The soymilk diet: A previously unknown etiology of acute pancreatitis

Abstract

We present a case of daily, large ingestions of soymilk that likely led to acute pancreatitis. Soybean contains trypsin inhibitor that when ingested will reduce the activity of trypsin in the intestine. A decrease in intestinal proteolytic activity removes the negative feedback on the pancreatic acinar cells, leading to an inappropriate increase in intrapancreatic trypsin secretion. When trypsin activation exceeds the capacity of pancreatic secretory trypsin inhibitor, the subsequent cascade of events can lead to acute pancreatitis.

Keywords: soymilk, pancreatitis, trypsin inhibitor, trypsinogen, pancreatic secretory trypsin inhibitor

Case

A woman in her 40s with no significant past medical history presented to the emergency department (ED) with one hour of sudden-onset, left-sided abdominal pain. The pain was described as severe, constant, and radiated to the epigastric area. There was associated eructation. The patient reported difficult bowel movements but denied fever, vomiting, obstipation, dysuria, and frequency. Her last menses was two years prior, and she was not sexually active. She denied cigarette smoking, alcohol, and illicit drug use. There was no family history of serious medical illness.

The patient's vital signs were heart rate 99 per minute, blood pressure 96/51 millimeters of mercury, respiratory rate 16 per minute, and temperature 97.3 degrees Fahrenheit. The patient was alert, oriented, and appeared in distress due to pain. Cardiopulmonary exam was normal. There were normal bowel sounds and mild epigastric tenderness, but no rigidity or costovertebral angle tenderness. The extremities were warm. The ED clinicians ordered a complete blood count, comprehensive metabolic profile, lipase, and venous blood gas with lactate level.

Point-of-care ultrasonography demonstrated an absence of gallstones and no hydronephrosis. The electrocardiogram and chest radiograph were normal. The clinicians' initial impression was dyspepsia or other benign gastrointestinal condition, and they ordered one liter of 0.9% saline and ketorolac intravenously, aluminum hydroxide/magnesium hydroxide/simethicone suspension and famotidine orally, and sodium phosphate enema rectally. The initial blood test results demonstrated mildly elevated lactate (1.8 millimoles per liter) but normal complete blood cell count, chemistry, and hepatic function. The patient walked unassisted to the bathroom, had a bowel movement, and reported an improvement in symptoms. The repeat examination remained unchanged.

The laboratory technician called to notify the clinicians of a significantly elevated lipase level of >6,000 units per liter (reference level 11 to 82 units per liter). Considering the absence of risk factors, clinical presentation, and fairly benign

examination, the ED clinicians decided to confirm the lipase level and order a lipid profile. The repeat lipase level returned at 5,500 units per liter, and the triglyceride level was 74 milligrams per deciliter. Upon further questioning, the patient admitted to starting a diet five days ago that strictly included oatmeal and approximately 64 ounces of Silk® soymilk (56 grams soy protein) per day in an effort to “be more healthy”. She was given one more liter of intravenous lactated Ringers solution, and despite the recommendation of hospitalization and discussion of risks and benefits, the patient chose to go home, agreeing to discontinue the soymilk diet. Two days later, the patient reported persistent, mild pain to her primary physician who convinced her to be hospitalized. Computed tomography of the abdomen confirmed the diagnosis of acute pancreatitis. The lipase level trended downward, and the patient was discharged home within 24 hours. Upon contact by phone six weeks later, the patient reported no further symptoms.

Discussion

Pancreatic digestive proteases are stored as inactivated precursors (i.e., trypsin as trypsinogen) in zymogen granules within pancreatic acinar cells. Under normal physiologic conditions, protease activation is regulated. A small quantity of trypsinogen is converted to active trypsin and inactivated by pancreatic secretory trypsin inhibitor (PSTI), thereby preventing injury to pancreatic acinar cells. Trypsin that is secreted from the acinar cells binds to protease activated receptor-2 (PAR-2), which is present on the surfaces of the acinar cells. Upon PAR-2 activation, cytokines are produced and exocrine function is regulated via a negative feedback loop. If

intrapancreatic trypsin activation exceeds the capacity of PSTI (due to excessive stimulation of pancreatic acinar cells), a subsequent cascade of events will lead to the activation of various proteases that can subsequently result in autodigestion and acute pancreatitis.[1,2]

The soybean is an excellent source of protein, but it has a component that is a known trypsin inhibitor. Most commercially available soy products retain as high as 20% of trypsin inhibitor activity after preparation from raw soybeans.[3] Feeding purified trypsin inhibitor to rats results in hypertrophy and hyperplasia of acinar cells[4] and concurrent increase in their secretion of digestive proteases, including trypsin.[5] In the few human studies, direct infusion of the purified inhibitor into the duodenum also induced a significant increase in the pancreatic secretion of trypsin.[6,7] Presumably, in the presented case, a large, daily ingestion of soybean trypsin inhibitor may have reduced proteolytic activity in the intestine, thereby removing the negative feedback on the pancreatic acinar cells.[7,8] This resulted in an inappropriate increase in intrapancreatic trypsin secretion that overwhelmed the normal levels of PSTI and likely led to clinically apparent, acute pancreatitis. This case appears to be the first report in the medical literature of soymilk-related pancreatitis.

References

1. Hirota M, Ohmuraya M, Baba H. The role of trypsin, trypsin inhibitor, and trypsin receptor in the onset and aggravation of pancreatitis. J Gastroenterol. 2006;41(9):832-6.

2. Hirota M, Ohmuraya M, Hashimoto D, et al. Roles of Autophagy and Pancreatic Secretory Trypsin Inhibitor in Trypsinogen Activation in Acute Pancreatitis. Pancreas. 2020;49(4):493-7.
3. Rackis JJ and Gumbmann MR. Protease inhibitors: physiological properties and nutritional significance, in Antinutrients and Natural Toxicants in Foods, Ory RL, Ed., Food and Nutrition Press, Westport, CT, 1982, 203.
4. Yanatori Y, Fujita T. Hypertrophy and hyperplasia in the endocrine and exocrine pancreas of rats fed soybean trypsin inhibitor or repeatedly injected with pancreozymin. Arch Histol Jpn. 1976;39(1):67-78.
5. Nitsan Z, Liener IE. Enzymic activities in the pancreas, digestive tract and feces of rats fed raw or heated soy flour. J Nutr. 1976;106(2):300-5.
6. Liener IE, Goodale RL, Deshmukh A, et al. Effect of a trypsin inhibitor from soybeans (Bowman-Birk) on the secretory activity of the human pancreas. Gastroenterology. 1988;94(2):419-27.
7. Reseland JE, Holm H, Jacobsen MB, et al. Proteinase inhibitors induce selective stimulation of human trypsin and chymotrypsin secretion. J Nutr. 1996;126(3):634-42.
8. Green GM, Lyman RL. Feedback regulation of pancreatic enzyme secretion as a mechanism for trypsin inhibitor-induced hypersecretion in rats. Proc Soc Exp Biol Med. 1972;140(1):6-12.