Endocrinología, Diabetes y Nutrición 72 (2025) 101536

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

SCIENTIFIC LETTER

Combined adalimumab and etonogestrel/ethinylestradiol therapy associated with hypertriglyceridemia-induced pancreatitis in a young woman with hidradenitis suppurativa

Tratamiento combinado de adalimumab y etonogestrel/etinilestradiol asociado a pancreatitis inducida por hipertrigliceridemia en una mujer joven con hidradenitis supurativa

Hypertriglyceridemia is a well-established cause of acute pancreatitis, with a reported incidence of up to 7% of all cases. Triglyceride (TG) levels >11.3 mmol/L pose a risk of pancreatitis. Causes of hypertriglyceridemia include rare genetic disorders and more common secondary factors, such as obesity, alcohol abuse, uncontrolled diabetes mellitus, hypothyroidism, and multiple drugs.[1] Hidradenitis suppurativa (HS) is a chronic and debilitating inflammatory skin disease characterized by painful lesions in apocrine gland-bearing regions that often progress into scaring, sinus tract formations, and suppuration. HS presents significant phenotype overlap with metabolic syndrome (MetS) and shares inflammatory pathway activity.[2]

Drug-related metabolic adverse events are typically mild.[3,4] However, the combined use of drugs with known effects on lipid metabolism can lead to a synergistic increase in TG levels and potentially severe consequences, particularly in patients with pre-existing metabolic risk factors. We present a case of hypertriglyceridemia-induced pancreatitis in a young woman on combined therapy with adalimumab and an etonogestrel/ethinylestradiol vaginal ring.

A 34-year-old woman presented to the emergency department with acute, dull abdominal pain radiating to the back and nausea. She had a personal history of HS, with painful abscesses in her armpits, under the breast, and on the inguinal, suprapubic, and perineal regions. Six weeks prior to admission, she initiated treatment with adalimumab 40 mg weekly because antibiotic treatment with local 1% clindamycin and systemic doxycycline proved unsuccessful. For several years she had been using the etonogestrel/ethinylestradiol vaginal ring for contraception. She denied alcohol abuse. However, she smoked approximately 10 cigarettes daily. On presentation, the patient's pulse rate was 104 bpm, blood pressure 140/85 mmHg, and 97% oxygen saturation while on 4 L/min oxygen via nasal catheter. She had obesity, stood at 158 cm, weighted 93 kg, her body mass index was 37.3 kg/m^2, and her waist circumference, 158 cm. The initial blood test could not be interpreted due to lipemic serum. Abdominal ultrasound confirmed the presence of liver steatosis and excluded cholecystolithiasis and cholecystitis. Subsequent computed tomography scan revealed the inflammation of the proximal pancreas with approximately 30% necrosis, along with retroperitoneal fat inflammation measuring 10 cm in diameter (Fig. 1). Thoracic X-ray revealed atelectasis of the lower left lobe. Treatment included parenteral hydration, analgesics, and plasmapheresis. Following initial management, lab test results showed elevated white blood cell count 15.5 $\times$ 10^9/L (normal range 4–10 $\times$ 10^9/L), C-reactive protein (CRP) 135 mg/L (<5 mg/L), amylase 2.22 μkat/L

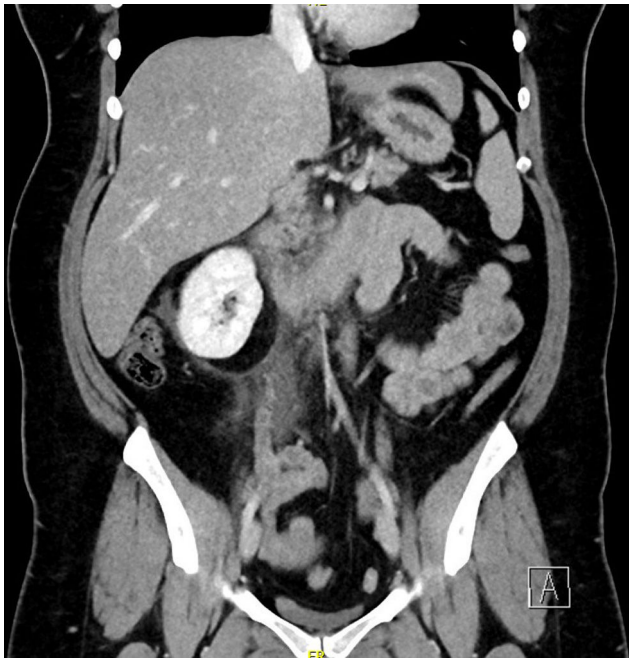

Figure 1 Abdominal computed tomography scan (coronal view) showing inflammation of the pancreas and retroperitoneal fat.

(0.52–1.78 μkat/L), and lipase 4.68 μkat/L (<1.07 μkat/L). Liver function tests were normal. Additionally, TG and total cholesterol levels were significantly high at 49.1 mmol/L (<1.7 mmol/L) and 19.5 mmol/L (<5 mmol/L), respectively. She denied special dietary habits, including high fat or ketogenic diet. During hospitalization, all prior drugs were discontinued, TG levels dropped down to 8.0 mmol/L, while CRP transiently increased up to 368 mg/L before gradually going back to normal. Antibiotic therapy was not required. A new abdominal CT was performed 21 days after the first CT scan confirmed the presence of a necrotic proximal pancreas. The percentage of the necrotic area was <30%. Follow-up visits documented an additional trend of normalization of TG levels, reaching 3.0 mmol/L at the 1-year follow-up. The lipid profile before pancreatitis was not measured, so comparing it to pretreatment levels was not possible.

Adalimumab is a fully human IgG1 monoclonal antibody that targets tumor necrosis factor-alpha (TNF-α). Adalimumab has been approved for various inflammatory conditions, including HS.[5] There has been only one reported case of pancreatitis due to adalimumab-induced hypertriglyceridemia. The patient had extremely high triglyceride levels of 4425 mg/dL (50 mmol/L). However, of note, the patient had a past medical history of alcohol use disorder. Additionally, at the time of presentation, the patient was intoxicated with alcohol levels of 22 mg/dL.[6] As it is well known, alcohol abuse can independently cause hypertriglyceridemia. Stinco et al. reported a case of adalimumab causing increased triglycerides levels of 689 mg/dL (7.79 mmol/L) in a patient with psoriatic arthritis, which eventually led to the discontinuation of treatment after 3 months.[7] Data on the effect of TNF-α on the lipid profile in HS are lacking. Nonetheless, a retrospective cohort study of patients treated with anti-TNF-α in rheumatic patients showed a moderate increase in TG and total cholesterol, with the most significant increase occurring within the first 6 months.[3] Although the mechanism of action of adalimumab on the lipid profile is not completely understood, it probably has to do with the TNF-α mediated inhibition of adipose lipoprotein lipase and, consequently, with elevated levels of triglycerides.[3]

In our case, combined hormonal contraception – specifically the etonogestrel/ethinylestradiol vaginal ring – was used. This type of contraception is common. A previous case reported on a young woman with diabetic ketoacidosis (DKA) who experienced hypertriglyceridemia-associated pancreatitis. The main cause of hypertriglyceridemia was DKA, but the additional risk factor was the hormonal contraception therapy provided by the etonogestrel/ethinylestradiol vaginal ring.[8] The effect of estradiol on lipid metabolism is well known. It mediates the increase of triglycerides by stimulating the secretion of hepatic triglyceride-rich lipoprotein.[8] Additionally, etonogestrel has lower androgenicity and consequently does not counteract the rise in triglyceride levels as much as any other progestogen.[4]

HS *per se* is associated with a higher prevalence of various MetS and insulin resistance. There is more than a 2-fold risk of developing MetS.[2] Prevalence of dyslipidemia in HS is up to 30.7%.[9] Low-grade subclinical inflammation – similar to MetS-related inflammation – is strongly involved in its pathogenesis.[2] HS patients should be screened for MetS parameters such as dyslipidemia, diabetes, and hypertension.[10]

As far as we know, this is the first reported case of hypertriglyceridemia-induced pancreatitis associated with concurrent treatment with adalimumab and combined hormonal contraception in the absence of other contributing factors. Our case highlights the potential for a synergistic effect on lipid metabolism when combining drugs with known side effects on lipid profiles. This possibility should be considered carefully, particularly in patients susceptible to metabolic complications. According to limited data, we recommend regular monitoring of lipid profile or, at least, TG and total cholesterol before treatment, 4 weeks and 6 months after starting therapy, and then annually during treatment.

Patient consent

A written informed consent form was signed by the patient after being explained to her.

Funding

None declared.

Conflict of interest

None declared.

References

1. Kiss L, Fűr G, Pisipati S, Rajalingamgari P, Ewald N, Singh V, et al. Mechanisms linking hypertriglyceridemia to acute pancreatitis. Acta Physiol (Oxf). 2023;237:e13916, http://dx.doi.org/10.1111/apha.13916.
2. Mintoff D, Benhadou F, Pace NP, Frew JW. Metabolic syndrome and hidradenitis suppurativa: epidemiological, molecular, and therapeutic aspects. Int J Dermatol. 2022;61:1175–86.
3. Hassan S, Milman U, Feld J, Eder L, Lavi I, Cohen S, et al. Effects of anti-TNF-α treatment on lipid profile in rheumatic diseases: an analytical cohort study. Arthritis Res Ther. 2016;18:261.
4. Tuppurainen M, Klimscheffskij R, Venhola M, Dieben TO. The combined contraceptive vaginal ring (NuvaRing) and lipid metabolism: a comparative study. Contraception. 2004;69:389–94.
5. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC, et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa. N Engl J Med. 2016;375:422–34, http://dx.doi.org/10.1056/NEJMoa1504370.
6. Sahu KK, Lal A, Mishra AK, Zhang P. Adalimumab-related hypertriglyceridemia and acute pancreatitis. QJM. 2020;113:298–9, http://dx.doi.org/10.1093/qjmed/hcz267.
7. Stinco G, Piccirillo F, Patrone P. Hypertriglyceridaemia during treatment with adalimumab in psoriatic arthritis. Br J Dermatol. 2007;157:1273–4, http://dx.doi.org/10.1111/j.1365-2133.2007.08188.x.
8. Maslonka M, Salameh H, Bhatt A, Larson SA. Hypertriglyceridemia induced acute pancreatitis associated with diabetic

ketoacidosis and a vaginal estrogen contraceptive device (NuvaRing): successfully treated with insulin infusion, plasmapheresis, and ring removal: 1316. Am J Gastroenterol. 2016;111:S587.
9. Kimball AB, Sundaram M, Gauthier G, Guérin A, Pivneva I, Singh R, et al. The comorbidity burden of hidradenitis suppurativa in the United States: a claims data analysis. Dermatol Ther (Heidelb). 2018;8:557–69, http://dx.doi.org/10.1007/s13555-018-0264-z.
10. Garg A, Malviya N, Strunk A, Wright S, Alavi A, Alhusayen R, et al. Comorbidity screening in hidradenitis suppurativa: evidence-based recommendations from the US and Canadian Hidradenitis Suppurativa Foundations. J Am Acad Dermatol. 2022;86:1092–101.

Darko Siuka[a,b], Matej Rakusa[b,c,*]

[a] *Department of Gastroenterology, University Medical Centre Ljubljana, Ljubljana, Slovenia*
[b] *Department of Internal Medicine, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*
[c] *Department of Endocrinology, Diabetes and Metabolic Disease, University Medical Centre Ljubljana, Ljubljana, Slovenia*

* Corresponding author.
E-mail address: matej.rakusa@gmail.com (M. Rakusa).