

Case Report / Olgu Sunumu

Propylthiouracil-Induced neutropenia coinciding with newly diagnosed Crohn's disease

Propiltiourasil tedavisine sekonder nütropeni ve Crohn hastalığı birlikteliği

Hacı Mehmet ÇİTİL ^{1*} Mustafa Eray DAĞDEVİREN ¹ Cevat GENÇER ¹ Lezan KESKİN ¹
Bahadır ÖNDEŞ ² Burhan Hakan KANAT ² Gökhan SÖĞÜTLÜ ²

¹Malatya Turgut Özal University, School of Medicine, Department of Internal Medicine, Malatya, Turkey.

²Malatya Turgut Özal University, School of Medicine, Department of General Surgery, Malatya, Turkey.

*Sorumlu Yazar / Corresponding Author, E-mail: mehmet4436@gmail.com

ARTICLE INFO

Article History:

Received: 06.12.2025

Accepted: 23.12.2025

Publication: 31.12.2025

Citation:

Çitil M. H., Dağdeviren M. E., Gençer C., Keskin L., Öndeş B., Kanat B. H., Söğütü G. Propylthiouracil-Induced neutropenia coinciding with newly diagnosed Crohn's disease: a case report. Journal of MTU. 2025;4(3):113-117.
<https://doi.org/10.58651/jomtu.1835987>

MAKALE BİLGİLERİ

Makale Geçmişi:

Geliş Tarihi: 06.12.2025

Kabul Tarihi: 23.12.2025

Yayın Tarihi: 31.12.2025

Atıf Bilgisi:

Çitil M. H., Dağdeviren M. E., Gençer C., Keskin L., Öndeş B., Kanat B. H., Söğütü G. Propiltiourasil tedavisine sekonder nütropeni ve Crohn hastalığı birlikteliği. Journal of MTU. 2025;4(3):113-117.
<https://doi.org/10.58651/jomtu.1835987>

ABSTRACT

Agranulocytosis is a serious side effect of antithyroid drugs (ATDs) in patients with hyperthyroidism. Diabetic ketosis is an acute complication of diabetes mellitus (DM) that can be triggered by conditions such as infection, stress, and noncompliance with treatment. Crohn's disease (CD) is a chronic inflammatory disease of the digestive system and can present with life-threatening complications such as intestinal perforation. A 42-year-old woman with a history of DM, epilepsy, and hyperthyroidism presented with fatigue, sore throat, and joint pain. This is a rare case of Crohn's disease diagnosed after an intestinal perforation during insulin infusion, plasmapheresis, and steroid therapy following diabetic ketoacidosis and neutropenia. This case highlights the coexistence of these three rare conditions in a single patient.

Keywords: Diabetic ketosis, agranulocytosis, neutropenia, crohn's disease

ÖZET

Agranülositoz, hipertroidi hastalarında antitiroid ilaçların (ATİ) kullanımına bağlı ortaya çıkan ciddi bir yan etkidir. Diyabetik ketoz, diyabetes mellitusun (DM) akut komplikasyonlarından biri olup, enfeksiyon, stres, tedavi uyumsuzluğu gibi durumlarla tetiklenebilir. Crohn hastalığı (CH), sindirim sisteminin kronik enflamatuvar bir hastalığı olup, intestinal perforasyon gibi hayatı tehdit eden komplikasyonlarla kendini gösterebilir. DM, epilepsi ve hipertroidi tanımlı 42 yaşında kadın hasta halsizlik, boğaz ağrısı, eklem ağrısı şikâyeti ile başvurdu. Diyabetik ketoz ve nütropeni ile yatırılarak insülin infüzyonu, plazmaferez ve steroid tedavisi sırasında gelişen intestinal perforasyon sonucu crohn tanısı alan nadir bir olgudur. Bu olgu, nadir görülen bu üç durumun eş zamanlılığını vurgulamaktadır.

Anahtar Kelimeler: Diyabetik ketoz, agranülositoz, nütropeni, crohn hastalığı

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease caused by inadequate insulin secretion, impaired insulin action, or both. In cases of inadequate or non-compliant treatment, complications such as diabetic ketoacidosis and hyperosmolar coma may occur (1).

The antithyroid drugs (ATDs) used to treat hyperthyroidism are propylthiouracil (PTU) and methimazole. One of the most serious side effects is agranulocytosis, defined as a reduction in granulocyte count to $<0.5 \times 10^9/L$, which is observed in 0.2–0.5% of patients taking ATDs (2).

Crohn's disease is an idiopathic inflammatory bowel disease characterized by chronic transmural inflammation that can affect any part of the digestive system from the mouth to the anus. Crohn's disease can cause complications such as abscesses, fistula formation, and perforation as a result of recurrent intestinal infections (3). In this case report, we present a case of agranulocytosis due to PTU use and sudden abdominal pain during diabetic ketosis treatment, which resulted in a diagnosis of Crohn's disease after laparotomy. This case highlights the association between Graves' disease, another autoimmune disease associated with late autoimmune diabetes (LADA), and Crohn's disease, a serious gastrointestinal disease, and the importance of treatment management in critical situations.

CASE

A 42-year-old woman with a 15-year history of type 2 diabetes mellitus, a 2-year history of epilepsy, and a 1-year history of hyperthyroidism. She was receiving a combination of insulin aspart and degludec (2×16 units), vildagliptin + metformin 50/1000 milligram (mg) tablets (2×1 tablets), dapagliflozin (10 mg) tablets (1×1 tablets), propylthiouracil (50 mg) tablets (3×1 tablets), metoprolol (50 mg) tablets (2×1 tablets), and levetiracetam tablets (2×1 tablet). The patient presented to an external center with complaints of fatigue, sore throat, and joint pain for the past month and odynophagia for the past two weeks. Laboratory tests revealed a neutrophil count of $310/mm^3$, and she was referred to our center with preliminary diagnoses of neutropenia and antithyroid drug-induced agranulocytosis. In the examinations performed in the endocrinology outpatient clinic, blood glucose level was 323 mg/dL, complete urinalysis revealed +3 ketonuria in urine, blood gases revealed pH: 7.499 (7.35-7.45), bicarbonate: 22.8 mmol/L (22-28 mmol/L), hemoglobin 12.5 g/dL (12.2-18.1 g/dL), neutrophil count $310/mm^3$ (2000-6900/ mm^3), TSH: <0.005 mU/L (0.27-4.2 mU/L), FT3: 4.03 pg/mL (2.04-4.4 pg/mL), FT4: 1.42 pg/mL (0.8-1.71 pg/mL). Thyroid ultrasonography revealed an enlarged thyroid gland with distinct lobulated contours, distinctly heterogeneous parenchyma, and a 5-mm hyperechoic nodule localized to the right lobe of the thyroid. The patient was admitted to the endoc-

rinology ward with preliminary diagnoses of propylthiouracil-induced agranulocytosis, hyperthyroidism, and diabetic ketosis. Systemic examination revealed weight loss, fatigue, night sweats, dizziness, dry mouth, sore throat, heat intolerance, polydipsia, exertional dyspnea, palpitations, bloating, dysuria, and cough symptoms. Upon admission, the patient's blood pressure was 110/80 mmHg, pulse was 84/min, respiratory rate was 22/min, temperature was 36.6°C, and oxygen saturation was 95%. Her general condition was moderate; she was conscious, oriented, and cooperative; her Glasgow Coma Score (GCS) was 15/15; and auscultation of lung and heart sounds was normal. Aphthous lesions were observed in the oral cavity. Abdominal examination revealed no tenderness. A thyroid receptor-blocking antibody (TRAB) test sent during hospitalization was found to be positive at 17 U/L (0-1.5 U/L), and Graves' disease was diagnosed. The patient was started on diabetic ketosis therapy, insulin infusion and hydration therapy. A hematology consultation was requested for the patient, who was suspected to have neutropenia due to ATI, and a peripheral blood smear revealed lymphocytes of 72%, monocytes of 24%, fragmented blood cells of 4%, an elevated platelet count, and mild hypochromia, anisocytosis, and poikilocytosis in the erythrocytes. The patient's C-peptide level was 0.02 ng/mL (1.1-4.4 ng/mL), and diabetes autoantibodies were ordered for the patient, who had previously used oral antidiabetic medication. The patient was diagnosed with LADA based on the following antibody measurements: anti-insulin antibody, 2.1 U/mL; anti-GAD antibody, >250 U/mL; and islet cell antibody, 0.54. Furthermore, during hospitalization, the patient's C-reactive protein (CRP) level was 25.8 mg/dL (0-0.5 mg/dL), a complete urinalysis revealed 16 red blood cells, and the patient described dysuria. Urine and blood cultures were also obtained. Meropenem 3×1 g treatment was initiated on the recommendation of an infectious disease specialist. Total plasma exchange (plasmapheresis) was planned for the patient's neutropenia secondary to antithyroid therapy and existing hyperthyroidism. The presence of hyperthyroidism prevented the ketone levels from turning negative during daily TIT monitoring, making it difficult to maintain blood sugar regulation. Plasmapheresis was performed using 42 units of fresh frozen plasma in three separate sessions every other day. Because plasmapheresis was not the primary treatment, surgical thyroidectomy was planned as soon as the white blood cell count normalized. On the 10th day of insulin infusion therapy, a complete urinalysis revealed a negative ketone level, and a surgical thyroidectomy was planned. Lugol's solution was started.

On the 10th day of follow-up, a neutrophil count of $3500/mm^3$ was detected, and a general surgeon was consulted regarding thyroidectomy, which was planned. Lugol's solution was started before surgery, and abdominal pain developed 6 hours after

the first dose. A standing abdominal radiograph was subsequently obtained, revealing air-fluid levels. Abdominal ultrasonography was performed. The patient was reported to have free fluid in all quadrants, measuring 5 cm in the deepest part, edema in the walls of the bowel loops in the right quadrant, and a contrast-enhanced abdominal computed tomography scan revealed dense free fluid and free air densities within the abdomen, more prominent in the lower quadrants. General surgery was consulted, and the patient underwent emergency surgery for a preliminary diagnosis of gastrointestinal perforation. Laparotomy revealed that the abdomen was filled with intestinal contents. A widespread transmural ulcerated lesion and perforation point were identified in a 20-cm area 10 cm proximal to the ileocecal region. The abdomen was cleaned, and an ileostomy was performed, extending 20 cm proximal to the ileocecal valve. Following surgery, the patient was transferred to the intensive care unit and then to the endocrine ward for blood sugar regulation and hyperthyroidism management.

Table 1. Daily neutrophil change of the patient

1st day (/mm ³)	2nd day	3rd day	4th day	5th day	6th day	7th day	8th day	9th day	10th day
0.31	0.44	0.66	1.01	1.11	1.77	1.28	1.49	1.97	3.5

DISCUSSION

Crohn's disease was diagnosed as the underlying cause of the gastrointestinal perforation that developed in a patient presenting with neutropenia and diabetic ketosis. This case highlights the challenges of the diagnostic process due to the atypical onset and complications associated with Crohn's.

The most serious and potentially life-threatening adverse effect of antithyroid drugs is agranulocytosis, defined as a reduction in the absolute neutrophil count to less than $0.5 \times 10^9/L$ (4).

In our case, the patient had no previous history of inflammatory bowel disease, and perforation was the first serious complication.

The most serious side effect of inflammatory bowel disease is agranulocytosis and a decrease in neutrophil count to $<0.5 \times 10^9/L$ (2).

Methimazole and propylthiouracil are ATIs used to treat hyperthyroidism and Graves' disease. Despite their effectiveness, agranulocytosis, one of the most important undesirable side effects of both drugs, is a critical decrease in granulocytes (5).

In our case, the patient was using 150 mg/day PTU, and the neutrophil count was critically low at $310/mm^3$.

The pathogenesis of ATI-induced agranulocytosis has not been fully elucidated, and immunological mechanisms and direct toxic effects are thought to play roles (2).

On the 4th day of follow-up, abdominal pain recurred, and she was re-consulted with general surgery. Abdominal ultrasonography was performed. The fluid was 5 cm thick, prominently dense, with septate septa and localized loculations in the Morrison's pouch and between the bowel loops in the lower abdominal quadrants. These findings were also reported as diffuse wall thickening in the bowel loops of the lower quadrants. General surgery was performed, and simultaneous intra-abdominal and thyroidectomy surgeries were performed. The abdominal abscesses were removed, and the patient was transferred to the intensive care unit and then to the general surgery ward for postoperative follow-up. The patient's initial post-surgical pathology report revealed findings consistent with Crohn's, including severe activation, necrosis, and multiple perforations. The patient, whose general condition was good, was discharged with a prescription of 75 micrograms (mcg)/day of levothyroxine sodium after thyroidectomy, 3×10 units of insulin glulisine and 1×14 units of insulin glargine U300 for DM, and mesalazine 500 mg tb 3×1 and budesonide 3 mg tb 3×1 for Crohn's disease.

Inflammatory bowel disease (IBD) refers to nonspecific chronic intestinal inflammatory conditions, including Crohn's disease and ulcerative colitis. Genomic studies have shown that inflammatory bowel disease (IBD) is associated with the underlying pathogenesis of IBD. Many of these genes are also associated with the risk of developing diabetes mellitus. A recent nationwide Danish cohort study reported an increased risk of DM in patients with Crohn's disease, independent of glucocorticoid use (6).

The incidence of Crohn's disease has been increasing in recent years, with gender-specific distribution in both developed and developing countries. Crohn's disease is more common in women and is associated with other autoimmune diseases and is more frequently associated with gastrointestinal complications such as abscesses and perforations (7).

In patients with diabetes mellitus, uncontrolled hyperglycemia and severe hyperglycemia due to insulin deficiency or impaired insulin action have negative effects on intestinal barrier function (8).

Neutropenia can develop through several mechanisms. Chronic inflammation can lead to decreased bone marrow reserve and suppressed neutrophil production. Furthermore, infections, medications, metabolic diseases, and autoimmune mechanisms can also trigger the development of neutropenia (9).

In our case, the patient was not receiving immunosuppressive therapy, and the resolution of neutropenia after discontinuation of propylthiouracil suggested that the condition was drug-related.

The management of intestinal perforation, neutropenia, and diabetic ketosis requires a multidisciplinary approach.

Intestinal perforation in Crohn's disease is rare, with a reported incidence of 1.5% to 16%, and nearly all cases involve a single perforation of the small intestine. Resection of the perforated segment is generally preferred over simple suturing because of the relatively low success rate and increased risk of morbidity associated with primary repair. Surgical intervention is unavoidable for intestinal perforation; however, preoperative correction of metabolic disorders, initiation of broad-spectrum antibiotics, and resuscitation are critical. In our case, diabetic ketosis treatment, appropriate antibiotic therapy, and hemodynamic stabilization were initially established, and surgery was planned. Adequate tissue sampling for pathological examination at the time of surgery is essential for diagnosing CD (10).

When Crohn's disease treatments are compared with placebo, some treatments reduce the risk of relapse in patients. Anti-TNF and thiopurine monotherapies are more effective in achieving remission and reducing the need for surgical intervention (12).

In general, patients with Crohn's disease are at a high risk of opportunistic infections due to malnutrition, advanced age, congenital immunodeficiency, neutropenia, chronic diseases, diabetes mellitus, and immunosuppressive medication use. Therefore, appropriate antibiotic therapy, blood sugar regulation, and nutritional support significantly reduce the risk of complications (13).

This case demonstrates the wide spectrum of atypical presentations of Crohn's disease. In young- to middle-aged women, especially those who develop acute abdominal symptoms following abdominal pain and have concomitant systemic diseases such as diabetes and hyperthyroidism, the possibility of an underlying inflammatory bowel disease should be considered. In such atypical cases, early diagnosis and appropriate treatment are crucial for reducing morbidity and mortality.

CONCLUSION

This case illustrates the unusual coexistence of LADA, Graves' disease complicated by PTU-induced agranulocytosis, and Crohn's disease with intestinal perforation. The late recognition of autoimmune diabetes, despite long-standing misclassification as type 2 DM, emphasizes the need for autoantibody screening. Plasma exchange is an effective bridge therapy for uncontrolled hyperthyroidism in patients with agranulocytosis. The interplay between metabolic dysfunction and immune dysregulation may have contributed to the complex presentation of the patient. Reporting such rare cases enhances clinical awareness and aids in

managing challenging scenarios.

Ethics Committee Approval: It is a case report and does not require ethics committee approval. Written informed consent was obtained.

Financial Resource/ Sponsor's Role: No financial support was received for the study.

Conflict of Interest: The authors declare that there is no personal or financial conflict of interest within the scope of the study.

Author Contributions: Idea/Concept: Lezan KESKİN, Hacı Mehmet ÇİTİL; Design: Hacı Mehmet ÇİTİL, Lezan KESKİN; Supervision/Consulting: Burhan Hakan KANAT, Bahadır ÖNDEŞ; Data Collection and/or Processing: Lezan KESKİN, Mustafa Eray DAĞDEVİREN; Analysis and/or Interpretation: Cevat GENÇER, Gökhan SÖĞÜTLÜ; Literature Review: Lezan KESKİN, Eray DAĞDEVİREN; Writing of the Article: Hacı Mehmet ÇİTİL; Critical Review: Hacı Mehmet ÇİTİL; Resources and Funding: No financial support was received for this study

REFERENCES

- 1) Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, Roh EJ, Elkamhaway A, Al-Karmalawy AA. Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. *Biomed Pharmacother*. 2023 Dec;168:115734. doi: 10.1016/j.biopha.2023.115734. Epub 2023 Oct 17. PMID: 37857245.
- 2) MacKay M, Clewis MC, Sweet P. Antithyroid Drug-Induced Agranulocytosis: A Case Report. *Cureus*. 2023 Nov 4;15(11):e48264. doi: 10.7759/cureus.48264. PMID: 38054132; PMCID: PMC10695326.
- 3) Cockburn E, Kamal S, Chan A, Rao V, Liu T, Huang JY, Segal JP. Crohn's disease: an update. *Clin Med (Lond)*. 2023 Nov;23(6):549-557. doi: 10.7861/clinmed.2023-0493. PMID: 38065612; PMCID: PMC11298500.
- 4) Kim JW, Lee HS, Ye BD, Yang SK, Hwang SW, Park SH, et al. Incidence of and risk factors for free bowel perforation in patients with Crohn's disease. *Dig Dis Sci* 2017;62:1607-14.
- 5) Yoshimura Noh J, Inoue K, Suzuki N, Yoshihara A, Fukushima M, Matsumoto M, Imai H, Hiruma S, Ichikawa M, Koshibu M, Sankoda A, Hirose R, Watanabe N, Sugino K, Ito K. Dose-dependent incidence of agranulocytosis in patients treated with methimazole and propylthiouracil. *Endocr J*. 2024 Jul 12;71(7):695-703. doi: 10.1507/endocr.EJ24-0135. Epub 2024 May 3. PMID: 38710619.
- 6) Jess T, Jensen BW, Andersson M, Villumsen M, Allin KH. Inflammatory Bowel Diseases Increase Risk of Type 2 Diabetes in a Nationwide Cohort Study. *Clin Gastroenterol Hepatol* . 2020;18:881-888.e1. doi: 10.1016/j.cgh.2019.07.052.
- 7) Silaghi A, Constantin VD, Socea B, Banu P, Sandu V, Andronache LF, Dumitriu AS, Paunica S. Inflammatory Bowel Disease: Pathogenesis, Diagnosis and Current Therapeutic Approach. *Journal of Mind and Medical Sciences*. 2022; 9(1):56-77.
- 8) Francis KL, Alonge KM, Pacheco MC, Hu SJ, Krutzsch CA, Morton GJ, Schwartz MW, Scarlett JM. Diabetes exacerbates inflammatory bowel disease in mice with diet-induced obesity. *World J Gastroenterol*. 2023 Sep 7;29(33):4991-5004. doi: 10.3748/wjg.v29.i33.4991. PMID: 37731997; PMCID: PMC10507503.
- 9) Mithoowani S, Cameron L, Crowther MA. Neutropenia. *CMAJ*. 2022 Dec 19;194(49):E1689. doi: 10.1503/cmaj.220499. PMID: 36535676; PMCID: PMC9829051.
- 10) Lightner AL, Vogel JD, Carmichael JC, Keller DS, Shah SA, Mahadevan U, Kane SV, Paquette IM, Steele SR, Feingold DL. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Crohn's Disease. *Dis Colon Rectum*. 2020 Aug;63(8):1028-1052. doi: 10.1097/DCR.0000000000001716. PMID: 32692069.
- 11) Ranasinghe IR, Tian C, Hsu R. Crohn Disease. [Updated 2024 Feb 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
- 12) Regueiro M, Velayos F, Greer JB, Bougatsos C, Chou R, Sultan S, Singh S. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017 Jan;152(1):277-295.e3. doi: 10.1053/j.gastro.2016.10.039. Epub 2016

Nov 10. PMID: 27840073.

13) Kucharzik T, Ellul P, Greuter T, Rahier JF, Verstockt B, Abreu C, Albuquerque A, Allocca M, Esteve M, Farraye FA, Gordon H, Karmiris K, Kopylov U, Kirchgesner J, MacMahon E, Magro F, Maaser C, de Ridder L, Taxonera C, Toruner M, Tremblay L, Scharl M, Viget N, Zabana Y, Vavricka S. ECCO Guidelines on the Prevention, Diagnosis, and Management of Infections in Inflammatory Bowel Disease. *J Crohns Colitis*. 2021 Jun 22;15(6):879-913. doi: 10.1093/ecco-jcc/ijab052. Erratum in: *J Crohns Colitis*. 2023 Jan 27;17(1):149. doi: 10.1093/ecco-jcc/ijac104. PMID: 33730753.