Hyperkalemia Occurring in a Patient with Psoriatic Arthritis Following Indomethacin Use

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ABSTRACT

Objective: To report a case of hyperkalemia possibly due to indomethacin use.

Case Summary: A 52-year-old white woman with psoriatic arthritis for 16 years and diabetes mellitus for 3 years was admitted to the university hospital due to swelling and pain of wrists, elbows, knees and ankles for the last one month. The patient had been receiving methotrexate irregularly, but discontinued it 3 months ago. Physical examination and laboratory evaluations were compatible with diagnosis of exacerbation of psoriatic arthritis and type 2 diabetes mellitus. Two days after initiation of indomethacin and methotrexate, hyperkalemia developed with increase of blood urea nitrogen and decrease of creatinine clearance. Indomethacin was discontinued, and this resulted in normalization of laboratory findings between day 5 and 10 after discontinuation.

Conclusion: The development of hyperkalemia caused by indomethacin is probably unusual, but it is important because indomethacin is a commonly used medication. This potentially serious complication can be prevented by careful attention to renal function and potassium balance in patients receiving indomethacin and other nonsteroidal anti-inflammatory drugs (NSAIDs), especially in patients with type 2 diabetes mellitus or preexisting renal disease.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for treatment of various kinds of diseases. These drugs inhibit prostaglandin synthesis and have some toxic effects on the kid-

neys. Due to inhibition of prostaglandin synthesis, renin secretion is diminished and this leads to hyperkalemia as a result of hyporeninemic hypoaldosteronism mechanism.[1] In this article, we describe a case of azotemia, hyperkalemia, and increased creatinine levels that developed in a patient with diabetes after the use of indomethacin for treatment of exacerbation of psoriatic arthritis.

CASE REPORT

A 52 year-old female patient was admitted to University hospital due to swelling and pain of wrists, elbows, ankles, and knees in February 2002.

Previous History

The patient declared that she had had such complaints with remissions and exacerbations for about 16 years and she was diagnosed with psoriatic arthritis 5 years ago. She used methotrexate (MTX) and prednisolone irregularly, but she discontinued all drugs 3 months ago. She stated that her complaints increased, especially in the last one month. She was diagnosed with type 2 diabetes mellitus 3 years ago, with fasting blood glucose levels above 140 mg/dL (all values were between 160 and 200 mg/dL), but she did not use any antidiabetic medications because it was thought that her disease could be related with the drugs that she had been using.

Status at Time of Admission

Her blood pressure was 130/80 mmHg; heart rate, 75 beats per minute; respiratory rate, 18/min; and body temperature, 36.6°C. The pathological findings on physical examination were as follows: swelling of both knees and ankles, heat increase of left ankle, and tenderness and ache with passive movements of these joints. Vesicular lesions on erythematous base were found at the extensor sites of wrists and at the gluteal region. Laboratory studies disclosed the following results: hemoglobin, 8.9 g/dL; hematocrit, 26%; leukocyte count, 38500/μL; thrombocyte count, 656000/μL; mean corpuscular volume, 76.5 fl; fasting blood glucose, 277 mg/dL; hemoglobinA_{1C}, 8.9 mg/dL; total protein, 7.6 g/dL; albumin, 2.7 g/dL; blood urea nitrogen (BUN), 38 mg/dL; serum creatinine, 0.9 mg/dL; potassium, 4.9 mmol/L; sodium, 139 mmol/L; erythrocyte sedimentation rate, 95 mm/h; and C-reactive protein 200 mg/dL. Throat and urine cultures were negative for pathogenic microorganisms, and blood culture was sterile. Other laboratory findings were within normal limits.

Urinalysis showed pH 5.0, specific density 1020, protein + and 4 to 5 leukocytes, 2 to 3 erythrocytes per high-power field.

Clinical Course

The patient was hospitalized due to these findings. She was thought to have exacerbation of psoriatic arthritis and methylprednisolone 20 mg/day, indomethacin 100 mg/day, and MT X 15 mg/week were initiated. In the second day of the therapy, BUN increased up to 89 mg/dL, serum creatinine up to 1.7 mg/dL and potassium up to 7.3 mmol/L. The maximum level of BUN during the follow-up was 89 mg/dL, and that of serum creatinine and potassium were 2 mg/dL and 8.4 mmol/L, respectively. The electrocardiogram revealed no abnormality except peaked T waves. Abdominal ultrasonography revealed no pathological finding. Creatinine clearance was 23 mL/min, urinary potassium excretion was 16 mmol/day (20-80), and urinary microprotein excretion was 503 mg/day (28-141). It was thought that these findings could result from indomethacin use, so it was discontinued. Intravenous perfusion of dextrose solution tamponated with insulin was initiated for the treatment of hyperp-

kalemia. Serum potassium level decreased to normal on day 5. Laboratory findings 10 days after discontinuation of indomethacin were as follows: potassium, 4.7 mmol/L; BUN, 24 mg/dL; serum creatinine, 0.9 mg/dL; creatinine clearance, 48 mL/min; and urinary potassium excretion, 72 mmol/day. Arthritis and dermatological findings of the patient resolved with methylprednisolone and MTX treatment, and the patient was discharged and called for controls. All laboratory findings of the patient, including serum creatinine, BUN, potassium, urinary potassium excretion, urinary microprotein excretion, creatinine clearance, fasting blood glucose, and hemoglobinA_{1C}, were found to be normal at the end of 3 months.

DISCUSSION

As with other NSAIDs, long-term administration of indomethacin to animals has resulted in abnormal renal pathology. Morphologically, analgesic nephropathy is characterized by papillary necrosis and tubulointerstitial inflammation.[1] In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome. A second form of renal toxicity has been seen in patients with prerenal and renal conditions, leading to a reduction in renal blood flow or blood volume and decreasing glomerular filtration rate, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion.[2] In these patients administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. The administration of NSAIDs in patients with hypovolemia (from cardiac insufficiency, hemorrhage, nephrotic syndrome, or ascitic cirrhosis) can lead to kidney failure.[3] Also patients with type 2 diabetes mellitus, advanced age, extracellular volume depletion from any cause, congestive heart failure, septicemia, pyelonephritis, or concomitant use of any nephrotoxic drug are at great risk.[4]

When we look over the causes that may result in hyperkalemia, we see that diabetic nephropathy, indomethacine, and MTX must be researched as possible causes of hyperkalemia in differential diagnosis. As understood from the history of the patient, the patient's type 2 diabetes mellitus became overt through the use of steroids and there was no complication related to type 2 diabetes mellitus (no neuropathy and fundoscopic examination was normal). So hyperkalemia does not seem to be related to diabetic nephropathy. MTX can cause nephropathy and hyperkalemia at doses more than 500 mg/m^2.[5] However, our patient used MTX at only a 15 mg/week dose. The reduced urinary potassium excretion level of the patient during hyperkalemic term reveals that prostaglandin synthesis was inhibited by indomethacin and this resulted in hyporeninemic hypoaldosteronism. As indomethacin was discontinued, all pathological laboratory findings returned to normal levels. Microproteinuria was detected during the period of hyperkalemia and increased creatinine level, but this also disappeared one week after discontinuation of indomethacin. Use of the Naranjo ADR Probability Scale indicated a probable relationship between hyperkalemia and indomethacin.[6]

There are articles about hyporeninemic hypoaldosteronism cases following indomethacin use for treatment of gouty arthritis.[7,8]

CONCLUSION

The development of hyperkalemia caused by indomethacin is probably unusual, but it is important because indomethacin is a commonly used medication. This potentially serious compli-

cation can be prevented by careful attention to renal function and potassium balance in patients receiving indomethacin and other NSAIDs, especially in patients with type 2 diabetes mellitus or preexisting renal disease.[6]

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