A Rare Case Of Acute Pancreatitis Cause by Newly Diagnosed Graves' Disease: A Successful Therapeutic Option

*Azzaki Abubakar *,**, Fauzi Yusuf*,**, Desi Maghfirah*,**, Andrie Gunawan*,**, Hendra Zufry***, Meutia Nailan Edward****, Khek Yu Ho******

*Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine, Syiah Kuala University, Banda Aceh, Aceh, 23111, Indonesia
**Gastroenterohepatology Division, Departemen of Interna Medicine, General Hospital dr. Zainoel Abidin, Banda Aceh, Aceh, 23111, Indonesia
***Endocrin, Metabolic and Diabetes Division, Departemen of Interna Medicine, General Hospital dr. Zainoel Abidin, Banda Aceh, Aceh, 23111, Indonesia
****School of Medicine, Department of Internal Medicine, Syiah Kuala University, Banda Aceh, Aceh, 23111, Indonesia
*****Department of Medicine, National University of Singapore, Singapore

Corresponding author:
Azzaki Abubakar. Gastroenterohepatology Division, Department Of Interna Medicine, Syiah Kuala University / General Hospital dr. Zainoel Abidin, Jl. Teuku Moh. Daud Beureueh No.108, Bandar Baru, Kec. Kuta Alam, Kota Banda Aceh, Aceh 24415. Email : azzaki.abubakar@usk.ac.id

ABSTRACT

Acute pancreatitis is a frequent disorder whose severity level varies from mild to life-threatening. This condition is characterized by abrupt inflammation of the pancreas. A 53-year-old male was having upper right abdominal pain and epigastric pain which began four hours after hospitalization. This case highlights the complexities of managing acute pancreatitis in a patient with Graves' disease, where hyperthyroidism may worsen pancreatitis and vice versa. Graves' disease is an autoimmune disorder causing hyperthyroidism, which can complicate pancreatitis management, particularly when treated with methimazole, which has been associated with acute pancreatitis. This case suggests a potential link between untreated Graves' disease and idiopathic acute pancreatitis. In patients presenting with unexplained pancreatitis, evaluation for hyperthyroidism may be warranted. The novelty of this case lies in the exclusion of all conventional etiologies and the possible role of autoimmune thyroid disease in pancreatic inflammation.

Keywords: *Acute pancreatitis, graves' disease, hyperthyroidism*

ABSTRAK

Pankreatitis akut terjadi dengan tingkat keparahan yang bervariasi mulai dari derajat ringan hingga mengancam jiwa. Pankreatitis akut terjadi dengan peradangan pada pankreas yang terjadi secara mendadak. Pada laporan kausus ini seorang pria berusia 53 tahun mengalami nyeri perut kanan atas dan nyeri epigastrium yang terjadi 4 jam sebelum masuk rumah sakit. Laporan kasus ini menjelaskan mengenai kompleksitas dalam penanganan pankreatitis akut pada pasien penyakit Grave, Dimana hipertiroidisme dapat memperburuk pankreatitis atau sebaliknya. Penyakit Graves merupakan gangguan autoimun yang menyebabkan hipertiroidisme, dan dapat memperumit penanganan pankreatitis, terutama ketika diobati dengan metimazol yang telah dikaitkan

dengan kejadian pankreatitis akut. Kasus ini mengindikasikan kemungkinan hubungan antara penyakit Graves yang belum diobati dengan pankreatitis akut idiopatik. Pada pasien yang mengalami pankreatitis tanpa penyebab yang jelas, evaluasi fungsi tiroid perlu dipertimbangkan. Keunikan kasus ini terletak pada tersingkirnya seluruh penyebab konvensional dan kemungkinan peran penyakit tiroid autoimun dalam proses peradangan pancreas.

Kata Kunci; *Pankreatitis akut, penyakit grave, hipertiroidisme*

INTRODUCTION

Graves' disease is a well-known autoimmune condition that causes the thyroid gland to produce too many thyroid hormones as a result of aberrant immune system stimulation. Most patients with Graves' disease typically exhibit classic signs and symptoms of hyperthyroidism. Rarely, initial presentation may solely manifest as Graves' orbitopathy or pretibial myxedema. Symptoms vary based on age of onset, severity, and duration of hyperthyroidism. In elderly patients, symptoms may be subtle or nonspecific, such as fatigue, weight loss, and new-onset atrial fibrillation, termed apathetic thyrotoxicosis. While methimazole is considered the definitive drug for treating hyperthyroidism, it carries the risk of inducing acute pancreatitis in some patients. This serious inflammatory condition of the pancreas has been increasingly recognized as a potential adverse effect of methimazole.[1]

Acute pancreatitis arises from several primary causes since its etiologies include infections and autoimmune pancreatitis. Moderate to severe epigastric stomach discomfort is frequently reported by patients, along with nausea and appetite loss[1]. The Burch-Wartofsky Score (BWS) is a clinical tool used to assess the severity of thyroid storm, a life-threatening complication of hyperthyroidism. One of the assessments of thyroid storm is gastrointestinal symptoms in the form of abdominal pain so that the diagnosis of acute pancreatitis can overlap with the symptoms of thyroid storm.

The purpose of this case study is to demonstrate the difficulties and achievements in treating acute pancreatitis due to Graves' disease. We report an uncommon instance of acute pancreatitis caused by Graves' disease in a male patient who had never been diagnosed with hyperthyroidism. Aggressive medical therapy centred on the treatment of acute pancreatitis and antithyroid medications proved to be successful in treating this life-threatening illness.

CASE ILLUSTRATION

A 53-year-old man with a history of poorly controlled hypertension presented with sudden, severe epigastric stabbing pain radiating to the pit of the stomach, beginning four hours after admission. He described the pain as continuous, worsened by food intake, lasting over 20 minutes, and accompanied by diaphoresis. He denied receiving radiation to the shoulder, jaw, or neck. He reported no prior episodes of similar pain. On further questioning, the patient noted a two-year history of slowly progressive exophthalmos and a visible anterior neck swelling. He had experienced intermittent diplopia and visual "shadows," for which he saw an ophthalmologist, with partial symptomatic relief. He was not yet on any anti-thyroid medications (e.g., carbimazole, propylthiouracil, or iodine compounds).

Clinical instruments such as the Wayne Index, Burch-Wartofsky Score (BWS), Japan Thyroid Association (JTA) score, Akamizu Score, and Acute Physiology and Chronic Health Evaluation II (APACHE II) are used to evaluate different facets of thyroid conditions and essential illness. The Wayne Index helps evaluate hyperthyroidism likelihood based on symptoms and is useful in resource-limited settings, with a score of 35 in this case. Timely management depends on both the BWS and JTA scores, which are used to determine the severity of thyroid storm. The BWS score is 35, but the JTA score was not relevant in this instance. Although it was not applicable in this case, the Akamizu Score, which is also used to evaluate thyroid storms, similarly directs diagnosis and treatment. Lastly, a highly proven instrument for predicting in-hospital mortality in intensive care units, the APACHE II score is used in critical care to evaluate the severity of the disease.

Blood laboratory results on June 5, 2024, revealed pancreatic enzymes: amylase 264 U/L, lipase 665 U/L; thyroid function: FT4 81.4 pmol/L, TSH 0.017 μIU/mL, TRAb 8.5 UI/L; autoimmune panels: serum IgG4 0.8 g/L (normal), ANA and ASMA both negative; calcium metabolism: serum calcium 9.2 mg/dL, intact PTH 45 pg/mL (both within normal limits); and other laboratory results: hemoglobin at 12.2 g/

dl, hematocrit at 39%, SGOT at 52 U/L, SGPT at 41 U/L, total bilirubin at 0.72 mg/dl, direct bilirubin at 0.55 mg/dl, indirect bilirubin at 0.17 mg/dl, random blood sugar at 145 mg/dl, urea at 33 mg/dl, creatinine at 0.73 mg/dl, sodium at 141 mmol/L, potassium at 4.3 mmol/L, chloride at 105 mmol/L, and albumin at 3.41 g/dl. Further tests on June 6 showed elevated procalcitonin at 4.92 ng/ml, Urinalysis indicated a pH of 5.0, proteinuria at +1, and hematuria. A thorax x-ray from June 5, 2024, showed a normal heart size, pulmonary infiltrates in both parahilar regions, a thickened and elevated right diaphragm, and no cardiac abnormalities, with a diagnosis of pneumonia and an elevated right diaphragm.

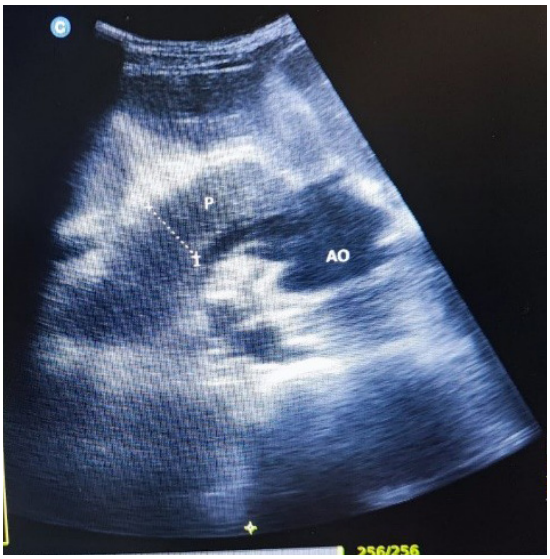

Figure 1. An abdominal ultrasound was then performed, There is an enlargement of the pancreas with inhomogeneous echogenicity and irregular edges. which showed no evidence of cholelithiasis or biliary duct dilatation

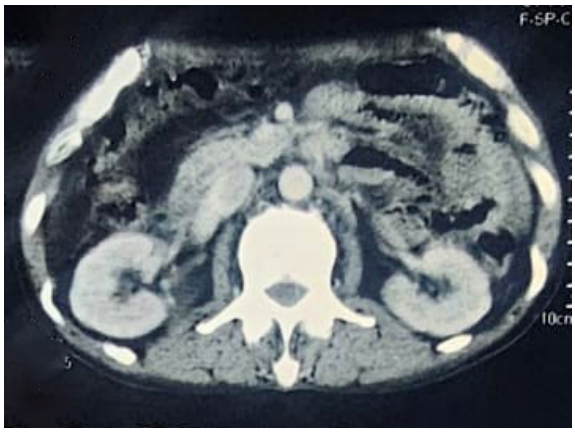

Figure 2. Abdominal CT scan showed a swollen pancreas with peripancreatic inflammatory fat stranding, suggestive of acute pancreatitis.

The patient's ultrasound result recorded on June 7, 2024 as seen in **figure 1**, shows that liver size was normal with uneven regular edges, acute angle with an increase of echo-parenchymal intensity. The result also reveals gall bladder condition with a thickened wall but non-existing stone, masses or cysts. In additions the spleen was also normal in size and no fluid in the abdominal cavity. The pancreas and both kidneys were normal in size. Later on June 11, 2024, a CT scan with and without contrast, as seen in **figure 2**, showed that the liver was within normal limits, with perfect density and a smooth surface. The portal and hepatic veins were normal, and the intra- and extra-hepatic biliary systems were typical in normal conditions without masses or abscesses. Small cysts were visible in the right and left lobes of the liver. The gallbladder was normal in size, with thickened walls and no stones. The spleen appeared normal in size and density, with a smooth surface, and no masses, abscesses, or cysts were detected. The pancreas appeared normal in size and density, with a smooth surface and no evidence of masses, abscesses, or cysts. The conclusions indicated right pleural effusion, cholecystitis, thoracolumbar spondylosis, and degenerative disc disease.

The patient was diagnosed with acute pancreatitis in the context of newly diagnosed Graves' disease, after comprehensive exclusion of other potential etiologies. Abdominal ultrasound and contrast-enhanced CT showed no evidence of gallstones or biliary duct dilatation, ruling out gallstone and biliary-tract causes. Autoimmune pancreatitis was excluded based on normal serum IgG4 levels and negative results for ANA and ASMA. Disorders of calcium metabolism and MEN-1 were considered but excluded based on normal serum calcium and intact PTH levels. Finally, drug-induced pancreatitis was deemed unlikely as the patient had not received any anti-thyroid medications (carbimazole, propylthiouracil) or iodine compounds before the onset of symptoms.

The first treatment consisted of bed resting and low-fat soft diet which provides 1700 kcal/day. Rehydration was also managet with RL fluid at 150 cc/hour for the initial 24 hours and them reduced to 75 cc.hour on the second day and 37.5 cc/hour on the third day. Medications included IV Ampicillin Sulbactam 2 g every 6 hours, IV lansoprazole 40 mg every 12 hours, paracetamol drip 1 g every 8 hours, oral domperidone 10 mg three times a day, oral thyrozol 10 mg twice a day, and oral propranolol 10 mg one times a day.

DISCUSSION

Acute pancreatitis (AP) is most commonly caused by gallstones and chronic alcohol consumption, accounting for the majority of cases worldwide. Other notable etiologies include hypertriglyceridemia, hypercalcemia, drug-induced pancreatitis, autoimmune processes, and post-procedural complications. However, in a subset of patients estimated at approximately 15–20% the etiology remains idiopathic despite comprehensive evaluation. [2,3] In this case, a 53-year-old male presented with features of acute pancreatitis alongside newly diagnosed Graves' disease, raising questions about a possible causal association.

To consider such a link, it is essential to systematically exclude all conventional causes. Imaging studies, including abdominal ultrasound and contrast-enhanced CT scan, revealed no evidence of cholelithiasis or biliary duct dilation, effectively ruling out gallstone-related or obstructive pancreatitis. Laboratory testing revealed normal serum triglyceride and calcium levels, ruling out metabolic causes such as hypertriglyceridemia and hypercalcemia, as well as potential manifestations of multiple endocrine neoplasia type 1 (MEN-1). There was no history of alcohol use, trauma, recent endoscopic procedures, or exposure to pancreatic toxins. Autoimmune pancreatitis was considered but deemed unlikely due to the absence of radiologic features, a normal serum IgG4 concentration, and negative autoantibodies (ANA and ASMA).

While radiographic studies are not diagnostic for acute pancreatitis (AP), they are valuable for identifying underlying etiologies and excluding other conditions. Chest X-rays may reveal pleural effusion or basal atelectasis, and abdominal X-rays can show pancreatic calcifications or sentinel loops. Transabdominal ultrasound is the preferred initial modality, especially for detecting gallstones, although its sensitivity may be limited by bowel gas in up to 30% of cases. In severe or complicated presentations, multiphase contrast-enhanced CT is recommended to assess pancreatic necrosis and vascular complications, ideally after a delay of at least 48 hours. MRI with MRCP offers detailed anatomical visualization, and ERCP is reserved for suspected biliary obstruction with cholangitis. In idiopathic cases, endoscopic ultrasound (EUS) may detect microlithiasis or pancreatic tumors when other imaging is inconclusive.[4]

Early intensive fluid resuscitation is the cornerstone of treatment for acute pancreatitis. Lactated Ringer's solution is the suggested fluid; unless otherwise specified, it is administered as a maintenance dosage at a rate of 3 milliliters per kilogram per hour, or 250 to 500 milliliters per hour, during the first 24 hours after being given as a bolus of 15 to 20 mL/kg. Monitoring includes regular assessments of laboratory results, mainly hematocrit, urea nitrogen in the blood, and urine output every 4-6 hours between the first IV fluid resuscitation phase encounter to adjust fluid administration. When initial resuscitation is not adequately performed, there is a significant chance that multi-organ dysfunction syndrome (MODS) will develop, which calls for more intensive care. Another crucial element is nutrition control. Until symptoms including nausea, vomiting, ileus, and abdominal discomfort subside, patients usually avoid oral intake. In moderate cases, early feeding is encouraged and carefully started with a soft, low-fat, low-residue food, increasing as tolerated.[5–9]

Prophylactic antibiotics are generally unnecessary; empiric use is reserved for suspected infections until culture results are available, particularly in cases of infected necrosis. Pain management is paramount, with the WHO analgesic ladder guiding treatment. Non-steroidal anti-inflammatory medications (NSAIDs) are the first line of treatment, followed by strong opioids when necessary, with interventions customized to meet the needs of each patient.[6,7]

Treatment strategies for Graves' disease are tailored to address its specific symptoms and to lower thyroid hormone production effectively. Symptomatic patients, especially those with elevated heart rates, cardiovascular history, or elderly individuals, typically receive beta-adrenergic blockers like Atenolol or Propranolol to manage symptoms and reduce heart rate. Atenolol, prescribed at 25 to 50 mg once daily, is favored for its convenience and selective action on beta-1 receptors. Since propranolol can prevent peripheral conversion of T4 to T3, it can also be given at doses of 10-40 mg every 6-8 hours. If beta blockers are not working or are not tolerated, calcium channel blocker, or CCBs, such verapamil and diltiazem, are thought to be substitutes.[7,9] Definitive treatments include antithyroid medications (e.g., methimazole), radioactive iodine (RAI) therapy, or thyroidectomy, chosen based on individual clinical factors.[3,5,9,10]

In this case, the patient received supportive therapy including bed rest, a low-fat diet, and fluid resuscitation with Ringer's Lactate. Medical management included IV ampicillin-sulbactam to prevent infection, lansoprazole, paracetamol, domperidone, methimazole (tyrosol), and propranolol.

Prompt infection management was crucial to prevent complications such as thyroid storm. While ampicillin-sulbactam offers broad antibacterial coverage, clinicians must monitor for adverse reactions and adjust therapy based on patient-specific risks. Methimazole remains the standard for hyperthyroidism treatment, though rare complications like agranulocytosis and drug-induced pancreatitis require careful monitoring during use.

For over 70 years, thionamide compounds like methimazole have been integral in managing hyperthyroidism, reducing both comorbidities and mortality associated with the disease. Despite their general tolerability, serious side effects such as agranulocytosis and drug-induced liver injury have been noted in a small percentage of users. Methimazole is considered the definitive drug for treating hyperthyroidism. Despite its effectiveness in managing hyperthyroidism, including Graves' disease, and its generally favorable side-effect profile compared to other antithyroid medications, methimazole's association with risk of inducing acute pancreatitis necessitates careful monitoring and consideration by healthcare providers.[6]

Of particular note, antithyroid drugs such as carbimazole and methimazole have been reported as rare but documented causes of acute pancreatitis. A few case reports have described the onset of pancreatitis following exposure to these medications, and one population-based cohort study found a slight increase in risk of AP during the initial months of methimazole therapy.[13,14] Similarly, isolated cases have been associated with iodine-containing agents, particularly radioactive iodine (I-131), and pancreatitis.[15] However, in the present case, the patient had not received any form of antithyroid therapy or iodine before admission, further supporting that drug-induced pancreatitis was not a contributing factor.

To our knowledge, this case adds to the very limited number of reported instances suggesting a possible association between Graves' disease and acute pancreatitis in the absence of pharmacologic triggers. While causality cannot be definitively established, the temporal relationship, along with the exclusion of more common etiologies, warrants further investigation. Clinicians should consider evaluating thyroid function in patients presenting with idiopathic pancreatitis, particularly if signs of thyrotoxicosis are evident. Continued reporting and research are necessary to determine whether a true causal link exists or whether such presentations are merely coincidental.

CONCLUSION

Graves' disease is an autoimmune condition that causes abnormal immune system stimulation which resulted in excessive thyroid hormones production. The fundamental cause is the generation of autoantibodies, particularly thyroid-stimulating immunoglobulins (TSI or TSHR antibodies), which attach to and activate thyroid cells' TSH receptors. subsequently, Triiodothyronine (T3) and thyroxine (T4), two thyroid hormones, are synthesized and secreted in greater amounts, resulting in hyperthyroidism.

Methimazole has the potential to cause acute pancreatitis in certain patients, despite being the gold standard for treating hyperthyroidism, especially in diseases like Graves' disease. This severe pancreatic inflammatory disease is becoming more well acknowledged as a possible side effect of methimazole. Medical professionals must closely monitor and take into account methimazole correlation to acute pancreatitis despite its efficacy in treating hyperthyroidism, including Graves' disease, and its usually positive side-effect profile when compared to other antithyroid medicine.

REFERENCES

1. Khandelwal A, Inoue D, Takahashi N. Autoimmune pancreatitis: an update. Abdom Radiol (NY). 2020 May;45(5):1359–70.
2. Zilio MB, Eyff TF, Azeredo-Da-Silva ALF, Bersch VP, Osvaldt AB. A systematic review and meta-analysis of the aetiology of acute pancreatitis. HPB (Oxford) [Internet]. 2019 Mar 1 [cited 2025 Jul 16];21(3):259–67. Available from: https://www.researchgate.net/publication/327818552_A_systematic_review_and_meta-analysis_of_the_aetiology_of_acute_pancreatitis
3. Mederos MA, Reber HA, Girgis MD. Acute pancreatitis: a review. JAMA [Internet]. 2021 Jan 26 [cited 2025 Jul 16];325(4):382–90. Available from: https://pubmed.ncbi.nlm.nih.gov/33496779/
4. Valverde-López F, Wilcox CM, Redondo-Cerezo E. Evaluation and management of acute pancreatitis in Spain. Gastroenterol Hepatol [Internet]. 2018 Dec 1 [cited 2025 Jul 16];41(10):618–28. Available from: https://pubmed.ncbi.nlm.nih.gov/30149943/
5. Agito K, Manni A. Acute pancreatitis induced by methimazole in a patient with subclinical hyperthyroidism. J Investig Med High Impact Case Rep [Internet]. 2015 May 19 [cited 2025 Jul 16];3(2). Available from: https://pubmed.ncbi.nlm.nih.gov/26425645/
6. Brix TH, Lund LC, Henriksen DP, Folkestad L, Bonnema SJ, Hallas J, et al. Methimazole and risk of acute pancreatitis. Lancet Diabetes Endocrinol [Internet]. 2020 Mar 1 [cited 2025 Jul 16];8(3):187–9. Available from: https://pubmed.ncbi.nlm.nih.gov/32035032/

7. Talathi SS, Zimmerman R, Young M. Anatomy, abdomen and pelvis, pancreas. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Apr 5 [cited 2025 Jul 16]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532912/
8. Davies TF, Andersen S, Latif R, Nagayama Y, Barbesino G, Brito M, et al. Graves' disease. Nat Rev Dis Primers [Internet]. 2020 Dec 1 [cited 2025 Jul 16];6(1). Available from: https://pubmed.ncbi.nlm.nih.gov/32616746/
9. de-Madaria E, Buxbaum JL, Maisonneuve P, García García de Paredes A, Zapater P, Guilabert L, et al. Aggressive or moderate fluid resuscitation in acute pancreatitis. N Engl J Med. 2022 Sep 15;387(11):989–1000.
10. Barrie J, Jamdar S, Smith N, McPherson SJ, Siriwardena AK, O'Reilly DA. Misuse of antibiotics in acute pancreatitis: insights from the United Kingdom's National Confidential Enquiry into patient outcome and death (NCEPOD) survey. Pancreatology. 2018 Oct;18(7):721–6.
11. Pecere A, Caputo M, Sarro A, Ucciero A, Zibetti A, Aimaretti G, et al. Methimazole treatment and risk of acute pancreatitis: a population-based cohort study. J Clin Endocrinol Metab [Internet]. 2020 Dec 1 [cited 2025 Jul 16];105(12). Available from: https://www.thyroid.org/patient-thyroid-information/ct-for-patients/july-2021/vol-14-issue-7-p-5-6/
12. Chng CL, Kek PC, Khoo DHC. Carbimazole-induced acute pancreatitis and cholestatic hepatitis. Endocr Pract [Internet]. 2011 Nov [cited 2025 Jul 16];17(6):960–1. Available from: https://www.researchgate.net/publication/351268475_Carbimazole-Induced_Acute_Pancreatitis_and_Cholestatic_Hepatitis
13. Liu Y, Lou X. The occurrence of acute pancreatitis after iodine 131 treatment of hyperthyroidism. Acta Endocrinol (Buchar) [Internet]. 2022 Apr 1 [cited 2025 Jul 16];18(2):250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9512377/
14. Antonelli A, Fallahi P, Elia G, Ragusa F, Paparo SR, Ferrari SM. Graves' disease: clinical manifestations, immune pathogenesis (cytokines and chemokines) and therapy. Best Pract Res Clin Endocrinol Metab. 2020;34(1):101388. doi:10.1016/j.beem.2020.101388
15. Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH. 2018 European Thyroid Association guideline for the management of Graves' hyperthyroidism. Eur Thyroid J. 2018;7(4):167–86. doi:10.1159/000490384