Probable Loop Diuretic–Induced Pancreatitis in a Sulfonamide-Allergic Patient

Paul Juang, Robert L Page II, and Ronald Zolty

OBJECTIVE: To report the case of a patient with a prior allergy to a sulfonamide antibiotic who subsequently developed the same reaction when administered various loop diuretics.

CASE SUMMARY: A 57-year-old female with cardiomyopathy and "sulfa" (trimethoprim/sulfamethoxazole) allergy documented as pancreatitis presented with symptoms consistent with pancreatitis after use of furosemide. She subsequently developed similar symptoms after multiple rechallenges with various loop diuretics including furosemide, bumetanide, and torsemide. The patient was placed on ethacrynic acid until she was desensitized to furosemide. She had been receiving oral furosemide for 5 months at the time of this report, with no complications. According to the Naranjo probability scale, this reaction was probable.

DISCUSSION: Reactions associated with arylamine sulfonamide–containing antibiotics have been commonly reported; however, cross-reactions with non-arylamine sulfonamide–containing medications have been rare. The time delay by which symptoms of pancreatitis presented following administration of loop diuretics suggests an immunologic pathway. In addition, while cases of loop diuretic–induced pancreatitis, including furosemide, have been published, the allergic manifestations with both sulfonamide antibiotics and non-antibiotics in our patient suggest possible cross-reactivity between these 2 drug classes.

CONCLUSIONS: The mechanism by which loop diuretics induce pancreatitis appears to be via an immunologic pathway. While the true correlation remains unknown, allergic cross-reactivity may occur between sulfonamide antibiotics and non-antibiotics, such as loop diuretics. Torsemide appears to also be a part of a long list of agents that can cause pancreatitis.

KEY WORDS: loop diuretics, pancreatitis, sulfonamide.

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The loop diuretics furosemide, bumetanide, torsemide, and ethacrynic acid exert their action upon the sodium/potassium/chloride cotransporter at the ascending loop of Henle.[1] In both the hospital and outpatient setting, this class of drugs is ubiquitously used across a large spectrum of diseases, from treatment of fluid overload in heart failure to management of hypercalcemia and pulmonary edema. As seen in Figure 1, furosemide, bumetanide, and torsemide share a common sulfonamide moiety; however, unlike the sulfonamide antibiotics, they do not possess an arylamine group (NH_2) at the N^4 position.[2] Because the true immunologic cross-reactivity between sulfonamide antibiotics (arylamines) and other sulfonamide (non-arylamines) medications has not been shown, current data suggest the incidence to be low.[2] We present the case of a woman with a prior allergy to a sulfonamide antibiotic documented as pancreatitis who developed pancreatitis after administration of furosemide and other loop diuretics.

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Case Report

A 57-year-old female presented to our hospital with signs and symptoms of decompensated heart failure consistent with volume overload, increasing shortness of breath, and weight gain (4.5 kg) over the past week. The patient's past medical history was significant for dilated cardiomyopathy, atrial fibrillation, sick sinus syndrome, biventricular pacemaker placement, hypertension, hyperlipidemia, irritable bowel syndrome, chronic renal insufficiency (baseline serum creatinine 2.2 mg/dL), gout, gastroesophageal reflux disease, anemia of chronic disease, pancreatitis, and Hashimoto's thyroiditis.

She also had a documented history of "sulfa" allergy associated with the sulfonamide antibiotic trimethoprim/sulfamethoxazole (TMP/SMX) that resulted in rash and pancreatitis. Her medical records indicated that she had been previously admitted twice for pancreatitis several years earlier when the sulfonamide antibiotic was administered. The time frame for developing pancreatitis was within 2 weeks of antibiotic initiation. Prior to the present admission, the woman had been stabilized with carvedilol 6.25 mg twice daily, valsartan 40 mg daily, warfarin 5 mg daily, sotalol 80 mg twice daily, pantoprazole 40 mg daily, ethacrynic acid 100 mg daily, and spironolactone 12.5 mg daily for greater than one year. She had been initially prescribed ethacrynic acid rather than furosemide due to the sulfa allergy; however, due to an inability to obtain ethacrynic acid consistently from her local pharmacy, the patient was not adherent to her diuretic therapy. Her hyperlipidemia was currently diet controlled, and irritable bowel syndrome was managed with fiber supplements. The patient had also been receiving levothyroxine for hypothyroidism associated with Hashimoto's thyroiditis; however, she had stopped the medication on her own one week prior to admission. She did not smoke or consume alcohol.

On admission, laboratory values were within normal limits with the exception of a low serum sodium level (133 mEq/L) and elevated serum creatinine (SCr; 2.2 mg/dL) and blood urea nitrogen (BUN; 48 mg/dL). Both the patient's liver function tests and complete blood cell count were within normal limits with the exception of a low hemoglobin level (9.1 g/dL) and hematocrit (27.3%), which were consistent with her anemia of chronic disease. Furthermore, a brain natriuretic peptide level was elevated at 1490 pg/mL. Vitals signs included blood pressure 130/85 mm Hg and heart rate 65 beats/min.

Due to the severity of the woman's heart failure (ejection fraction <20%, New York Heart Association functional class IV), physicians decided to admit her to the intermediate care unit, discontinue carvedilol and sotalol, and begin dobutamine 4 µg/kg/min. The hospital medication regimen included ferrous sulfate 325 mg daily, ascorbic acid 500 mg daily, magnesium gluconate 500 mg daily, pantoprazole 40 mg daily, docusate 100 mg twice daily, digoxin 62.5 µg daily, spironolactone 50 mg daily, erythropoietin alfa 30 000 units weekly, valsartan 40 mg daily, levothyroxine 25 µg daily, conjugated estrogen 0.3 mg daily, isosorbide dinitrate 20 mg 3 times daily, and continuous infusion of heparin. Due to a shortage of both oral and intravenous ethacrynic acid, intravenous therapy with furosemide 40 mg twice daily was immediately initiated.

Five weeks after admission, the patient began to experience nausea and vomiting with continuous severe epigastric and abdominal pain with radiation to the back. Results of liver function tests were within normal limits with the exception of elevated levels of amylase 437 IU/L and lipase 1030 IU/L. Other laboratory values, including serum magnesium and calcium levels and a complete blood cell count, were within normal limits with the exception of Scr 1.8 mg/dL and BUN 38 mg/dL. A fasting lipid panel conducted at the same time as those tests revealed total cholesterol 169 mg/dL and triglycerides 91 mg/dL. The trends in lipase levels are depicted in Figure 2. An abdominal computed tomography (CT) scan revealed edema, pancreatic duct stranding, and thickening of the fascial plane consistent with pancreatitis. All oral intake was immediately discontinued. Digoxin, pantoprazole, and levothyroxine were converted to intravenous formulations, and all other medications, including conjugated estrogen and intravenous furosemide, were discontinued. Ondansetron 4 mg was administered intravenously every 4 hours as needed.

Within 2 days of discontinuing furosemide, the patient's abdominal pain, nausea, and vomiting resolved; however, due to increases in peripheral and pulmonary edema, intravenous bumetanide was initiated. Within 24 hours, the patient developed myalgia. After 3 days of therapy, bumetanide was discontinued and intravenous torsemide was initiated; one dose of metolazone was administered. No complications were observed until day 4 of torsemide therapy when the patient began to experience severe abdominal pain, similar to the previous episode. The serum lipase level was elevated at 567 IU/L and a second abdominal CT scan, performed. This scan revealed findings similar to those of the first scan but exhibited an additional fat-stranding pattern in the peripancreatic tissues and nearby mesenteric tissues that was consistent with pancreatitis. No changes in the drug therapy had occurred after torsemide was started. Torsemide was immediately discontinued. Two days later, the patient's symptoms resolved and lipase values returned to within normal ranges. However, within 5 days of torsemide discontinuation, the patient again developed fluid overload. Intravenous ethacrynic acid, which had now become available, was initiated. The patient had no further complications and was discharged 6 days later on ethacrynic acid 20 mg intravenously twice daily, dobutamine 6 µg/kg/min, levothyroxine 50 µg daily, spironolactone 50 mg daily, digoxin 62.5 µg daily, erythropoietin alfa 60 000 units weekly, ferrous sulfate 325 mg daily, ascorbic acid 500 mg

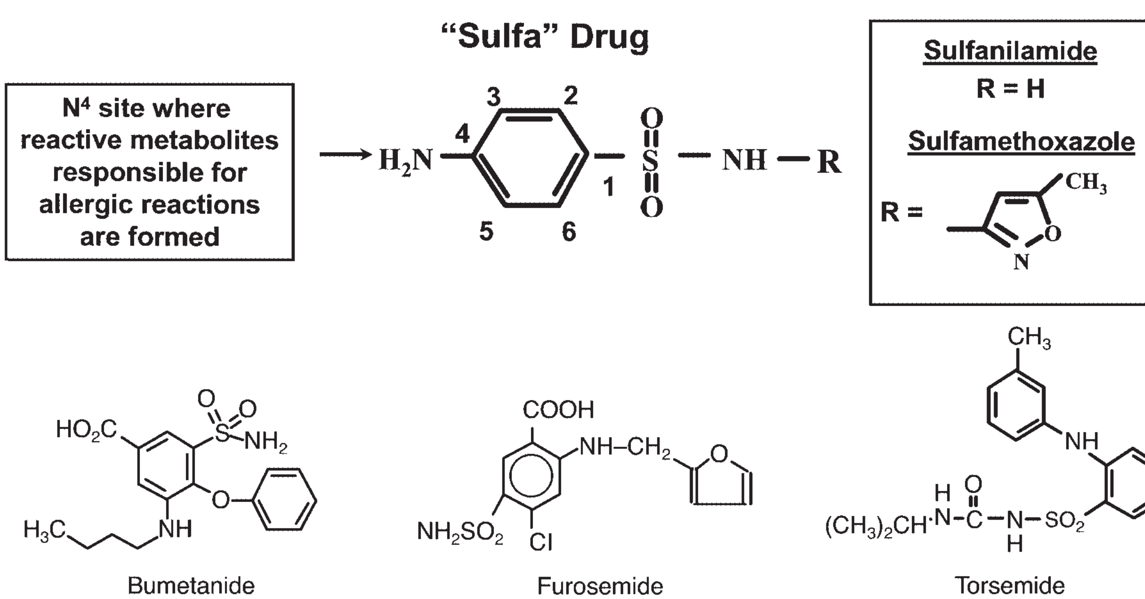

Figure 1. Comparison of arylamine versus non-arylamine sulfonamide medications.[6]

daily, magnesium gluconate 500 mg daily, lansoprazole 30 mg daily, isosorbide dinitrate 20 mg 3 times daily, valsartan 40 mg daily, warfarin 5 mg daily, and loperamide, hydromorphone, and ondansetron on an as-needed basis. Arrangements were made at a nearby home infusion facility, which included nursing services, so that the patient could receive intravenous ethacrynic acid and dobutamine.

One month after discharge, the woman was readmitted to a different hospital with heart failure exacerbation and was mistakenly given 4 doses of intravenous furosemide, with no other changes in medications. She quickly developed abdominal pain with an elevated lipase level of 903 IU/L within one day of the last furosemide dose. Ethacrynic acid was restarted and oral intake was stopped for 2 days; she was then transferred to our institution. Pancreatic symptoms resolved and lipase values returned to within normal range within 4 days of stopping furosemide. Endoscopic retrograde cholangiopancreatography (ERCP) revealed dilated pancreatic ductal branches, a pseudocyst, and widespread substantial pancreatic ductal abnormalities that are consistent with chronic pancreatitis. A pancreatic duct stent was placed, and the patient was discharged with prescriptions for pancreatic enzymes along with her previous chronic medications.

Four weeks later, the woman was readmitted to our institution with signs and symptoms consistent with heart failure exacerbation. Upon examination, she experienced mild abdominal pain and isolated elevated lipase levels that had been present since stent placement. After consulting the gastroenterology service, clinicians decided to remove the stent. Changes to the drug regimen included increasing the doses of levothyroxine to 75 µg daily and digoxin to 125 µg daily. However, because diuretic therapy was necessary, a rapid furosemide desensitization regimen,[3] derived from penicillin and TMP/SMX desensitization protocols,[2] was attempted. The patient tolerated the desensitization protocol with no complications and was discharged with oral furosemide. She had experienced no subsequent bouts of pancreatitis for 5 months when this report was prepared. A prescription for ethacrynic acid was also given to the patient at discharge in case she developed any signs or symptoms of pancreatitis.

Discussion

The pathogenesis by which medications induce an immunologic response is thought to occur via hapten formation.[4] Large (>1000 Da) molecules can intrinsically induce an immunologic response, while smaller molecules can covalently bind to high-molecular-weight structures to induce a response or be metabolized to an immunologic byproduct.[4] Sulfonamides possess a sulfonyl (SO_2) group bound with an amine or amide (NH_2 or NHR) along with an aromatic ring (Figure 1).[2] Sulfonamides can be differentiated into 2 classes based on their structural components. Sulfonamide antibiotics (eg, TMP/SMX, sulfadiazine, sulfisoxazole, sulfacetamide) are unique in their structure in that they possess a primary arylamine group at the N^4 position from the sulfonamide function group and are referred to as arylamines.[2] It is thought that the metabolism of sulfonamide antibiotics occurs via acetylation, hydroxylation, and glucuronidation reactions.[5] The primary arylamine is oxidized to form a highly reactive hydroxylamine intermediate that further oxidizes to form a nitroso metabolite. This nitroso metabolite has an affinity for cysteine residues on proteins and has been shown to be highly immunogenic in animal models. Other sulfonamide-containing medications, such as the loop diuretics celecoxib, acetazolamide, hydrochlorothiazide, tolbutamide, glipizide, glyburide, probenecid, and sulfasalazine, are non-arylamines. Because of their structural difference, the non-antibiotic sul-

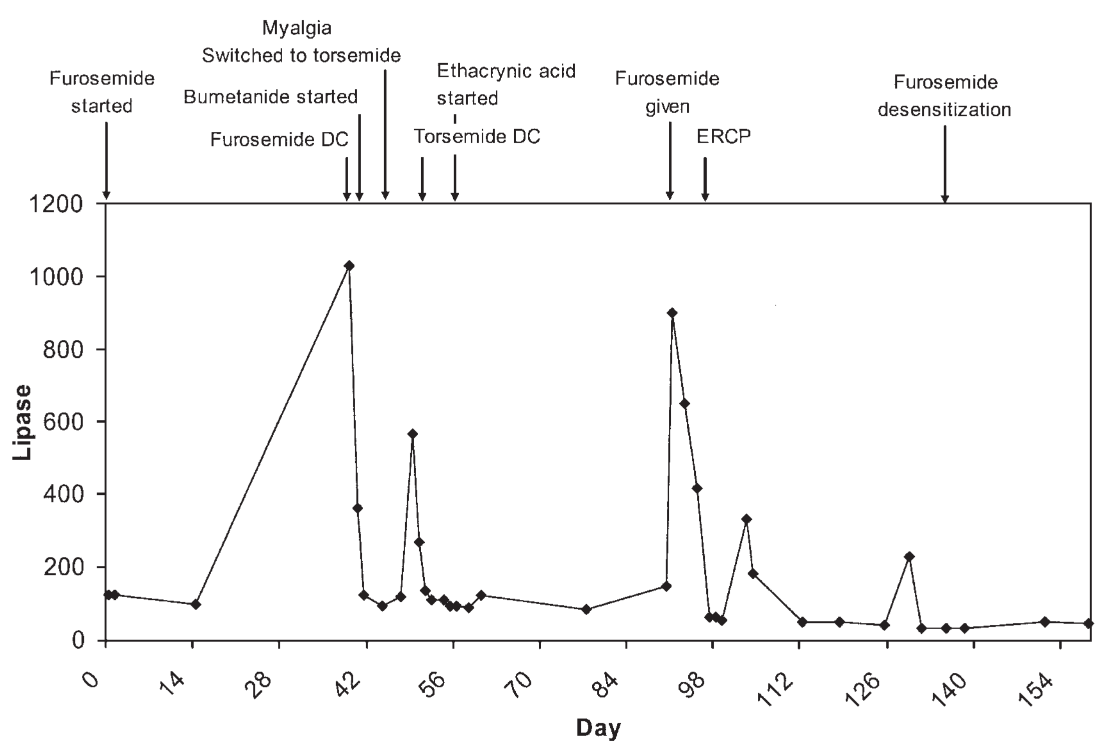

Figure 2. Serum lipase concentrations (IU/L) versus time (days) before and after beginning various loop diuretics. Day zero is first day of admission. DC = discontinued; ERCP = endoscopic retrograde cholangiopancreatography.

fonamides do not share the same metabolic hapten formation as sulfonamide antibiotics. A recent review by Johnson et al.[6] provided an excellent review of all sulfonamides and their chemical structures. In the case of furosemide, its furan subgroup appears to be responsible for exerting haptengic action, but the pathogenesis of the other loop diuretics is unclear.[7] Theoretically, cross-sensitivity in patients allergic to arylamines and non-arylamines can exist, but the absolute risk of reaction appears to be low.[7-9]

The mechanism by which loop diuretics produce pancreatitis is not definitively known, but previous studies have shown that furosemide infusions result in increased pancreatic secretion and increases in serum amylase levels in addition to decreased pancreatic circulation due to extracellular volume contraction.[10-13] In general, drugs that result in pancreatic toxicity can do so by provoking an idiosyncratic reaction, becoming an intrinsic pancreatic toxin, impeding pancreatic secretion, or precipitating bile stones or sludge.[14-16] Furosemide and sulfonamides have been typically associated with idiosyncratic reactions that are due to hypersensitivity.[16] In vitro sensitization of lymphocytes in a patient with an allergy to sulfamethoxazole indicated that sulfonamide-induced pancreatitis may be due to type IV (delayed hypersensitivity) reactions.[17] In addition, loop diuretic–induced pancreatitis typically presents within a month of initiation of therapy, and the symptoms recur soon after rechallenge.[16] Other symptoms of hypersensitivity, such as rash, eosinophilia, and lymphadenopathy, have not been reported. The other types of idiosyncratic reactions, those caused by the formation of a toxic metabolite, typically occur after several months of therapy, and rechallenge results in the recurrence of symptoms several weeks later. Based on the timing of reactions, it is likely that the mechanism by which loop diuretics induce pancreatitis is an immunologic rather than a metabolic pathway.

Pancreatitis associated with sulfonamide loop diuretics, primarily furosemide and bumetanide, have been reported (Table 1).[18-22] In addition, Cooperman and Rubin[23] reported their experiences with the use of ethacrynic acid and furosemide. Their patients developed nausea, vomiting, and epigastric pain associated with furosemide use that dissipated with drug withdrawal. In examining the reported cases, we observed an expected relationship in patients with a previous history of alcohol intake with subsequent furosemide-induced pancreatitis.[18,21] There were cases, however, of patients with no history of pancreatic or biliary tract inflammation who developed furosemide-induced pancreatitis.[19,20,22] There appears to be no dose–effect relationship for development of furosemide-induced pancreatitis, as doses varied from 40 to 1000 mg/day, which provides further support for an immunologic mechanism. There also appears to be no association between the occurrence of furosemide-induced pancreatitis with other factors, such as age and gender. Finally, it appears the resolution of symptoms following discontinuation of the offending drug is fairly rapid, from 24 hours to 4 days following drug discontinuation.

The concept of cross-reactivity between sulfonamide antibiotics and non-antibiotics remains a controversial topic, as few definitive studies have demonstrated cross-reactivity.[9,24] As of December 2, 2005, 8 case reports have documented cross-reactivity in patients allergic to a sulfonamide medication after receiving a sulfonamide non-antibiotic. Patients

Table 1. Published Cases of Loop Diuretic–Induced Pancreatitis

Reference	Pts.	Drug	Allergy	Time of Administration	Symptoms	Rechallenge
Wilson (1967)[18]	age 23 y, male, HTN, CHF, COPD	furosemide 40 mg/day po	NA	day 24	abdominal pain, elevated amylase and blood urea levels	no
Jones (1975)[19]	age 64 y, female, MI	furosemide 80 mg/day po	NA	days 28–38	abdominal discomfort, elevated amylase and lipase levels	no
Strunge (1975)[20]	age 53 y, female, CHF, CRI	furosemide up to 1000 mg/day	NA	NA	abdominal distension, epigastric pain	no
	age 72 y, female, angina	furosemide up to 240 mg/day	NA	NA	postmortem acute inflammation of pancreas	no
Buchanan (1977)[21]	age 46 y, male, DM, ARF	furosemide 500 mg, 1 dose	NA	12 h later	abdominal pain, elevated amylase level	no
	age 56 y, male, CHF	furosemide 250 mg, 1 dose	NA	NA	abdominal pain, elevated amylase level	no
	age 49 y, male, varices	furosemide 250 mg, 1 dose	NA	18 h later	abdominal pain, elevated amylase level	no
Stenvinkel (1988)[22]	age 34 y, male, pulmonary edema	furosemide 750 mg/day, furosemide 500 mg/day, bumetanide 6 mg/day	NA	following day	abdominal pain, elevated amylase level	yes

ARF = acute renal failure; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CRI = chronic renal insufficiency; DM = diabetes mellitus; HTN = hypertension; MI = myocardial infarction; NA = not available.

with previous allergies to "sulfa" drugs, presenting as rash, swelling, nausea, vomiting, or dyspnea, have developed similar symptoms after subsequent administration of acetazolamide, furosemide, bumetanide, glyburide, or hydrochlorothiazide.[25-28] Case reports have also found positive cross-reactivity, via oral sensitivity test or skin prick test, between indapamide, furosemide, or sulfonylureas with sulfonamide antibiotics, loop diuretics, or benzothiadiazines.[29-32]

As of December 2, 2005, only one clinical trial has examined the cross-reactivity between sulfonamide antibiotics and non-antibiotics. A retrospective cohort study examined the risk for subsequent reaction to sulfonamide non-antibiotics following a previous reaction to sulfonamide antibiotics (predominantly TMP/SMX).[33] Of 969 patients with allergic reactions to sulfonamide antibiotics, 9.9% of patients (adjusted OR 2.8; 95% CI 2.1 to 3.7) exhibited a subsequent allergic reaction to sulfonamide non-antibiotics. In examining the loop diuretics, the unadjusted odds ratio was 6.9 (95% CI 3.0 to 15.9). Interestingly, patients who experienced a prior hypersensitivity reaction to sulfonamide antibiotics had a lower risk (adjusted OR 0.7; 95% CI 0.5 to 0.9) of developing hypersensitivity reactions following subsequent administration of sulfonamide non-antibiotics compared with similar reactions following administration of penicillins. It is felt that patients with previous reactions to sulfonamides or penicillins may have a predisposition to later allergic reactions to sulfonamide non-antibiotics. In the recent review of sulfonamide cross-reactivity, 33 sulfonamide non-antibiotics, in 7 different classes, were critically examined to determine whether there is cross-reactivity between sulfonamide antibiotics and non-antibiotics.[6] The authors concluded that the case reports supporting the concept failed to definitively support the cause-and-effect concept of cross-reactivity between the drug classes. It would appear that our patient developed cross-reactivity between a sulfonamide antibiotic and a loop diuretic; however, with recent available literature and the lack of detailed information regarding her previous reactions to sulfonamide antibiotics, this cannot be a definite conclusion.

It is important to highlight that our case report does exhibit some limitations. First, both loop diuretics (mainly furosemide) and oral estrogens have been associated with pancreatitis, occurring 12 hours to 38 days after exposure to loop diuretics and 2–78 weeks for estrogen exposure.[18-22,34]

Second, pancreatitis is also a major complication of ERCP, occurring in up to 7% of patients.[34] The literature also suggests that receiving potent pancreatotoxic drugs (eg, estrogen, azathioprine, valproic acid, mesalazine, morphine derivatives, prednisone) can increase the occurrence of post-ERCP pancreatitis.[35] While we cannot rule out the presence of a new-onset loop diuretic allergy in this patient, we can exclude both estrogen exposure and ERCP as potential causes. Estrogen-induced pancreatitis has been associated with elevated serum cholesterol levels, with triglyceride levels greater than 200 mg/dL.[34] This was not the case with our patient. In addition, estrogen idiosyncratic reactions have been associated with the formation of toxic metabolites, which would not have resulted in recurrence of symptoms in such prompt fashion and would have slowly dissipated with the discontinuation of the medication.[16] Our patient had experienced multiple episodes of pancreatitis prior to the ERCP. Furthermore, she exhibited the same reaction to loop diuretics as she did to TMP/ SMX. Her second challenge resulted in a reaction after 4 days of torsemide, and her last challenge resulted in a reaction after 4 doses of furosemide. Due to the similarity in reaction with exposure to both sulfonamide antibiotics and multiple sulfonamide non-antibiotics, this may suggest cross-reactivity between these agents. This report may be the first to present torsemide cross-reactivity with sulfonamide antibiotics.

An interesting question would be whether the pancreatitis was due to a hypersensitivity reaction or an adverse effect due to toxic metabolites. We cannot conclusively rule out that this was an adverse reaction due to loop diuretics; however, the presentation of symptoms was consistent with sulfonamide- or furosemide-induced delayed hypersensitivity reactions. In our patient, the onset of symptoms was 5 weeks after initiation of furosemide, and the time delay in the development of a reaction decreased with subsequent rechallenges. The timing of the symptom presentation coupled with the usual lack of other hypersensitivity symptoms would indicate an immunologic pathway. An objective assessment of the probability of adverse drug reactions at the time of the first hospitalization (after the multiple rechallenges) indicated a probable case of loop diuretic–induced pancreatitis.[36]

Conclusions

Loop diuretic–induced pancreatitis has been well documented, but the reaction mechanism—hypersensitivity versus metabolic—has not been well elucidated. The timing of presentation of symptoms in our patient points to an immunologic pathway leading to a hypersensitivity reaction. As the patient had previous similar symptoms after administration of TMP/SMX, this would lead to the possibility of cross-reactivity between sulfonamide antibiotics and non-antibiotics. Previous data have included case reports that indicated cross-reactivity with studies and review articles dispelling this association. As the importance of the cross-reactivity potential between sulfonamide antibiotics and non-antibiotics remains in contention, it is our recommendation that clinicians be cognizant of the potential for cross-sensitivity when initiating loop diuretics in patients who had experienced a previous allergic reaction to sulfonamide antibiotics.

Close supervision is warranted in patients who receive concomitant therapy. This observation period may extend as long as one month after therapy initiation. If an allergic reaction develops, the loop diuretic should be discontinued and ethacrynic acid initiated, or loop diuretic desensitization should be considered. A careful history is necessary to document the nature of a previous sulfa allergy, especially in patients with a history of pancreatitis.

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EXTRACTO

OBJETIVO: Describir el caso de una paciente con alergia previa a un antibiótico de sulfamida que posteriormente desarrolló la misma reacción alérgica cuando se le administraron diferentes diuréticos del asa.

CASO CLÍNICO RESUMIDO: Una mujer de 57 años, con una miocardiopatía y una pancreatitis comprobada por alergia a productos que contienen "sulfas," presentó síntomas también indicativos de pancreatitis, tras el uso de furosemida. Posteriormente, desarrolló síntomas similares tras múltiples reexposiciones a varios diuréticos de asa como furosemida, bumetanida, y torasemida. La paciente recibió ácido etacrínico hasta que se desensibilizó a la furosemida. Actualmente, ha estado recibiendo furosemida por vía oral durante los últimos 5 meses sin ningún tipo de complicaciones. El algoritmo de causalidad de Naranjo indica que la relación de causalidad en esta paciente es probable.

DISCUSIÓN: Con frecuencia, se han descrito reacciones asociadas con antibióticos del tipo sulfamidas con arilamina; sin embargo, las reacciones cruzadas con otros fármacos que contengan sulfamidas, pero sin arilamina, han sido escasas. El retraso con el que aparecen los síntomas de pancreatitis tras la administración de diuréticos de asa podría indicar una vía inmunológica. Además, aunque en la literatura médica hay casos de pancreatitis inducida por diuréticos de asa, especialmente por furosemida, las manifestaciones alérgicas tanto con antibióticos del grupo de las sulfamidas como con sulfamidas que no son antibióticos en esta paciente sugieren una posible reactividad cruzada entre estos 2 tipos de medicamentos.

CONCLUSIONES: El mecanismo por el que los diuréticos de asa inducen el desarrollo de pancreatitis parece ser inmunológico. Aunque aún no se conoce la verdadera relación, puede ocurrir una reactividad alérgica cruzada entre los antibióticos del grupo de las sulfamidas y sulfamidas que no son antibióticos, como los diuréticos de asa. La torasemida también parece formar parte de la larga lista de fármacos que pueden causar pancreatitis.

Violeta Lopez Sanchez

RÉSUMÉ

OBJECTIF: Signaler le cas d'une patiente ayant déjà présenté une allergie à un antibiotique sulfamidé qui a développé ultérieurement une réaction allergique similaire lors de l'administration de plusieurs diurétiques de l'anse.

PRÉSENTATION SOMMAIRE DU CAS: Une patiente âgée de 57 ans souffrant d'une cardiomyopathie et ayant comme antécédent une allergie aux "sulfa" documentée sous forme de pancréatite s'est présentée avec des symptômes eux aussi compatibles avec une pancréatite après l'utilisation de furosémide. Elle a développé à nouveau des symptômes similaires après de multiples expositions à divers diurétiques de l'anse incluant le furosémide, le bumétanide, et le torsémide. On a dû utiliser l'acide éthacrynique chez la patiente jusqu'à ce qu'elle soit désensibilisée au furosémide. Elle reçoit maintenant le furosémide depuis 5 mois sans complications. Avec l'échelle de Naranjo, on obtient ce qui correspond à un lien probable.

DISCUSSION: Des réactions associées à des antibiotiques contenant un groupement sulfamidé arylamine ont été signalées fréquemment mais les réactions croisées avec les médicaments contenant un groupement sulfamidé non-arylamine sont rares. Le délai avec lequel les symptômes de pancréatite se sont présentés après l'administration des diurétiques de l'anse laisse penser à un mécanisme immunologique. De plus, bien que des cas de pancréatite induite par les diurétiques de l'anse, principalement le furosémide, aient été publiés dans la littérature, le fait que les manifestations allergiques se soient présentées chez cette patiente autant avec les antibiotiques sulfamidés qu'avec les médications sulfamidés non antibiotiques suggèrent la possibilité d'une réactivité croisée entre les 2 classes de médicaments.

CONCLUSIONS: Le mécanisme par lequel les diurétiques de l'anse causent une pancréatite semble être de nature immunologique. Bien que la vraie corrélation demeure inconnue, une réactivité allergique croisée peut se produire entre les antibiotiques sulfamidés et les sulfamidés non-antibiotiques, tels les diurétiques de l'anse. Le torsémide semble lui aussi faire partie d'une longue liste d'agents qui peuvent causer une pancréatite.

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