Mepolizumab-associated acute pancreatitis: a case report

Fiore Casale[1], Irum Jan[2]*

European Journal of Medical Case Reports
Volume 6(2):39–42
https://doi.org/10.24911/ejmcr/173-1633552787

ABSTRACT

Background: Drug hypersensitivity reactions commonly generate systemic syndromes but can also affect specific organs. Mepolizumab, a monoclonal antibody targeting interleukin-5, is a safe and effective Food and Drug Administration-approved biologic therapy for severe eosinophilic asthma.

Case Presentation: A 49-year-old female developed acute pancreatitis complicated by acute hypoxic respiratory failure secondary to fluid overload. Following 72 hours of intravenous fluids and analgesic administration, an urticarial rash developed on the patient's trunk, raising concern for a drug-related exanthem. After medication reconciliation, it was deemed that she had a hypersensitivity reaction to mepolizumab.

Conclusion: In several clinical trials, mepolizumab demonstrated few hypersensitivity reactions. This patient presentation highlights the importance of strong clinical suspicion for drug hypersensitivities, especially in patients failing to respond to the standard of care for common medical conditions.

Keywords: Allergy, hypersensitivity, mepolizumab, pancreatitis, DRESS.

Received: 06 October 2021 **Accepted:** 18 December 2021 **Type of Article:** CASE REPORT **Specialty:** Internal Medicine

Correspondence to: Irum Jan
*Department of Internal Medicine, University of New Mexico, Albuquerque, NM.
Email: irum.jan@va.gov
Full list of author information is available at the end of the article.

Background

Adverse drug reactions are common and often predictable based on a drug's mechanism of action. However, 10%-15% are unpredictable reactions dependent on environmental and genetic susceptibilities, and often due to drug hypersensitivities [1,2]. Over 500 medications have been implicated in causing acute pancreatitis, with mesalazine and azathioprine being the most well-documented, while few biologics have ever been implicated [3,4]. Mepolizumab, a monoclonal antibody which inhibits interleukin-5, has been approved the by Food and Drug Administration for the treatment of severe eosinophilic asthma, with the most common adverse effects including headaches, nasopharyngitis, musculoskeletal and connective tissue disorders, and non-allergic infusion reactions [5-7]. Though scarce, pharyngeal swelling and hypersensitivity reactions have also been reported [7]. Here, we will describe a novel case of acute pancreatitis secondary to delayed-type hypersensitivity to mepolizumab.

Case Presentation

A 49-year-old female with severe persistent asthma, gastroesophageal reflux disease, diabetes mellitus, post-traumatic stress disorder, hypoadrenalism, and obesity presented to the emergency department with severe shortness of breath and abdominal discomfort. Pulmonology managed her asthma, prescribing oral prednisone 2.5 mg three times daily (based on asthma-specific dosing recommendations) for a recent exacerbation, and administering a second treatment with mepolizumab 2 weeks prior to admission. In the past, she visited rheumatology clinic for an extensive work-up of her restrictive pulmonary function tests, diffuse arthralgias, and wheezing, which was unrevealing. Medications included an albuterol nebulized inhaler, fluticasone/salmeterol inhaler, glipizide, loratadine, mepolizumab 100 mg every 4 weeks, montelukast, omeprazole, rosuvastatin, and a tiotropium inhaler. She had no known allergies and family history was not significant for any autoimmune disorders. The patient denied use of alcohol, tobacco, and recreational drugs.

On examination, the patient was tachycardic (maximum: 118 beats/minute), tachypneic (maximum: 25 breaths/minute), and hypertensive to 180/100 mm Hg. She appeared dyspneic and in distress, but lungs were clear to auscultation in all fields with mild end-expiratory wheezes. The abdomen was distended with diffuse tenderness and focal severe tenderness at the epigastrium. No shifting

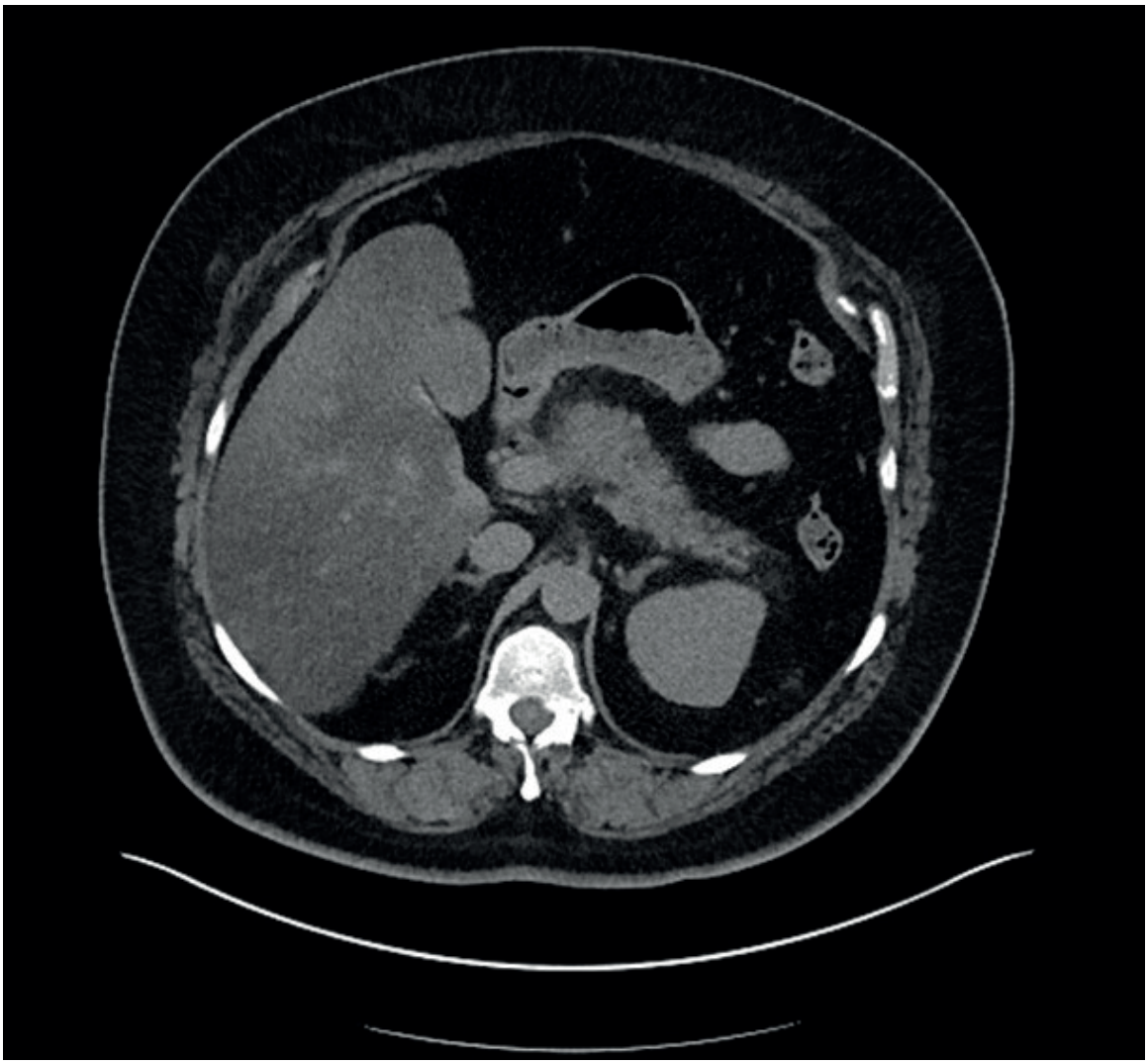

Figure 1. *Abdominal CT demonstrating an edematous and inflamed pancreatic gland.*

dullness could be appreciated. Bilateral lower extremities had pitting edema to the knee. Elevated laboratory values included glucose (305 mg/dl), alkaline phosphatase (186 U/l), aspartate transaminase (50 U/l), lipase (1,372 U/l), C-reactive protein (20.7 mg/l), erythrocyte sedimentation rate (52 mm/hour), lactate dehydrogenase (726 U/l), gamma-glutamyl transferase (189 IU/l), IgE (1,930 IU/ml), rheumatoid factor (41.7 IU/ml), aldolase (8.2 U/l), IgG-4 (90.6 mg/dl), and complement functional activity (>60 U/ml). Serum triglycerides, antinuclear antibodies, antineutrophil cytoplasmic antibodies, and serum anti-cyclic citrullinated peptide were normal. Abdominal computerized tomography (CT) revealed an acutely edematous pancreatitis (Figure 1), conferring a diagnosis of acute pancreatitis.

Treatment included nebulized albuterol and ipratropium, aggressive intravenous (IV) lactated ringers (100 cc/hour), and morphine with hydromorphone for pain management. Without symptomatic improvement after 3 days of aggressive treatment with 9 l of IV fluids and in the setting of poor diuretic output, there were concerns for cardiovascular strain from this intravascular expansion and possible worsening of her condition. Concurrently, the patient developed a diffuse truncal urticaria. A repeat abdominal CT revealed worsening acute pancreatitis. Gastroenterology was consulted, who completed a thorough medication reconciliation, and attributed the patient's presentation to a hypersensitivity-reaction to her second dose of mepolizumab, the only new medication within the past year. After 9 days of hospitalization, the patient's abdominal pain resolved, and she returned to her baseline weight and room air oxygen requirement (Table 1).

Discussion

Drug-hypersensitivity reactions are relatively common, often presenting with cutaneous signs and symptoms [8]. However, drug eruptions can affect any organ system, and may cause acute pancreatitis [3,9]. Nonetheless, it remains unknown which genetic and environmental factors determine what organ systems are affected [8]. To the authors' knowledge, this is the first report of acute pancreatitis secondary to a mepolizumab delayed-hypersensitivity reaction. Given lack of alcohol use and lack of gallbladder disease, it was presumed that this presentation was either autoimmune or drug mediated. However, our patient did

Table 1. *Timeline of the patient's clinical course.*

Week 0	Administered first dose of mepolizumab
Week 4	Administered second dose of mepolizumab
Week 6	Patient admitted to hospital
Day 1	Patient presents for severe dyspnea and abdominal pain
Day 2	Patient diagnosed with acute pancreatitis; started IV fluids and pain management
Day 3	Patient develops urticaria
Day 4	Repeat CT scan shows worsening acute pancreatitis; Gastroenterology consulted
Day 5	Gastroenterology attributed presentation to mepolizumab-associated hypersensitivity reaction
Day 7	Patient dyspnea and abdominal pain starts to resolve
Day 9	Patient discharged

not respond to the standard-of-care therapy after 72 hours, indicating that a separate process was occurring [10,11]. Following the development of diffuse truncal urticaria, concerns for a drug-related hypersensitivity reaction arose. It is possible that the patient had subclinical drug rash with eosinophilia and systemic symptoms (DRESS) presentation and/or delayed-type drug hypersensitivity due to concomitant inflammatory suppression from use of oral corticosteroids, which is the gold standard therapy for these hypersensitivity reactions [12].

Recent large clinical studies utilizing mepolizumab demonstrated that the most common adverse events include headache and nasopharyngitis [12]. However, there are reports of decompensated heart failure and death secondary to acute pancreatitis, which were considered unrelated to mepolizumab [8]. Further studies are needed to discern which populations are at risk for developing hypersensitivity reactions to mepolizumab and the overall safety of long-term mepolizumab treatment for severe asthma.

Conclusion

We hope this case encourages physicians to consider drug hypersensitivity etiologies for common acute medical problems and highlights the need for strong clinical suspicion for hypersensitivity reactions in patients on biologic therapies.

What is new?

Biologic therapies are generally considered as safe and do not typically exhibit drug hypersensitivity reactions. Specifically, mepolizumab has not been shown to cause pancreatitis or drug hypersensitivity reactions. Here, the authors report a patient who presented with pancreatitis secondary to mepolizumab therapy, and possible subclinical DRESS.

List of Abbreviations

CT	Computerized tomography
DRESS	Drug rash with eosinophilia and systemic symptoms
IV	Intravenous

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent for publication

Written and informed consent was taken from patient to publish this case report.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author details

Fiore Casale[1], Irum Jan[2]

1. Department of Internal Medicine, School of Medicine, University of New Mexico, Albuquerque, NM
2. Department of Internal Medicine, University of New Mexico, Albuquerque, NM

REFERENCES

1. Yawalkar N. Drug hypersensitivity. Acta Clin Belg. 2009;64(6):529–33. https://doi.org/10.1179/acb.2009.090
2. Naisbitt DJ, Olsson-Brown A, Gibson A, Meng X, Ogese MO, Tailor A, et al. Immune dysregulation increases the incidence of delayed-type drug hypersensitivity reactions. Allergy. 2020;75(4):781–97. https://doi.org/10.1111/all.14127
3. Nitsche CJ, Jamieson N, Lerch MM, Mayerle JV. Drug induced pancreatitis. Best Pract Res Clin Gastroenterol. 2010;24(2):143–55. https://doi.org/10.1016/j.bpg.2010.02.002
4. Simons-Linares CR, Elkhouly MA, Salazar MJ. Drug-induced acute pancreatitis in adults: an update. Pancreas. 2019;48(10):1263–73. https://doi.org/10.1097/MPA.0000000000001428
5. Pavord ID, Korn S, Howarth P, Bleecker ER, Buhl R, Keene ON, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet. 2012;380(9842):651–9. https://doi.org/10.1016/S0140-6736(12)60988-X
6. Henriksen DP, Bodtger U, Sidenius K, Maltbaek N, Pedersen L, Madsen H, et al. Efficacy, adverse events, and inter-drug comparison of mepolizumab and reslizumab anti-IL-5 treatments of severe asthma - a systematic review and meta-analysis. Eur Clin Respir J. 2018;5(1):1536097. https://doi.org/10.1080/20018525.2018.1536097
7. Harrison T, Canonica GW, Chupp G, Lee J, Schleich F, Welte T, et al. Real-world mepolizumab in the prospective severe asthma REALITI-A study: initial analysis. Eur Respir J. 2020;56(4):2000151. https://doi.org/10.1183/13993003.00151-2020

8. Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International consensus on drug allergy. Allergy. 2014;69(4):420–37. https://doi.org/10.1111/all.12350

9. Dykewicz MS, Lam JK. Drug hypersensitivity reactions. Med Clin North Am. 2020;104(1):109–28. https://doi.org/10.1016/j.mcna.2019.09.003

10. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet. 2015;386(9988):85–96. https://doi.org/10.1016/S0140-6736(14)60649-8

11. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on initial management of acute pancreatitis. Gastroenterology. 2018;154(4):1096–101. https://doi.org/10.1053/j.gastro.2018.01.032

12. Shiohara T, Mizukawa Y. Drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS): an update in 2019. Allergol Int. 2019;68(3):301–8. https://doi.org/10.1016/j.alit.2019.03.006

Summary of the case

1	**Patient (gender, age)**	Female, 49-year-old
2	**Final diagnosis**	Acute pancreatitis
3	**Symptoms**	Abdominal pain, edema, urticaria, dyspnea
4	**Medications**	Mepolizumab, IV fluids
5	**Clinical procedure**	N/A
6	**Specialty**	Internal Medicine