Acute Bilateral Compartment Syndrome Secondary to Polydipsia-Induced Severe Hyponatremia

Catherine Girard-Martel [1, 2], Melanie Gagnon [1]

Key Words: Compartment Syndrome, Hyponatremia, Primary Polydipsia, Psychogenic Polydipsia, Antipsychotics

Introduction

Acute compartment syndrome (ACS) occurs when the tissue pressure within a closed muscle compartment exceeds the perfusion pressure and results in muscle and nerve ischemia. ACS has an annual incidence of 3.1 per 100,000 and predominantly affects young men under the age of 35 because of their significant muscle mass (1). Bone fracture is the leading cause (75%) of ACS (1); however, several other nontraumatic etiologies have also been reported, including: thrombosis, bleeding diatheses, anticoagulation leading to hemorrhage/hematoma, ischemia-reperfusion injury, surgical positioning, limb compression, extravasation of intravenous fluids and drug injection (1). A few cases have also been described in diabetic patients with poor glycemic control (2), and one case has been reported secondary to primary hypothyroidism and adrenal insufficiency (3). To our knowledge, only two previous cases of ACS secondary to severe hyponatremia have been reported and both were patients with schizophrenia and primary polydipsia (4, 5). The case we present is the first of its kind in North America. Despite the rare progression to ACS, clinicians need to be aware of this possibility when seeing patients presenting with rhabdomyolysis in association with hyponatremia because treatment must be initiated promptly.

[1]CIUSSS Saguenay, Quebec City, Canada
[2]Foothills Medical Center-Critical Care, Calgary, Alberta, Canada

Address for correspondence: Dr. Catherine Girard-Martel, CIUSSS Saguenay, 305 Rue Saint Vallier, Chicoutimi, QC, Canada, G7H 5H6
Phone: 418-541-1234, #3535; Fax: 418-541-1019;
E-mail: catherine.girard-martel@usherbrooke.ca

Submitted: March 4, 2014; Revised: June 18, 2014;
Accepted: November 17, 2014

Case Report

A 43-year-old male presented to the emergency department with episodes of falling without any specific trauma to the legs and bilateral anterior leg pain over the preceding three days. His past medical history was significant for schizophrenia, metabolic syndrome and mild anemia secondary to hemorrhoids. Relevant medications included: olanzapine, sertraline, spironolactone/hydrochlorothiazide and rosuvastatin. He had experienced dry mouth as a side effect of his medications and had been drinking over 6L of water a day. Moreover, he had consumed approximately 4L of beer a day in the three days prior to his emergency room visit.

He complained of bilateral leg pain without any visible abnormalities on examination of both anterior tibial compartments. He was, however, unable to actively flex or dorsiflex both feet. Passive stretching of extensor muscles elicited severe pain. Neurologic exam demonstrated diffuse hypoesthesia of the feet without generalized muscle rigidity. Laboratory testing revealed mild leucocytosis ($18.6x10^9$/L), anemia (93 g/L), severe hyponatremia (114 mmol/L), increased serum lactate (5.8 mmol/L), and a significantly elevated creatine kinase level (9,068 UI/L). Given diagnostic concern for ACS, a surgical consult was immediately obtained and intracompartmental pressures were measured at 100 and 120 mmHg, respectively, in both anterior tibial compartments. Additionally, all other compartment pressures of the lower extremities were abnormal (>30 mmHg).

Emergent bilateral fasciotomies of all compartments of the lower extremities were performed as soon as the diagnosis was confirmed. The patient's hyponatremia resolved with water restriction alone and he did not develop renal insufficiency as a complication of his rhabdomyolysis. Anemia

worsened during hospitalization and upper and lower gastrointestinal endoscopy revealed findings of portal hypertensive gastropathy and bleeding from congested internal hemorrhoids, both of which were as a result of a new diagnosis of cirrhosis. Healing of the wounds required skin grafting (see Figure 1) and took several months, but fortunately the patient recovered complete neuromuscular function.

Discussion

Patients in the two previously published cases also carried diagnoses of schizophrenia and primary polydipsia. In a prospective observational study from Canada, the prevalence of polydipsia among an outpatient population with chronic mental illnesses was 15.7% (14/89 patients) and 90.4% of the polydipsia patients had a primary diagnosis of schizophrenia (6). Patients with schizophrenia and primary polydipsia may be at increased risk of hyponatremia when a superimposed cause of reduced water excretion is present, such as selective serotonin reuptake inhibitors (SSRIs), thiazide diuretics, increased alcohol intake and cirrhosis in our case. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) can also coexist in schizophrenia. Several psychotropics can cause SIADH (antipsychotics, antidepressants, anxiolytics and SSRIs are some examples) (7) but psychotic exacerbations have also been associated with enhanced release of ADH in polydipsic schizophrenic patients (8).

Since the first described case in 1977, there have been several reports in the literature of patients with rhabdomyolysis in association with hyponatremia (9). The pathogenic mechanism causing the rhabdomyolysis in hyponatremia is controversial, but may involve abnormality of sodium:calcium exchange across the muscle cell, so that calcium accumulates intracellularly. When intracellular calcium ions reach a critical concentration, they activate neural proteases and lipases that serve to destroy the cell (10). In a retrospective study of 475 hospitalized patients with rhabdomyolysis at Johns Hopkins Hospital, myotoxins were the commonest cause, with illicit drugs/alcohol responsible for 34% of cases and prescribed drugs for 11% of cases. Antipsychotics (36%) were the most frequently prescribed class of drugs responsible for the cases of rhabdomyolysis, followed by statins (20%), SSRIs (15%) and zidovudine (13%) (11). Rhabdomyolysis is not a well-understood adverse effect of antipsychotic use, but proposed mechanisms suggest involvement of serotoninergic and/or dopaminergic blockade (12). In addition to the other causes of hyponatremia mentioned above, the increased risk of rhabdomyolysis associated with antipsychotic medication use in these three patients might explain their development of ACS.

Along with our case, the two previous reported cases involved the anterior compartments of the legs. In fact, the anterior tibial compartment is the most frequently affected muscular compartment in ACS from all causes. It may be

Figure 1 Fasciotomy Wounds Two Months Later

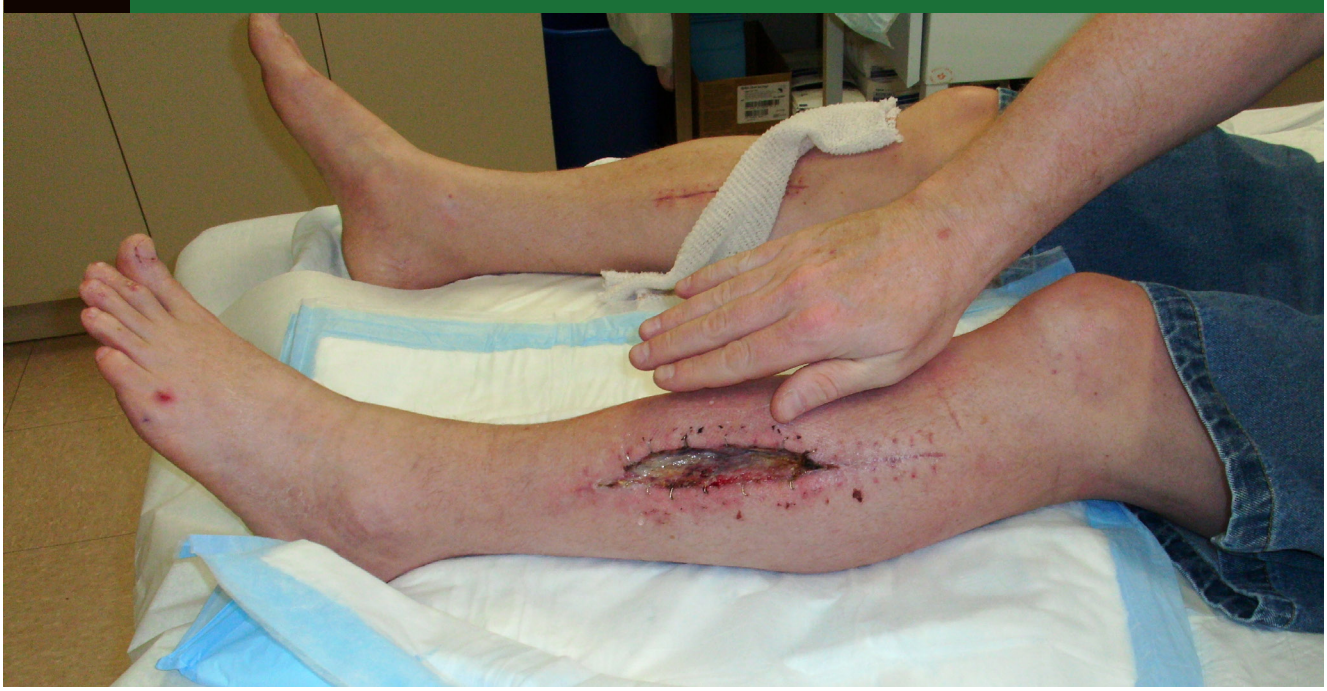
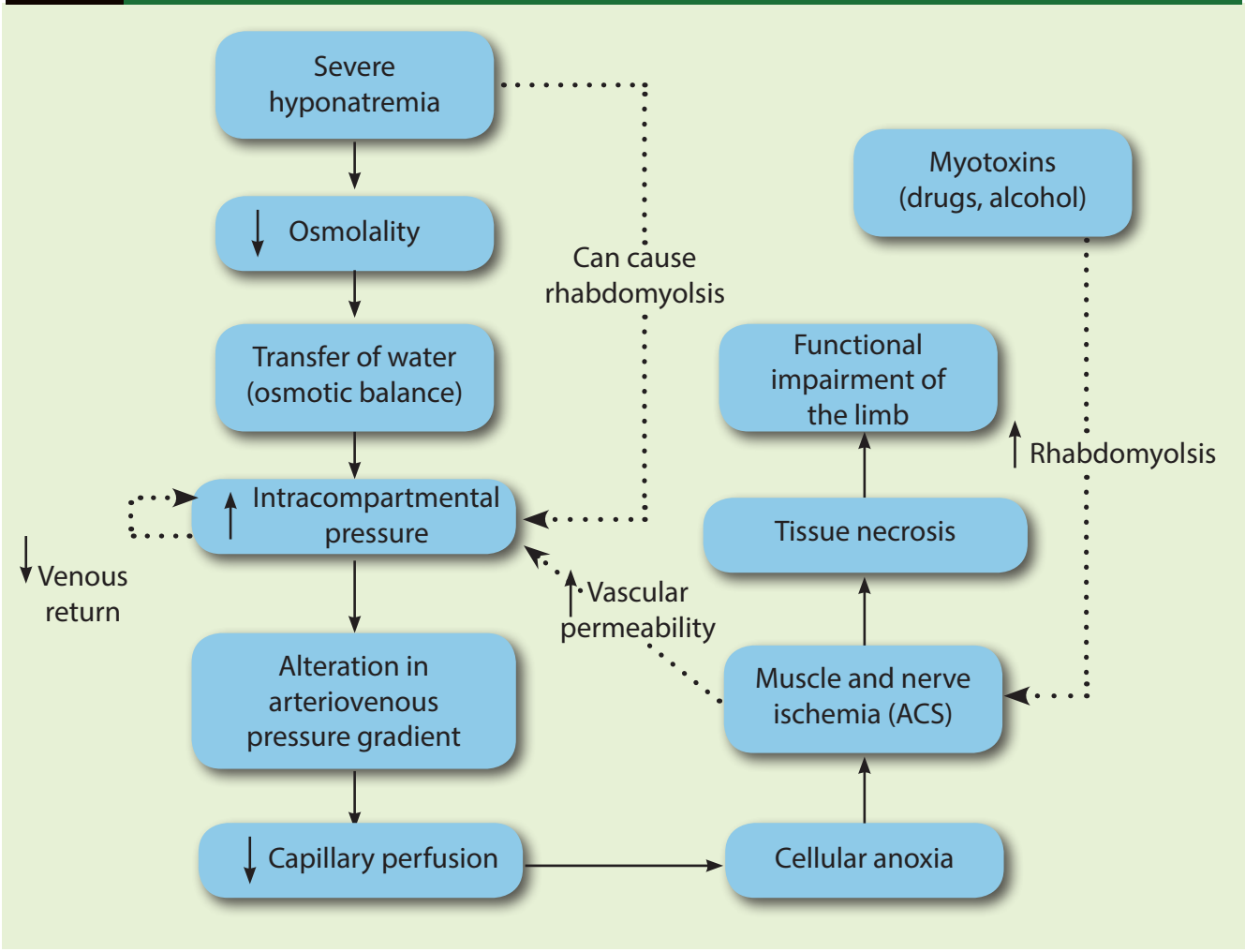


Figure 2 Physiopathological Hypothesis Underlying ACS in Severe Hyponatremia



more common in the forearm and leg because the musculature is constrained by firm, well-defined fascial boundaries in a relatively limited anatomical space (13). Therefore, the anterior tibial compartment should be carefully evaluated in patients with symptoms and signs suggestive of ACS. Interestingly, the patient we describe had a new diagnosis of liver cirrhosis made during hospitalization. Although strong evidence is lacking, according to a retrospective review by Baek et al. (14) patients with cirrhosis who develop rhabdomyolysis are at increased risk of recurrent rhabdomyolysis and mortality compared to patients without liver disease.

In our case, acute hyponatremia was probably the inciting event that led to the ACS. The physiopathology of hyponatremia-induced compartment syndrome has not been studied, but we propose that the acute decrease in blood osmolality unbalances the osmotic state and promotes water movement inside muscle cells (see Figure 2). This would be similar to the physiopathology of cerebral brain edema secondary to acute hyponatremia. Although a certain component of muscular cell necrosis is always present in ACS from any causes (secondary rhabdomyolysis), rhabdomyolysis infrequently leads to ACS. The patient's rhabdomyolysis was either associated with the hyponatremia at first, and then contributing to the development of ACS, or occurred later secondary to the ACS. In both possibilities, the rhabdomyolysis was likely worsened by alcohol consumption and polypharmacy consisting of an antipsychotic, a statin, an SSRI and a diuretic.

Conclusions

Physicians from several different medical specialties (e.g., family and emergency physicians, internists and psychiatrists) may encounter patients with nontraumatic causes of ACS. Patients with schizophrenia and polydipsia may be particularly at risk. After six hours of the development of ACS, complete functional recovery cannot be guaranteed, and beyond eight to twelve hours, the damage is irreversible. Although infrequent, nontraumatic ACS is, therefore, an important diagnostic entity to consider due to its time-sensitive nature.

Competing Interests

None.

Acknowledgments

The authors thank Dr. Jonathan Gaudet (University of Calgary) and Dr. John Robb (University of Sherbrooke) for their helpful comments.

References

1. Krasinski KL, Bytomski JR. Trauma: compartment syndrome. In: Miller M, Hart J, MacKnight J, editors. Essential orthopedics. 1st ed. Philadelphia: Saunders; 2010. p. 63-69.
2. Pamoukian VN, Rubino F, Iraci JC. Review and case report of idiopathic lower extremity compartment syndrome and its treatment in diabetic patients. Diabetes Metab 2000;26(6):489-492.
3. Muir P, Choe MS, Croxson MS. Rapid development of anterotibial compartment syndrome and rhabdomyolysis in a patient with primary hypothyroidism and adrenal insufficiency. Thyroid 2012;22(6):651-653.
4. Maiocchi L, Bernardi E. Acute anterior compartment syndrome associated with psychogenic polydipsia. Australas Psychiatry 2012;20(2):159-161.
5. Franck WM, Schick CH, Olk A, et al. [Generalized compartment syndrome after excessive drinking. A rare complication of psychological disorders?] German. Nervenarzt 2005;76(3):327-330.
6. Iftene F, Bowie C, Milev R, Hawken E, Talikowska-Szymczak E, Potopsingh D, et al. Identification of primary polydipsia in a severe and persistent mental illness outpatient population: a prospective observational study. Psychiatry Res 2013;210(3):679-683.
7. Jones E. Drug-induced syndrome of inappropriate antidiuretic hormone. Can Pharm J 2007;140(6):397-399.
8. Goldman MB, Robertson GL, Luchins DJ, Hedeker D, Pandev GN. Psychotic exacerbations and enhanced vasopressin secretion in schizophrenic patients with hyponatremia and polydipsia. Arch Gen Psychiatry 1997;54(5):443-449.
9. Strachan P, Prisco D, Multz AS. Recurrent rhabdomyolysis associated with polydipsia-induced hyponatremia—a case report and review of the literature. Gen Hosp Psychiatry 2007;29(2):172-174.
10. Hemat RAS. Principles of orthomolecularism. Urotext; 2009. p. 488.
11. Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. Medicine (Baltimore) 2005;84(6):377-385.
12. Packard K, Price P, Hanson A. Antipsychotic use and risk of rhabdomyolysis. J Pharm Pract 2014;27(5):501-512.
13. Padberg F, Walter ND. Metabolic and systemic consequences of acute limb ischemia. In: Hallet JW, Mills JL, Earnshaw J, Reekers J, Rooke T, editors. Comprehensive vascular and endovascular surgery. 2nd ed. Philadelphia: Mosby; 2009. p. 283-284.
14. Baek JE, Park DJ, Kim HJ, Lee JD, Chang SH. The clinical characteristics of rhabdomyolysis in patients with liver cirrhosis. J Clin Gastroenterol 2007;41(3):317-321.