

# Letters to the Editor

## Case Report: Late-Onset Metformin-Associated Diarrhea

**To the Editor:** A 72-year-old patient was diagnosed with type 2 diabetes mellitus 26 years ago and began taking metformin with no gastrointestinal adverse effects. Two years ago, the patient developed chronic diarrhea that occurred most days and only while awake. The diarrhea was associated with loose to watery explosive stools, with urgency but no incontinence, and intermittently formed stools. There was no abdominal pain and no blood or melena per rectum. Dietary modification did not help. The patient unintentionally lost 3.63 kg (8 lb) and had difficulty maintaining weight.

The patient had well-controlled hypertension, dyslipidemia, and stable stage 3a chronic kidney disease without albuminuria; he is being treated with ramipril (Altace), atorvastatin, and empagliflozin (Jardiance). Gastrointestinal history included nonsteroidal anti-inflammatory drug-related gastritis and benign colon polyps.

On presentation, the patient's vital signs and abdominal and rectal examinations were normal. Laboratory results showed a negative comprehensive enteric pathogen polymerase chain reaction panel, normal fecal fat and fecal pH, and positive fecal lactoferrin and fecal occult blood by a fecal immunochemical test. A colonoscopy showed one benign tubular adenoma. Multiple random colon biopsies were histologically normal. After the colonoscopy, the diarrhea persisted, and metformin was discontinued. Within two days, the diarrhea resolved without recurrence.

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This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

Diarrhea is a well-known adverse effect when metformin is initiated for type 2 diabetes, but it usually resolves with continued use. Only a few cases of chronic diarrhea have been reported after months or years of taking metformin.<sup>1-5</sup>

Late-onset metformin-associated diarrhea may be confused with diabetes-related diarrhea; however, diabetes-related diarrhea is more common in patients with type 1 diabetes and is often associated with dysautonomia.<sup>6</sup> The differential for late-onset metformin-associated diarrhea includes irritable bowel syndrome or microscopic colitis, which may be distinguished based on clinical course.

Many patients with type 2 diabetes who develop chronic diarrhea after taking metformin for years likely have late-onset metformin-associated diarrhea rather than diabetes-related diarrhea. A reasonable, cheap, and convenient approach to chronic diarrhea in patients with type 2 diabetes is to discontinue metformin for two weeks and await resolution, and then begin a diarrhea workup only if the diarrhea does not completely resolve.

**Robert J. Flaherty, MD**

Bozeman, Mont.

Email: [bob@rflaherty.com](mailto:bob@rflaherty.com)

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