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Approach to metabolic acidosis in pediatric patients

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Introduction:

Hello, and welcome to the PedsCases podcast on an approach to metabolic acidosis in pediatric patients! My name is Ro and I am a third-year medical student at the University of British Columbia. This podcast was developed in collaboration with Dr. Irina Simin, a pediatric resident at UBC, and Dr. James Harris, a community pediatrician based in Fraser Health and a clinical associate in the PICU at BC Children's Hospital and NICU at Surrey Memorial Hospital.

This podcast will discuss an approach to metabolic acidosis in the pediatric patient, using a case of diabetic ketoacidosis, or DKA, for reference. For more details about the presentation and treatment of DKA, please review the PedsCases podcast on DKA[1]. For a more thorough approach to acid-base physiology, compensatory mechanisms, and arterial blood gas interpretation, please reference the PedsCases podcast on "approach to acid-base disturbance"[2].

Objectives:

By the end of this podcast, listeners will be able to:

1. Define metabolic acidosis, and differentiate it from respiratory acidosis
2. Describe common clinical presentations of metabolic acidosis that should prompt blood gas interpretation
3. Outline the differential diagnosis for metabolic acidosis
4. Interpret lab findings to help guide diagnosis
5. Demonstrate an approach to the management of metabolic acidosis

With that, let's get into our case!

Case:

Jonah is a 10-year-old boy brought to the emergency department by his dad. He has been feeling unwell for a few days, but today he became confused and has had worsening fatigue. A couple of hours ago he developed non-bloody, non-bilious vomiting. His dad has never seen him like this before and is quite worried, so he brought him into the emergency department for assessment.

On further history, you find out that Jonah is previously healthy, with no known health conditions. His dad denies any known sick contacts, and there have been no fevers, injuries or toxic ingestions that he knows of. He says Jonah started having less energy over the past 3 days, but this has progressively worsened. His dad tried to get him to eat today, but Jonah could

not keep anything down. He has not had any diarrhea, and in fact, he hasn't had a bowel movement today at all. His dad reflects that Jonah has been peeing with increased frequency, now that you ask, though he hasn't complained of any pain with urination, and when asked about any blood in his urine, he shrugs and says, "I don't think so". He says he's probably peeing so much because he has been so thirsty and drinking a lot of water. Jonah's dad also reflects that he thinks Jonah might have lost some weight as his clothes appear to be looser than usual.

On family history, Jonah has a younger sister who has asthma but is otherwise healthy. His parents are both healthy as well.

On exam, you note that Jonah looks quite unwell. You check his vitals, which are as follows:

- HR: 125 BPM
- RR: 35 breaths per minute
- Blood pressure: 92/68
- Temperature: 37.1°C
- He is saturating 99% on room air

Jonah is displaying signs of respiratory distress, so you start with a respiratory exam. You note that along with his tachypnea, he has significant intercostal and supraclavicular retractions suggesting deeper rapid breaths. On percussion, the lungs are resonant bilaterally and on auscultation, his lungs are clear bilaterally to the bases, and you do not appreciate any crackles or wheezes.

You move on to the cardiovascular exam and note that Jonah's radial pulses are regular and symmetrical, but somewhat soft. His capillary refill is 3-4 seconds, and you auscultate a normal S1/S2 without any added heart sounds or murmurs.

His abdominal exam is benign, with no evidence of distention. You hear bowel sounds in all four quadrants, and his abdomen is soft and non-tender to superficial and deep palpation. There is no evidence of hepatosplenomegaly.

Neurologically, he is demonstrating slight confusion and an altered level of consciousness. He is drowsy but not lethargic. His GCS is 14.

Given his respiratory distress, you order some investigations:

- His venous blood gas, or VBG, and the rest of his labs come back as follows:

pH	7.14	Na^+	135 mmol/L	Cr	65 µmol/L
pCO_2	23 mmHg	K^+	3.0 mmol/L	Hgb	150 g/L
pO_2	44 mmHg	Cl^-	100 mmol/L	WBC	18 x 10^9/L
HCO_3	10 mmol/L	Glucose	25 mmol/L	Plt	460 x 10^9/L
BE	-21 mmol/L	BUN	22 mmol/L	Lactate	2.0 mmol/L

- Beta Hydroxybutyrate: 8.5
- Urinalysis is positive for glucose and ketones
- Liver enzymes, lipase, and CXR findings are within normal limits, ECG shows sinus tachycardia
- A blood culture is taken and pending

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Before we start interpreting these results, focusing on the VBG, let's go over some definitions:

- Metabolic acidosis is a process that increases the concentration of hydrogen ions and decreases the concentration of bicarbonate in the blood. This is in contrast to respiratory acidosis, which is a process that results in carbon dioxide buildup[3].
- Acidemia is a low blood pH (< 7.35) which occurs as a result of these processes.
- Base excess describes the amount of acid that must be added to a sample at standard conditions (in other words, 37 degrees and PCO2 40) to reach a pH of 7.40 and can be used to quickly identify metabolic vs. respiratory contributions of a pH disturbance. It can be interpreted as follows: if it is positive, it indicates metabolic alkalosis, or respiratory acidosis with renal compensation, and if it is negative, it indicates metabolic acidosis, or respiratory alkalosis with renal compensation[4].
- I also want to acknowledge that, technically, an arterial blood gas, or ABG, is the gold standard for acid-base interpretation[3]. However, the VBG or CBG serve as reasonable proxies, and are more often used clinically, especially in children.

So in this case, we can say that Jonah has acidemia, with a pH of less than 7.35, and we know that it is a metabolic acidosis driving this because his bicarbonate is below the normal range and he has a substantially negative base excess. Of note, his CO2 is low due to a compensatory hyperventilation pattern to blow off extra CO2.

Our second objective was to describe typical presentations of metabolic acidosis, so let's talk about which features of acute metabolic acidosis Jonah is presenting with. We can split it up into respiratory, neurologic, and cardiac effects. Jonah is presenting with tachypnea and hypocapnia. This is due to respiratory compensation that attempts to correct a metabolic acidosis. Patients may present with a breathing pattern of fast, deep respirations, referred to as Kussmaul respirations. Thinking about neurologic manifestations, Jonah is presenting with an altered mental state and fatigue. With severe cases of metabolic acidosis you may also see more profound altered mental status, lethargy, as well as seizures, ataxia, hypotonia, muscle weakness, vision, or hearing impairments. From a cardiac perspective, arrhythmias may be seen with severe acidemia (pH < 7.1), and tachycardia is a common manifestation[3]. In Jonah's case his tachycardia is likely compounded by dehydration.

While not as relevant in this case, it is important to note manifestations of chronic metabolic acidosis, which include poor growth and skeletal muscle wasting, decreased bone mineral content, and nephrolithiasis and nephrocalcinosis[3].

Let's bring it back to our case. Thinking of Jonah's presentation, and his accompanying lab values, we need to think about what might be causing this. Let's go over an approach to the differential diagnosis for metabolic acidosis:

The first step in thinking about the potential causes of a metabolic acidosis is to classify it as an anion gap metabolic acidosis (or AGMA) vs. a non-anion gap metabolic acidosis (or NAGMA). Note that you may also hear terms such as "high anion gap metabolic acidosis, HAGMA", or "wide anion gap metabolic acidosis, WAGMA". In this podcast, I will use AGMA to refer to metabolic acidosis with an anion gap above the normal range. The anion gap is the difference between measured cations (Na+, K+) and measured anions (HCO3-, Cl-), where the normal is 12 or 16, depending on whether K+ is included. Since sodium, potassium, bicarbonate and chloride are the commonly measured ions, and make up a significant portion of circulating ions, they are the ones that we include in our calculations. The anion gap represents the

unmeasured anions that are not included in our calculation, such as phosphate and albumin. Think of it this way: the human body does not have a net charge, so we know that there must be an equal number of anions and cations. In an AGMA, the anion gap is elevated above the normal range, suggesting that there are more unmeasured anions in circulation than expected whereas in a NAGMA, there are not[5,6]. Now, you might be wondering what the significance of all of this is in our workup, and it's because these categories guide our differential diagnosis[3,6]!

For an AGMA, a common mnemonic is CAT MUDPILES, which represents:

- Carbon monoxide or cyanide, or congenital heart failure
- Aminoglycosides
- Theophylline, Toluene (glue sniffing)
- Methanol
- Uremia (due to kidney failure)
- Diabetic/alcoholic/starvation ketoacidosis
- Paracetamol/acetaminophen
- Iron, isoniazid, inborn errors of metabolism
- Lactic acidosis (usually secondary to sepsis)
- Ethanol (due to lactic acidosis), ethylene glycol
- Salicylates/ASA/aspirin

For a NAGMA, a mnemonic we can use is ABCD:

- Addison's disease (adrenal insufficiency)
- Bicarbonate loss, which can be through the GI or renal systems, for example in severe diarrhea or renal tubular acidosis when the kidneys are unable to acidify urine
- Chloride excess
- Diuretics, such as acetazolamide

It's important to note that multiple processes may be occurring simultaneously and contributing to the overall pH of the blood, and you may see a mixed NAGMA and AGMA. You can characterize a secondary process with a delta/delta, which is a calculation that compares the relative change in anion gap to the relative change in the bicarbonate concentration and look for compensation. We will come back to this in a minute.

Looping back to our case, let's calculate Jonah's anion gap, which again is calculated by adding the concentrations of sodium and potassium, and subtracting the concentrations of bicarbonate and chloride. In our case, the result is 28. Remember that for an anion gap calculated with the inclusion of potassium, the normal range is 16 +/- 4, so we can identify that Jonah has an elevated anion gap metabolic acidosis, or AGMA, contributing to his acidemia.

Let's also calculate the delta/delta to look for concurrent processes. Delta/delta is calculated by the difference between the measured anion gap and the normal anion gap, divided by the difference between the normal concentration of bicarbonate and the measured concentration of bicarbonate.

Let's talk about how to interpret the delta/delta ratio[7]:

- If it's less than 0.4, this represents a normal anion gap metabolic acidosis (or NAGMA)
- If it's between 0.4 and 0.8, this represents a mixed NAGMA and AGMA, and suggests concurrent acidotic processes
- If the delta/delta ratio is between 0.8 and 2, this represents a pure AGMA

- And if it's greater than 2, this demonstrates concurrent AGMA and pre-existing metabolic alkalosis or compensated respiratory acidosis

Now that we have a framework for approaching the delta/delta ratio, let's calculate it for our case! Jonah's measured anion gap is 28, which is 12 above the normal value of 16, since we've included potassium. His bicarbonate concentration is 10, which is 14 below the normal value of 24. So, his delta/delta ratio is 12/14 = 0.857. Based on our definitions of delta/delta values above, we can interpret Jonah's acidemia to be the result of a pure AGMA.

Let's go back to our differential diagnosis to provide an explanation for Jonah's presentation. Because we have determined that Jonah's presentation and delta/delta ratio are consistent with a pure AGMA, we can focus our thinking on CAT MUDPILES.

Recall that on history, Jonah and his dad reported polyuria, polydipsia, vomiting, weight loss, and lethargy. Our physical exam identified respiratory distress in a Kussmaul breathing pattern, and signs of dehydration, and that notable investigations included the following:

- Bloodwork was significant for hyperglycemia, positive ketones, leukocytosis, uremia, elevated lactate and creatinine
- Urine was positive for glucose and ketones
- ECG showed sinus tachycardia

With this history, clinical presentation, and supporting investigations, you make a diagnosis of diabetic ketoacidosis, or DKA!

Given that we have a clear cause of metabolic acidosis from our current investigations, we would likely initiate treatment at this point. However, if a diagnosis was not evident from results of our initial investigations, we would consider further workup to investigate other causes from our CAT MUDPILES differential. A low index of suspicion should be considered when the diagnosis is uncertain. To further investigate other differentials under the umbrella of AGMA, we could consider the following:

- We would do a basic serum toxicology screen measuring acetaminophen, salicylates, and ethanol levels[3]
- We would also assess the osmolar gap, or OG, which can support suspicion of a toxic ingestion by identifying unmeasured osmoles. Going back to basics, osmolarity is the number of particles in 1 L of solvent. The osmolar gap is defined by the difference between the measured osmolarity and calculated osmolarity. The measured osmolarity is a value reported by the lab, and the calculated osmolarity is a sum that includes two times the concentration of sodium, plus the concentrations of urea, glucose, and ethanol. A normal osmolar gap is generally less than 10. An elevated OG indicates the presence of an osmotically active compound that is not being measured, such as one of the toxic alcohols: ethylene glycol, methanol, or isopropanol[8]. Note that other causes of metabolic acidosis can also elevate the osmolar gap, but a very high osmolar gap, for example over 20-30, increases the likelihood of a toxic ingestion of the above-mentioned alcohols, which can be found in household and industrial products such as hand sanitizer, rubbing alcohol, windshield wiper fluid, antifreeze, paint removers, and degreasing agents, among others.

Now that we've gone over some investigations to work up an underlying cause of metabolic acidosis, let's talk a little bit about management! The mainstay of management is to treat the

underlying pathology, whether that be septic shock, chronic kidney disease, toxic ingestion, or in our case, DKA[3].

Looping back to our case, after the diagnosis of DKA is made, the team follows the local DKA protocol, with careful consideration of Jonah's fluid deficit and ongoing fluid maintenance, as well as his insulin, potassium, and dextrose requirements. His electrolyte, acid-base and fluid status are frequently monitored and adjustments are made as required. His glucose is checked every hour, and insulin and dextrose rates are adjusted to achieve slow and steady progress toward target blood glucose range[9].

Six hours later in his course, Jonah has improved clinically, and his repeat labs come back as follows:

pH	7.28	Na^+	135 mmol/L	Cr	58 µmol/L
pCO_2	30 mmHg	K^+	5.0 mmol/L	Hgb	149 g/L
pO_2	40 mmHg	Cl^-	112 mmol/L	WBC	15 x 10^9/L
HCO_3	14 mmol/L	Glucose	16 mmol/L	Plt	462 x 10^9/L
BE	-10 mmol/L	BUN	20 mmol/L	Lactate	1.0 mmol/L

Note that the pH is still acidotic at 7.28. You quickly recalculate his anion gap, which is now 14, which is in the range of a normal anion gap (16 +/- 4). So, it seems like we've done a good job of treating the AGMA, but now we still have a NAGMA, which brings us back to our differential diagnosis for NAGMA. Remember the mnemonic ABCD, which stood for Addison's disease (or adrenal insufficiency), bicarbonate loss (GI or renal), chloride excess, or diuretics.

In this case, the history can be used to suggest a hyperchloremic metabolic acidosis, given the rehydration with normal saline. This is commonly seen in the treatment of DKA with normal saline, and is an accepted side effect of treatment, although it may contribute to delaying the resolution of the acidemia.

Generally speaking, in other cases of NAGMA, other aspects of a history such as a known bicarbonate loss through diarrhea can also be used to guide diagnosis and management. However, if the history is not convincing for a known cause of NAGMA, there are further steps that we can use to characterize the mechanism of bicarbonate loss. We can do this by calculating the urinary anion gap to help us differentiate between GI and renal causes of metabolic acidosis, and urine osmolar gaps to further characterize the process. For further details about these calculations, EMCrit Project's summary of Non-Anion-Gap Metabolic Acidosis is a great resource to reference[10].

As a general note on the topic of metabolic acidosis treatment, IV sodium bicarbonate is sometimes used in pediatric cases of severe acidemia and chronic kidney disease, but this use is limited due to high risk of electrolyte derangements, cerebral edema, and adverse cardiovascular events[3]. Note that, in general, this is not done with a pH that is above 7, though specific practices are site- and practitioner-dependent. The Canadian Pediatric Society actually recommends against its use for DKA metabolic acidosis specifically[9]. Routine use of bicarbonate is not recommended and expert opinion should be consulted.

Getting back to our case, you are satisfied with the progress that Jonah is making, and continue on with the DKA care plan. You return the next day and Jonah is looking and feeling much better, and his repeat labs show that his DKA and acidosis have corrected!

His family thanks you and shares that the endocrinology team has already started teaching around managing Jonah's new diagnosis of Type 1 diabetes.

For further details about the treatment of DKA, please refer to the PedsCases podcast about diabetic ketoacidosis!

With that, we have reached the end of our case! Let's review a few clinical pearls:

1. Remember that metabolic acidosis is any process that increases the concentration of hydrogen ions and decreases the concentration of bicarbonate in the blood, and that there can be multiple co-existing processes driving an acidemia.
2. The clinical presentation of metabolic acidosis can be broad and can have manifestations in the cardiac, respiratory, and nervous systems. Order blood-gas investigations if you are suspicious of acidosis!
3. The differential diagnosis for metabolic acidosis is broad. Use the anion gap and other acid-base calculations to help guide your investigations and diagnosis.
4. Remember that the most important aspect of managing metabolic acidosis is to treat the underlying cause!

I hope you feel more confident with the objectives, which were to:

1. Define metabolic acidosis, and differentiate it from respiratory acidosis
2. Describe common clinical presentations of metabolic acidosis that should prompt blood gas interpretation
3. Outline the differential diagnosis for metabolic acidosis
4. Interpret lab findings to help guide diagnosis
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Thank you so much for listening and thank you to Dr. Irina Simin, Dr. James Harris, and the PedsCases team for all of their support with this project!

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References

1. Rumley C. Diabetic ketoacidosis [Internet]. 2018 [cited 2024 Jun 5]. Available from: https://www.pedscases.com/diabetic-ketoacidosis
2. Girgulis K. Approach to acid base disturbance [Internet]. 2018 [cited 2024 Jun 5]. Available from: https://www.pedscases.com/approach-acid-base-disturbance-0
3. Yorgin P, Mak R. Approach to the child with metabolic acidosis [Internet]. Wolters Kluwer; 2023 [cited 2024 Jun 5]. Available from: https://tinyurl.com/2ejjscwk
4. Langer T, Brusatori S, Gattinoni L. Understanding base excess (BE): Merits and pitfalls. Intensive Care Medicine. 2022 May 31;48(8):1080–3. doi:10.1007/s00134-022-06748-4
5. Pandey DG. Biochemistry, anion gap [Internet]. U.S. National Library of Medicine; 2023 [cited 2024 Jun 5]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539757/
6. Nickson C. Anion Gap [Internet]. Medmastery; 2020 [cited 2024 Jun 5]. Available from: https://litfl.com/anion-gap/
7. Nickson C. Delta ratio [Internet]. Medmastery; 2021 [cited 2024 Jun 5]. Available from: https://litfl.com/delta-ratio/
8. Farkas J. Pulmcrit- toxicology dogmalysis: The Osmolal Gap [Internet]. 2017 [cited 2024 Jun 5]. Available from: https://tinyurl.com/46n4ya67
9. Gripp KE, Trottier ED, Thakore S, Sniderman J, Lawrence S. Current recommendations for management of paediatric diabetic ketoacidosis [Internet]. Canadian Paediatric Society; 2022 [cited 2024 Jun 5]. Available from: https://tinyurl.com/5872jrpw
10. Farkas J. Non-anion-gap metabolic acidosis (Nagma) [Internet]. 2023 [cited 2024 Jun 5]. Available from: https://emcrit.org/ibcc/nagma/

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