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Hypophosphatemia, hypokalaemia and rhabdomyolysis associated with a panic attack

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SUMMARY

Panic attacks have been associated with hypophosphatemia, which can lead to numerous complications if unrecognised. Here, we present the case of an otherwise-healthy man in his 20s who experienced a panic attack accompanied by hypophosphatemia and hypokalaemia and subsequently developed rhabdomyolysis. This trajectory highlights the clinical significance of panic attack-associated metabolic derangements and their potential for medical complications such as rhabdomyolysis.

BACKGROUND

Panic attacks are diagnosed clinically and usually without the need for laboratory testing; thus laboratory abnormalities are not typically identified. However, hypophosphatemia is a well-recognised laboratory finding in patients with acute panic attacks and panic disorder.[1 2] The prevalence and clinical significance of this finding are not well established, but hypophosphatemia poses risk for numerous medical complications including myopathies resulting in dysphagia, cardiac dysfunction and respiratory failure, as well as seizures and coma. There are reports of acute complications from panic-related hypophosphatemia including lactate elevation[3] and episodic weakness,[4] as well as immune-mediated signalling associated with panic disorder,[5 6] but panic-related rhabdomyolysis has not been reported. This case demonstrates an uncommon instance of rhabdomyolysis deemed secondary to metabolic derangements during an acute panic attack.

CASE PRESENTATION

A man in his early 20s with no prior medical conditions presented to the emergency department for palpitations, shortness of breath, throat tightening, lightheadedness, tingling in the extremities and a sensation that the world was closing in on him. His symptoms began that morning; he had just worked an overnight shift as a technician in a hospital, drank an energy drink and played a light game of basketball but denied strenuous physical activity. Immediately prior to the onset of symptoms, he was feeling abnormally anxious and emotional regarding a recent breakup. A video he recorded of himself during the car ride to the hospital showed him pale, mildly tremulous, anxious appearing, seated upright and speaking normally.

According to the patient, and per recent primary care notes, he had been experiencing significant anxiety in the preceding weeks but never had a panic attack before. He had a family history only of hypertension and stroke in his parents. He had last exercised using resistance bands at home 3 days prior to admission in a routine, not particularly strenuous workout. He had no recent illness, sick contacts, travel, atypical ingestions or notable supplement/drug use other than an energy drink and occasional marijuana from a legal local source.

On presentation, he was tachycardic to 135 bpm, tachypneic with a respiratory rate of 29 breaths/min, his blood pressure was 110/60 mm Hg, his peripheral oxygen saturation was 96% on room air and his temperature was 37.1°C. Physical examination was significant only for an anxious appearance, diffuse flushing across the face and chest and normal and symmetric strength in all extremities.

INVESTIGATIONS

A chest X-ray was without abnormality, and ECG showed sinus tachycardia. Laboratory test results are shown in table 1. Notably, he exhibited hypophosphatemia to 0.45 mmol/L, hypokalaemia to 2.8 mmol/L, leukocytosis to 20.2×10^9/L and creatine kinase (CK) was elevated to 1192 U/L. A venous blood gas measurement was obtained approximately 1 hour after the initial laboratory abnormalities were discovered and showed pH 7.41 (reference range 7.32–7.42), partial venous pressure of carbon dioxide 36.6 mm Hg (reference range 40–50 mm Hg) and a calculated bicarbonate of 23 mmol/L (reference range 22–26 mmol/L).

Given the concern for developing rhabdomyolysis, he was admitted to the hospital. On day 2 of hospitalisation, his serum CK level increased to 4942 U/L, and he began to experience diffuse muscle pains most prominent in the bilateral arms and chest. Given the elevated CK and new myalgias, he was diagnosed with rhabdomyolysis. Lab values trended over his 4-day admission (and follow-up outpatient labs on day 8) are shown in table 1.

DIFFERENTIAL DIAGNOSIS

With regards to his presenting symptoms, a diagnosis of panic attack was made based on The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria: he experienced a discrete transient period of intense discomfort with palpitations, shortness of breath, lightheadedness and fear of dying.

Regarding the observed hypophosphatemia and hypokalaemia, we considered the possibility of acute volume loss via vomiting or diarrhoea; however, the patient denied both of these. We also considered the possibility of euglycemic diabetic

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Table 1 Laboratory test results

Lab test	Reference range	Day 1	Day 2	Day 3	Day 4	Day 8
White blood cells	4–11 x 10^9/L	20.2	8.8	7.2	8.4	7.1
Haemoglobin	135–177 g/L	152	142	147	146	157
Platelets	150–400 x 10^9/L	421	282	273	284	309
Sodium	135–145 mmol/L	138	139	140	136	140
Potassium	3.5–5.5 mmol/L	2.8	3.9	4.3	4.2	4.2
Chloride	98–107 mmol/L	97	106	103	100	101
Bicarbonate	22–29 mmol/L	15	21	25	25	25
Urea nitrogen	2.14–7.14 mmol/L	6.43	4.64	2.86	5.0	3.57
Creatinine	59.23–103.43 µmol/L	94.59	69.84	59.23	66.30	72.49
Calcium	2.1–2.63 mmol/L	2.42	2.33	2.23	2.33	2.27
Magnesium	0.66–1.07 mmol/L	0.82	0.99	0.86	0.91	0.95
Phosphorus	0.81–1.45 mmol/L	0.45	1.36	1.10	1.55	0.94
Total bilirubin	0–20.52 µmol/L	15.39	10.26	6.84	6.84	8.55
AST (SGOT)	10–50 U/L	52	103	262	258	54
ALT (SGPT)	10–50 U/L	46	45	70	92	94
Alkaline phosphatase	40–130 U/L	82	70	62	63	66
Albumin	35–52 g/L	51	42	39	40	45
Creatine kinase	0–190 U/L	1192	4942	16 615	11 598	463
D-dimer	0–2.74 nmol/L	<1.48				
Lactate	0–2 mmol/L	1.48				
Serum beta hydroxybutyrate	0.2–2.8 mmol/L	<0.2				
TSH	0.27–4.2 IU/mL	1.18				

ALT (SGPT), Alanine aminotransferase (serum glutamic-pyruvic transaminase); AST (SGOT), Aspartate aminotransferase (serum glutamic-oxaloacetic transaminase); TSH, Thyroid-stimulating hormone.

ketoacidosis, which can present with potassium depletion and normoglycemia, however, he had no known risk factors and serum beta-hydroxybutyrate was undetectable. Acute intoxications were also investigated, such as salicylate poisoning which can cause rhabdomyolysis; blood tests were negative for salicylates and ethanol, and urine toxicology was negative for opiates, amphetamines, phencyclidine and cocaine, and positive only for THC. Acute hypokalaemia and hypophosphatemia can also result from refeeding syndrome, though he had no prolonged period of fasting and malnutrition and his metabolic derangements resolved with minimal repletion as noted below.

Regarding the rhabdomyolysis, possible aetiologies included physical exertion, seizure, toxins, infection and the observed metabolic derangements. After review of laboratory tests and extensive discussions with the patient and his family, there were no environmental exposures, ingestions, clinical signs or sufficiently strenuous activities to support the former hypotheses, leaving his observed metabolic derangements (hypophosphatemia and hypokalaemia) as the likely cause of his rhabdomyolysis.

TREATMENT

Treatment was focused on the patient's panic attack, electrolyte derangements and rhabdomyolysis. He was first given 1 L of intravenous Lactated Ringer's and 1 mg of intravenous midazolam as well as 2 g of intravenous magnesium sulfate, 60 mmol of oral potassium and 20 mmol of intravenous sodium phosphate. After these interventions, his anxiety, tachycardia and tachypnoea resolved. Standard treatment for rhabdomyolysis consists of fluid administration and avoidance of acute kidney injury.[7] Accordingly, during the admission, he received continuous crystalloid fluid infusion and no new medications.

OUTCOME AND FOLLOW-UP

At no point during his hospitalisation there were abnormalities on cardiac telemetry or a supplemental oxygen requirement. His examination showed full strength symmetrically in all extremities at all points. His CK level peaked at 16 615 U/L on day 3, then downtrended on day 4, and his symptoms resolved the same day. He was discharged with plans to orally hydrate, avoid strenuous exercise, obtain repeat outpatient laboratory tests and follow-up with primary care and mental health services. Two months following hospitalisation, a follow-up visit with his primary provider revealed no recurrent episodes of these symptoms and no new laboratory abnormalities.

DISCUSSION

We presented a case in which a panic attack presented with hypophosphatemia, hypokalaemia and rhabdomyolysis. Panic attacks have been associated with hypophosphatemia in numerous case reports, and hypophosphatemia has even been proposed as a biomarker for panic disorder,[1–4] with serum phosphate levels being negatively correlated with anxiety level.[1] To our knowledge, this is the first report linking rhabdomyolysis to a panic attack with hypophosphatemia, though it has been hypothesised as a possible complication.[3]

One proposed mechanism for acute panic-related hypophosphatemia is via hyperventilation causing intracellular alkalosis, which in turn stimulates phosphofructokinase activity, increasing the rate of glycolysis and depleting phosphorus.[3 4] In addition to hypophosphatemia, acute hyperventilation can cause potassium to shift into the intracellular space, resulting in clinically significant hypokalaemia.[8 9] Both hypophosphatemia[10–12] and

hypokalaemia[13–15] can cause rhabdomyolysis, likely in part via adenosine triphosphate depletion and relative muscle ischaemia.[16 17] This mechanism of hyperventilation-associated alkalosis is a likely aetiology for the hypophosphatemia, hypokalaemia and rhabdomyolysis in this patient.

Consistent with this hypothesis, the aforementioned venous blood gas showed a reduced carbon dioxide tension indicative of a possible respiratory alkalosis, with pH on the high end of the reference range. It is worth noting that this was derived from venous rather than arterial blood, which is suboptimal for evaluating acid-base status but can be useful in the emergency department setting[18 19]; and that the patient's symptoms were resolving at the time of this measurement and, therefore, his hypocarbia and alkalosis were likely more extreme at initial presentation. It is also worth noting that the initial laboratory results showed an elevated anion gap of 26 mmol/L (calculated as sodium−(chloride+bicarbonate), with a reference range of 5–15 mmol/L); this may have been reflective of the developing rhabdomyolysis, which causes overproduction of organic acids[20] and could hypothetically contribute to a mixed acid-base status with simultaneous respiratory alkalosis and metabolic acidosis. While we are limited in our ability to conclusively evaluate some of these mechanistic hypotheses, there was a clear temporal association between the panic attack, electrolyte derangements and rhabdomyolysis.

A possible alternate explanation for the observations in this patient is hypokalaemic or thyrotoxic periodic paralysis, in which attacks occur after exercise or stress and can occasionally lead to rhabdomyolysis;[15] however, they are characterised primarily by weakness, which was not a primary feature of his initial or presenting symptoms; he was able to comfortably walk, drive and record himself en route to the hospital without he or those around him noting weakness. In addition, he had no personal or family history suggestive of electrolyte disorders or myopathies, and no identifiable reason to be prone to these electrolyte derangements. Another possible contributor to this presentation was the energy drink consumed by the patient; these drinks usually contain stimulants and have been associated with rhabdomyolysis in conjunction with vigorous exercise.[21] While this mechanism could increase susceptibility to rhabdomyolysis, our patient did not perform abnormally heavy exercise, nor would this explain the observed electrolyte abnormalities. Finally, while not present in this patient, prior reports of panic-related hypophosphatemia have been associated with lactate elevation,[3] and with intermittent weakness, pain, paresthesias and shaking, which were initially misattributed to chronic fatigue, anxiety and Lyme disease.[4]

We concluded that this patient experienced a panic attack leading to acute hypophosphatemia and hypokalaemia which triggered rhabdomyolysis. This rare but important complication demonstrates the need to consider and evaluate for medical complications arising from an otherwise typically self-resolving psychiatric condition. We suggest that patients presenting with panic attack accompanied by low phosphate or potassium levels should be evaluated for rhabdomyolysis.

Learning points

- Panic attacks and panic disorder are associated with hypophosphatemia.
- Acute panic attacks can present with metabolic derangements sufficient to trigger rhabdomyolysis.
- Measurement of creatine kinase and blood gas analysis should be considered in patients with anxiety-related symptoms and abnormal phosphate or potassium levels.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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