

Title:

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### Acute pancreatitis secondary to SGLT2i - An increasingly common problem

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**Abstract:** Acute pancreatitis is an uncommon adverse effect of sodium-glucose linked transporter 2 inhibitors (SGLT2is). Their use has notably increased in recent years, hence clinical suspicion is key in patients recently started on these drugs. We report the case of an 83-year-old male patient who was admitted for a first acute pancreatitis episode of unclear etiology that eventually was attributed to dapaglifozin, a SGLT2i in widespread use.

Keywords: Acute pancreatitis. Dapaglifozin. Sodium-glucose linked transporter 2 inhibitors (SGLT2is).

## Dear Editor,

Acute pancreatitis (AP) is an inflammatory condition of the pancreas whose primary etiologic agents include lithiasis, alcohol, hypertriglyceridemia, hypercalcemia, and medications <sup>(1)</sup>. Drug-induced AP represents 2 % of all APs, with azathioprine, sulphonamides, tetracyclines, valproic acid, corticosteroids and furosemide being most commonly involved. Oral antidiabetic drugs are a rare cause of AP; however, its association with GLP-1 analogs and DPP-4 inhibitors <sup>(3,4)</sup> has been reported, with AP secondary to sodium-glucose cotransporter 2 inhibitors (SGLTis) being exceptional <sup>(4)</sup>.



We report the case of an 83-year-old male who visited for epigastric pain; he had a history of type-2 diabetes mellitus on treatment with metformin and dapaglifozin; he consumed neither alcohol nor other toxic substances. Blood chemistry showed lipase at 200 U/L, normal transaminases and bilirubin, normal lipid and ion panels, and CRP at 157 mg/L. A scan was performed that confirmed the presence of edematous acute pancreatitis (AP), and a minimum amount of bile sludge in the bladder with no bile duct dilation.

By further asking the patient we ascertained his having recently initiated dapaglifozin (SGLT2i), reportedly associated with AP cases. Having ruled out other causes, it was decided to discontinue the SGLT2i as a likely etiologic agent, which led to a positive course and hospital discharge without subsequent recurrence.

#### Discussion

SGLT2is act by reducing glucose absorption in the renal tubule, thus increasing urinary excretion and lowering plasma levels. Most common adverse effects include urinary tract infection, euglycemic ketoacidosis, and kidney failure <sup>(1)</sup>. Recent publications suggest that AP may be an adverse effect of SLGT2is <sup>(1-4)</sup> albeit with an unclear pathogenesis; the main theory is that it represents an idiosyncratic reaction mediated by both immune and cytotoxic events <sup>(3,5)</sup>.

A review was undertaken, which found only five cases of dapaglifozin-associated AP in the literature <sup>(1-4)</sup>. All reported cases involved males aged between 48 and 58 years — with our patient being the oldest in the series with 83 years of age — with a variable treatment duration from 3 to 120 days. All reported cases evolved favorably following the drug's discontinuation.

Further studies are needed to establish a causal relationship between SGLT2is and AP. Therefore, it is important that AP signs and symptoms be monitored in patients recently initiated on a SGLT2i, and then report their onset.



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# Table I.

	Sex	Age	Treatment duration (days)
Gutch et al., 2018	М	48	3
Sujanani et al., 2020	М	51	5
Barrett et al., 2021	М	50	120
Issa et al., 2024	М	58	7
Cortés et al., 2024 *	М	83	30

<sup>\*</sup>The case herein reported