

**BRIEF REPORTS**

# Ischemic Colitis Associated with Herbal Product Use in a Young Woman

*Courtney K. Ryan, CPT, USAF, MC; Brian Reamy, LT COL, USAF, MC; and James A. Rochester, MAJ, USAF, MC*

Ischemic colitis is most often thought of as a condition that occurs in elderly patients, usually as a result of some form of vascular disease. Ischemic colitis, however, also occurs in younger, otherwise healthy adults. When it occurs in this population, it is usually self-limited and is commonly called transient ischemic colitis. Some publications associate this transient form with estrogen or oral contraceptive use.<sup>1,2</sup> Other causes include vascular disease, diabetes, coagulopathy, cocaine use, and even long-distance running.<sup>3-6</sup> There have also been recent case reports associating transient ischemic colitis with use of decongestants containing pseudoephedrine.<sup>7-9</sup>

We report a case of ischemic colitis in a 26-year-old woman who did not have a known hypercoagulability disorder or vasculitis, was not on hormone therapy, and had not been taking cold medications. She was, however, taking a rapid fat-loss catalyst composed of several herbal products, some of which are known to cause vasoconstriction.

## Case Report

A 26-year-old woman came to the hospital with the complaint of diarrhea for the previous 10 hours. For the first 7 hours the patient had watery diarrhea, and in the more recent 3 hours the diarrhea became bloody. The patient was having episodes of the bloody diarrhea with increasing amounts of blood in her stools about every half-hour. She also had symptoms of crampy abdominal pain, as well as mild lightheadedness and dizziness. She denied any fevers, dysuria, chest pain, shortness of breath, nau-

sea, vomiting, or any recent diet changes. Her medical history was notable only for irritable bowel syndrome for 2 to 3 years. This diagnosis was based on symptoms and diet trials. Her irritable bowel syndrome had been well controlled by diet for the past 6 to 8 months. Also, there had never been a bloody component to her diarrhea associated with irritable bowel syndrome.

Six days before she was examined, she had completed a 10-day course of penicillin VK for a molar infection. She denied any history of tobacco, cocaine, or amphetamine use. Her exercise regimen was of low to moderate intensity. She was not taking oral contraceptives or any other hormone therapy. Her surgical history included two cesarean sections and a bilateral tubal ligation. She had no history of thrombotic events or any recent travel. She was not taking any current prescription medications; however, she had been taking herbal diet formulations for the past 2 months. She had started taking Metabolife 356, then she switched to a less-expensive brand called Xenadrine, which she took for the month before her admission. Metabolife 356 contains guarana, ma huang, Siberian ginseng, lecithin, ginger root, damiana, sarsaparilla root, goldenseal, gotu kola, spirulina, algae, bee pollen, nettle leaf, royal jelly, and bovine complex. This formulation is standardized to contain 12 mg of ephedrine group alkaloids and 40 mg of caffeine alkaloids.<sup>10</sup> Xenadrine contains bitter orange (standardized for 5 mg of synephrine), ma huang (standardized for 20 mg of ephedrine), guarana extract (standardized for 200 mg of caffeine), and white willow bark extract (standardized for 15 mg of salicin).<sup>11</sup>

When examined, the patient appeared to be an otherwise healthy, well-nourished woman in no acute distress. Her temperature, blood pressure, pulse rate, and respiration rate were within normal limits. Findings of her head, eyes, ears, nose and

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From the Family Practice Residency Program (CKR, BR, JAR), Malcolm Grow Medical Center, Andrews Air Force Base, Md. Address reprint requests to Courtney K. Ryan, MD, Andrews Air Force Base, 89 MDOS/SGOPF, Family Practice Clinic, 1075 West Perimeter Dr, Andrews AFB, MD 20762-6600.

throat examination, as well as cardiac and pulmonary findings, were within normal limits. Her abdomen was mildly tender to palpation without rebound tenderness or peritoneal signs in the upper portion of the lower left quadrant. Bowel sounds were active. The patient's extremities were normal, as were findings of neurologic, musculoskeletal, and skin examinations. A complete blood count and electrolyte, blood urea nitrogen, creatinine, liver enzyme, amylase, and lipase levels were also all within normal limits.

Flexible sigmoidoscopy showed superficial inflammation and hemorrhagic friable mucosa without ulceration in a patchy distribution approximately 10 cm long at the splenic flexure. No obstruction was evident. Bright red blood was also observed in the lumen of the splenic flexure. No mucosal injury or blood was found elsewhere on sigmoidoscopic examination. Biopsy specimens were collected from involved and normal-appearing areas. Acute abdominal radiographs showed no free air under the diaphragm, no air-fluid levels, no obstruction, preserved psoas shadows, and small-bowel gas in a nondiagnostic pattern. Stool was collected for culture.

The patient was admitted to the hospital. Food and fluids by mouth were withheld 24 hours, she was rehydrated with intravenous fluids, and her hemoglobin levels were checked serially. The bloody diarrhea resolved within 10 hours of onset. By the next day, the patient's abdominal pain had resolved. She started on clear liquids and then advanced to a full diet in the next 24 hours. She tolerated the full diet, had no return of symptoms or diarrhea, and was released within 48 hours.

Stool studies were negative for ova and parasites, *Giardia lamblia*, *Cryptosporidium* organisms, salmonella, shigella, yersinia, *Escherichia coli* H:0157, vibrio, and campylobacter. Flexible sigmoidoscopy biopsy results of affected areas showed superficial erosion with covering inflammatory exudate, fibrosis of the lamina propria mucosae, and focal glandular lining cells dropped out, all changes consistent with ischemic colitis. Biopsy results of normal-appearing areas were cytologically normal. The patient's next bowel movement after she was released was completely normal. The next one contained some blood, but not nearly the amount when initially examined. She had no other blood in her stool after that.

When the patient returned to clinic the following week, her stool was negative for occult blood on examination, and she no longer had any abdominal tenderness. She was advised to discontinue use of the herbal diet medications and to avoid any ephedrine- or pseudoephedrine-containing cold remedies or other combinations. A follow-up flexible sigmoidoscopy was scheduled for a few months after her hospitalization. She has had no recurrence of any of the symptoms she had before she was hospitalized, and she has been feeling well.

## Discussion

The active herbal ingredients in the supplements the patient was taking included ma huang, bitter orange, guarana extract, and white willow bark extract. Ma huang is a source of ephedrine, a long-acting sympathomimetic that acts primarily through the release of stored catecholamines. It is a mild stimulant and a pressor agent.<sup>12</sup> Ma huang is considered by the Food and Drug Administration as possibly safe when used orally for a maximum of 7 days and in maximum doses of 24 mg/d of ephedrine equivalent.<sup>13</sup> One rapid fat-loss product the patient was taking had labeling recommending the equivalent of up to 36 to 40 mg of ephedrine per day.

Bitter orange is a source of synephrine, which acts as a sympathomimetic. This type of medication causes increased blood pressure by increasing peripheral arterial resistance and decreasing venous capacitance.<sup>12</sup> Bitter orange has also been shown to have antifungal and antibacterial actions.<sup>13</sup>

Guarana extract is a source of caffeine. Caffeine raises peripheral vascular resistance and blood pressure by stimulating the release of catecholamines.<sup>12</sup> It also has many other effects, including central nervous system stimulation, increased heart rate and cardiac contractility, inhibition of platelet aggregation, stimulation of gastric acid secretion, and relaxation of extracerebral vascular and bronchial smooth muscle.<sup>13</sup> Guarana extract can interact with many drugs and herbal products. Specifically noted were other caffeine substances and ma huang. Guarana extract can also result in prolonged bleeding times.<sup>13</sup>

White willow bark extract contains flavonoids, tannins, and salicylates. Most of the information available on this extract is based on the pharmacologic properties of salicylates, or aspirin. Although

this component does not appear to have any vasoconstrictive properties, it is known to increase blood-clotting time, as does aspirin.<sup>13</sup>

Injury to the colon in a patient with ischemic colitis results from decreased splanchnic blood flow caused by blockage from hypercoagulation, vasoconstriction, or diversion. Areas compromised are typically found at the splenic flexure, the descending colon, or sometimes at the rectosigmoid junction. These areas are known as watershed areas between the superior and inferior mesenteric arteries and between the lower sigmoid artery and superior rectal artery. Patients with ischemic colitis usually complain of abdominal pain and hematochezia. The transient types will usually resolve within a few days without sequelae.

Other cases of ischemic colitis have been reported in younger populations in association with diabetes,<sup>4</sup> contraceptive use,<sup>2</sup> competitive long-distance running,<sup>6</sup> and cocaine use.<sup>5</sup> More recently, there have been a handful of cases linking ischemic colitis with decongestant use.<sup>7,8</sup> In each of these cases, the vasoconstrictive properties of pseudoephedrine were believed to be the likely cause of the ischemic colitis. Most of those cases involved the splenic flexure of the colon, the watershed area discussed previously as being the most sensitive to ischemic insult.

## Conclusion

Although our patient was not taking decongestant medications, the active ingredients of her herbal diet supplements contained ephedrine products similar to pseudoephedrine, as well as caffeine products. Both these entities have vasoconstrictive properties that could cause ischemic injury to areas of the bowel most sensitive to inadequate blood supply. Our patient did not have any other known risk factors or predispositions for ischemic colitis. The location of injury was typical, as evidenced by these previous studies. The patient has also had no recurrence of any symptoms of ischemic colitis after she stopped taking the herbal diet supplements, and she was advised to avoid any decongestants containing pseudoephedrine products.

It is important to keep in mind that many patients take a variety of herbal medications. Most patients think that because they do not need a prescription for herbal preparations, they are completely harmless. Herbal products have many active

ingredients with pharmacologic properties that can have potent effects in addition to potential adverse effects. To have a complete picture of the factors influencing our patients health, it is beneficial for physicians to know which herbal products in addition to pharmaceutical medications our patients are taking.

This case report suggests that use of such herbal products as bitter orange, ma huang, and guarana extract, which are known sympathomimetics and vasoconstrictors, could be risk factors for development of ischemic colitis in an otherwise healthy person. The studies discussed in this article illustrate that ischemic colitis in a patient with no known risk factors can be caused by a variety of mechanisms that reduce blood flow to the colon, whether by internal blockage, diversion, or decreased flow. The vasoconstrictive agents in cold remedies that can cause transient ischemic colitis are similar to those found in the herbal formulations this patient was using. This evidence helps support the probability that these similarly acting herbal products could do the same damage.

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