

Hyperkalemia Caused by Penicillin

A 44-year-old man presented to the emergency department with right testicular pain, dysuria, and scrotal ulcers. His medical history was significant for intravenous drug abuse, colitis, asthma, and a 16-year history of poorly controlled diabetes mellitus because of noncompliance with oral hypoglycemic agents. On arrival he was afebrile but hypotensive (right arm 70/40 mm Hg, left arm 87/43 mm Hg). His heart rate was 99 beats/min and respiratory rate was 22 breaths/min. Oxygen saturation on room air was 100%, and capillary blood glucose level was 26 mmol/L.

Sliding-scale insulin and intravenous ciprofloxacin were administered pending blood and swab culture results. Morphine was administered for pain control. Urology was consulted, and Fournier's gangrene was diagnosed. The patient was taken to the operating room (OR) for incision, drainage, and debridement of necrotic tissue. Microbiology results from the scrotal ulcers showed 4+ polymorphonuclear cells, 3+ red blood cells, and 4+ gram-positive cocci in pairs and chains, determined to be *Streptococcus pyogenes*. Ciprofloxacin was switched to intravenously administered gentamicin 580 mg daily and ampicillin 1g every 8 hours. On day 5, on the advice of the infectious disease consultant, ampicillin was replaced with penicillin G, 3 million units intravenously administered every 4 hours and clindamycin 600 mg every 8 hours, while gentamicin was continued. At this time, the patient's white cell count was $13.4 \times 10^9/L$ (predominantly polymorphonuclear leucocytes) and potassium level was 3.1 mmol/L. That same day he was taken to the OR for further debridement and tissue removal. Postoperative hypotension caused by excessive bleeding (systolic blood pressure 60-70 mm Hg) was corrected with intravenously administered fluids and blood transfusion. On day 9, he was taken to the OR again because of multiple bleeding sites, including an arterial bleed on the left side of the scrotum. These were cauterized, and the wound was packed. The patient required a total of 6 units of blood, and his potassium level was 3.8 mmol/L 1 day after blood transfusions. Skin grafting was done on day 15, and gentamicin was discontinued on day 16.

On the second postoperative day, sliding-scale insulin was switched to a regimen of Humulin R (Eli Lilly and Company, Indianapolis, Ind) 6 units subcutaneously twice daily and Humulin N (Eli Lilly and Company) 16 units subcutaneously twice daily. The following day, he was afebrile with a white cell count of $8.1 \times 10^9/L$. The intra-

venously administered antibiotics were discontinued, and an oral regimen of penicillin VK 600 mg 4 times per day for 14 days was begun. On the morning of day 21 (10 days after the blood transfusion) the patient's potassium level increased to 6.0 mmol/L, with the rest of his electrolytes remaining within the normal range. At this time, the patient was treated with 30 g of sodium polystyrene (Kayexalate, Sanofi-Synthelabo, New York, NY), and Humulin N was increased to 18 units in the morning and 16 units at night. The surgeon was advised to replace oral penicillin VK with amoxicillin, but this was not done for another 3 days. Thirteen hours later, the patient's potassium level had decreased to 5.2 mmol/L. He was discharged on day 27 when his potassium level was 4.7 mmol/L.

DISCUSSION

Hyperkalemia is common in diabetes. Its prevalence has been estimated to be 15% in diabetic patients.¹ Potassium filtered at the glomerulus is almost completely reabsorbed in the proximal tubule and ascending limb of loop of Henle and is then secreted into the distal convoluted tubule and collecting duct. The rate of potassium secretion is determined by a number of factors, including distal sodium delivery, aldosterone, and serum potassium. Chronic hyperkalemia in diabetic patients is most often attributable to hyporeninemic hypoaldosteronism and chronic renal impairment caused by diabetic nephropathy. Conditions including urinary tract obstruction, volume depletion, and drugs (eg, nonsteroidal anti-inflammatory agents and heparin) can acutely provoke hyperkalemia in susceptible individuals.

The risk of dangerous hyperkalemia in diabetic patients is particularly high with the concurrent administration of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and potassium-sparing diuretics. Hyperkalemia might be precipitated by an acute event or medication if the underlying renal insufficiency or hyporeninemic hypoaldosteronism is subclinical and not recognized because of normal serum potassium and creatinine values.

The cause of hyperkalemia in our patient was most likely the potassium load in penicillin G and penicillin VK; he also had an underlying propensity to hyperkalemia because of diabetes. Penicillin G is usually administered as the potassium salt and sometimes as the sodium salt of 6-phenylacetamidopenicillanic acid. Penicillin G contains 0.33 mmol of sodium and 1.7 mmol of potassium per million units.² Our patient received 30.6 mmol of potassium per day in penicillin G and 6.912 mmol of potassium per day in pen-

icillin V. Rapid intravenous infusion or oral administration of large amounts of semisynthetic penicillin derivatives is potentially dangerous in patients with diabetes and renal insufficiency. Similarly, the increased sodium load in semisynthetic penicillins may worsen fluid retention in patients with congestive heart failure. This is particularly true with carbenicillin or ticarcillin, each of which contains 5 mmol of sodium per gram.³ Four previous case reports of cardiac arrest caused by penicillin-induced hyperkalemia in the literature emphasize the importance of recognizing and avoiding this potentially lethal complication.⁴⁻⁶

CONCLUSIONS

It is important for physicians to be aware of the sodium or potassium load in penicillin preparations administered and to monitor patients' electrolytes closely if large doses of penicillin are being administered, particularly in patients with diabetes, renal insufficiency, or congestive heart failure.

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