signs will differ. The mechanism of toxicity, in this gentleman's case, included a direct stimulation of the respiratory center in the brainstem resulting in hyperventilation. If the arterial blood gases had been measured in an earlier phase of his illness they almost certainly would have demonstrated a respiratory

alkalosis, with a pH greater than 7.45 and a bicarbonate at normal or near normal levels. The body will typically attempt to compensate for a respiratory alkalosis by excreting bicarbonate, which occurred in this case.

On a cellular level, aspirin causes an uncoupling of oxidative phosphorylation and disrupts metabolism of glucose and fatty acids, which contributes to a metabolic acidosis. Aspirin will also inhibit platelet function and increase bleeding time. By unclear mechanisms aspirin toxicity can also cause pulmonary and cerebral edema.

- Doses which cause toxicity vary for acute and chronic poisoning situations. In an acute poisoning, doses of 150-500 mg/Kg can cause mild to severe toxicity. In the chronic ingestion category, doses of 100 mg/Kg per day for as little as 2 days can lead to toxicity. In a 70Kg person this would represent ingestion of only 20-25, 325mg aspirin tablets in a 24-hour period.
- Signs of acute toxicity include vomiting, increased respiratory rate, ringing in the ears, and decreased level of consciousness from lethargy to coma. Hypoglycemia and hyperthermia can occur. Chronic intoxication syndromes exhibit the symptoms and signs similar to those manifested in the acute intoxication but tend to be more subtle (as in this case) and are often confused with other diagnoses. Cerebral and pulmonary edema are more common in the chronic toxicity case.
- Lab tests are very helpful and should be considered in all overdose patients and in patients with an anion gap acidosis. When dealing with a patient who has experienced an acute ingestion there is a toxicity nomogram for determining level of toxicity. **The nomogram should not be used for chronic ingestion.**

Treatment is, of course, to support vital functions as needed. There is no specific antidote for aspirin toxicity but activated charcoal should be given for all acute cases in which the ingestion has been less than one-hour prior or involve enteric coated aspirin products as these can form bezoars resulting in delayed absorption and toxicity. Another treatment is urinary alkalinization with bicarbonate in the IV fluids. This mode of treatment is effective in increasing urinary excretion of the salicylate. In severe cases with very high levels and in cases with profound central nervous system changes, hemodialysis is the treatment of choice. It is both rapid and effective in removing the salicylate.

Hemodialysis is also recommended for any patient who develops signs of pulmonary or cerebral edema.

CONCLUSIONS

This was a tough case particularly because of the fact the patient is a poor historian. However a basic chemical panel which demonstrated a bicarbonate of 14 which is distinctly abnormal, helped direct the staff toward a series of tests and considerations which ultimately led to the correct diagnosis.

It is also important to note medical personnel should pay close attention to the patient and family when they provide a history. This patient's mother said "her son wasn't acting right" and she was correct. The patient's psychological and neurological history was a significant factor in terms of necessity to go to a "significant other," in this case his mother, to "fill in the blanks".

A clinical factor of importance was the increased respiratory rate (24). This is an abnormal respiratory rate. The diligent physician should undertake an investigation as to the reason the patient was breathing fast especially in view of the fact the breathing was unlabored and the breath sounds were normal. It is important to note the body's protective and normal response to a metabolic acidosis is to breathe fast, ("blow off" CO₂). This patient was ultimately placed on a ventilator and it would have been an error to ventilate him at a slow rate as this would have resulted in a worsening of the acidosis by taking away his capacity to compensate for the acidosis by hyperventilating.

KEY POINTS

- Subtle changes in mental status are important.
- Subtle changes in vital signs can be very helpful, particularly in toxicology syndromes.
- Pay close attention to abnormal electrolyte findings.
- Always consider the "anion gap" when confronted with acidosis.
- Obtain aspirin and acetoaminophen levels on all overdose patients.
- Believe the caretaker who states the patient is "not acting right."

Putting all of these key clues together resulted in the correct diagnosis and initiation of proper treatment with a positive outcome.

We would welcome any questions or comments about this case study. We would also welcome any suggestions relevant to developing a case study from an interesting case involving your unit and REACH.

Let us hear from you. Should you desire to read previously published case studies and the opportunity to receive additional CEUs, visit our website at www.reachair.com. You can do so online.

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CASE STUDY

POST TEST

SALICYLATE TOXICITY QUESTIONS: choose **all** correct answers

1. What is the upper limit of a normal anion gap?
 - A. 5 mEq/L
 - B. 10 mEq/L
 - C. 15 mEq/L
 - D. 20 mEq/L

2. Anion gap is calculated by...
 - A. Sodium – (chloride + BUN) = anion gap
 - B. Chloride – (sodium + potassium) = anion gap
 - C. (sodium – bicarbonate) + CO₂ = anion gap
 - D. Sodium – (chloride + bicarbonate) = anion gap

3. Late in the course of aspirin toxicity arterial blood gases will most likely demonstrate...
 - A. Partially compensated metabolic acidosis
 - B. Partially compensated respiratory acidosis
 - C. Partially compensated metabolic alkalosis
 - D. Partially compensated respiratory alkalosis

4. Which one of the following persons (70Kg) is likely to demonstrate signs of chronic salicylate toxicity?
 - A. One time ingestion of 100 - 325 mg aspirin tablets
 - B. Ingestion of 10 - 325 mg aspirin tablets over the course of 24 hours
 - C. Ingestion of 24 - 325 mg aspirin tablets over the course of 24 hours
 - D. Ingestion of 20 - 600 mg ibuprofen tablets over 24 hours

5. Early in the course of acute salicylate toxicity the most likely pH of arterial blood will be...
 - A. > 7.45
 - B. 7.40
 - C. < 7.35
 - D. < 7.25

6. Some signs of acute salicylate toxicity include: (Choose the one which does NOT apply)
 - A. Vomiting
 - B. Increased respiratory rate
 - C. Decreased level of consciousness
 - D. Hypoglycemia
 - E. Metallic taste

7. Treatment of severe salicylate toxicity could include: (Choose the one which does NOT apply)
 - A. Alkalinization of urine
 - B. IV infusion of bicarbonate
 - C. Slowing the rapid respiratory rate by chemical paralysis and sedation
 - D. Support of vital functions
 - E. Hemodialysis

