Journal of Community Hospital Internal Medicine Perspectives

Volume 14 | Issue 4 Article 21

2024

Calcitriol Unleashed: A Rare Culprit in Hypercalcemia Associated with Rare Primary Pancreatic Lymphoma - A Case Report

Dania Kaur
Department of Internal Medicine, North Alabama Medical Center, Florence, Alabama, USA, dania.kaur@namccares.com

Abhinav Vyas
Department of Internal Medicine, North Alabama Medical Center, Florence, Alabama, USA

Sowmya Sagireddy
Department of Internal Medicine, South Brooklyn Health, Brooklyn, New York, USA

Rabia Qazi
Department of Internal Medicine, North Alabama Medical Center, Florence, Alabama, USA

Sarah Elsayed
Department of Internal Medicine, North Alabama Medical Center, Florence, Alabama, USA

Calcitriol Unleashed: A Rare Culprit in Hypercalcemia Associated with Rare Primary Pancreatic Lymphoma - A Case Report

Authors

Dania Kaur, Abhinav Vyas, Sowmya Sagireddy, Rabia Qazi, Sarah Elsayed, Jyoti Verma, Prutha Pathak, and Rachna Valvani

CASE REPORT

Calcitriol Unleashed: A Rare Culprit in Hypercalcemia Associated With Rare Primary Pancreatic Lymphoma - A Case Report

Dania Kaur [a,*], Abhinav Vyas [a], Sowmya Sagireddy [b], Rabia Qazi [a], Sarah Elsayed [a], Jyoti Verma [a], Prutha Pathak [a], Rachna Valvani [a]

[a] Department of Internal Medicine, North Alabama Medical Center, Florence, AL, USA
[b] Department of Internal Medicine, South Brooklyn Health, Brooklyn, NY, USA

Abstract

Hypercalcemia of Malignancy is a complicated condition often linked to parathyroid hormone, parathyroid hormone-related peptide, or bone metastasis. This report presents a unique case of calcitriol-mediated hypercalcemia in an 89-year-old female with primary pancreatic lymphoma, highlighting the rarity and complexity of this presentation. Initially, the patient's condition was thought to be related to sarcoidosis, but the recurrence of hypercalcemia led to the discovery of pancreatic B-cell lymphoma as the underlying cause. It also emphasizes the need to explore new treatment options. Interestingly, it demonstrates the successful use of cinacalcet in treating calcitriol-induced hypercalcemia in malignancies, which could be a potential therapeutic option for such cases. It also serves as a reminder of the critical need for ongoing research and innovative therapeutic strategies to improve outcomes in managing hypercalcemia caused by malignancies. The case underscores the potential complexities of calcitriol-mediated hypercalcemia, especially in uncommon presentations like primary pancreatic lymphoma.

Keywords: Calcitriol-mediated hypercalcemia, Hypercalcemia of malignancy, Pancreatic lymphoma

1. Introduction

Hypercalcemia of Malignancy is a challenging clinical condition observed in around 20% of cancer patients. The primary contributors are parathyroid hormone (PTH), parathyroid hormone-related peptide (PTHrP), and bone metastasis. However, about 1% of Hypercalcemia of Malignancy is caused by calcitriol production.[1] We report a case of calcitriol-mediated hypercalcemia in a patient with primary pancreatic lymphoma. The involvement of calcitriol production in this case introduces a noteworthy complexity to the condition. Additionally, the rarity of primary pancreatic lymphoma underlines the exceptional nature of this presentation.

2. Case presentation

An 89-year-old female with a medical history notable for right breast cancer post-chemotherapy, hypertension, chronic kidney disease, and hyperlipidemia presented with a constellation of symptoms, including generalized weakness, decreased appetite, and an unintentional weight loss of 15 pounds over the preceding six months. She denied any fever, cough, sore throat, night sweats, abdominal pain nor hallucinations. Upon arrival at the Emergency Department, her vital signs indicated a blood pressure of 177/85 mmHg, with a saturation of 96% on room air. Laboratory assessments unveiled elevated creatinine 1.9 mg/dL (normal range 0.6–1.3 mg/dL) with a baseline of 1.5 mg/dL, blood urea nitrogen 37 mg/dL (normal range 4–22 mg/dL), calcium 13.2 mg/dL

Received 8 January 2024; revised 2 May 2024; accepted 14 May 2024.
Available online 2 July 2024

* Corresponding author.
E-mail address: dania.kaur@namccares.com (D. Kaur), avyas@namccares.com (A. Vyas), sowmyasagireddy2015@hotmail.com (S. Sagireddy), rabia.qazi@namccares.com (R. Qazi), sarah.elsayed@namccares.com (S. Elsayed), jyoti.verma@namccares.com (J. Verma), prutha.pathak@namccares.com (P. Pathak), rachna.valvani@namccares.com (R. Valvani).

https://doi.org/10.55729/2000-9666.1374

(normal range 8.5–10.5 mg/dL), and albumin 4.7 g/dL (normal range 3.4–5 g/dL). Other laboratory results have been indicated in Table 1. Immediate intervention involved the initiation of normal saline at a rate of 150 mL/h for hypercalcemia and acute kidney injury.

Further investigation into hypercalcemia included assessments of parathyroid hormone, parathyroid hormone-related peptide, and calcitriol. While parathyroid hormone and parathyroid hormone-related peptide yielded unremarkable results, calcitriol levels were elevated at 105 pg/ml (normal range 24.8–81.5 pg/ml)—intravenous hydration led to the resolution of acute kidney injury and hypercalcemia by the third day of hospitalization. Before discharge, the creatinine returned to the 1.5 mg/dL baseline, while calcium levels decreased to 10.3 mg/dL. The patient was discharged with a follow-up scheduled in the hematology-oncology clinic for an in-depth exploration of the underlying malignant hypercalcemia.

After five days, she visited the hematology-oncology clinic, where her calcium level was still high at 11.8 mg/dL. She was given a dose of zoledronate to help with hypercalcemia. A normal serum, urine electrophoresis, and a normal nuclear bone scan ruled out multiple myeloma and other paraproteinemias as a contributing cause. This led to a referral to an endocrinologist for hypercalcemia management. Since the oncological workup was negative, and the hypercalcemia was secondary to calcitriol, the treatment plan then focused on sarcoidosis, for which she was started on low-dose prednisone (10 mg/day) and cinacalcet (30 mg/day).

The patient came back to the hospital after three months with complaints of low appetite, nausea, abdominal distension, and subjective shortness of breath. Although the vital signs were stable, the patient had persistently high levels of calcium at 11.8 mg/dL, low levels of albumin at 2.9 g/dL (normal range is 3.4–5 g/dL), and corrected calcium at 12.4 mg/dL. A computed tomography (CT) scan of the abdomen and pelvis showed the presence of a large solid mass in the mid-upper abdomen, free fluid in the abdomen, and peritoneal densities, indicating likely metastasis (Figs. 1 and 2). These findings indicated the presence of a pancreatic tumor. Ascitic fluid cytology confirmed that the patient had B-cell lymphoma of pancreatic origin, and the immunostaining tests showed positive CD45 and CD20.

During the patient's subsequent hospitalization, their condition worsened, characterized by persistent hypercalcemia, hypoglycemia, and hyponatremia. Although there were plans for a PET scan

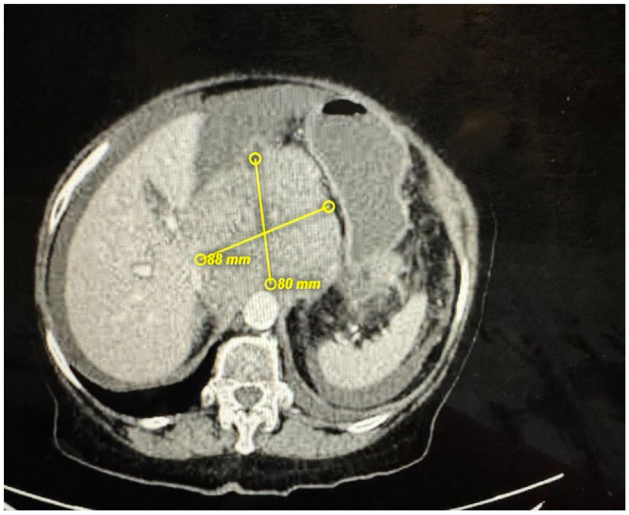

Fig. 1. An image showing the presence of a large pancreatic mass (88 mm × 80 mm).

Table 1. Laboratory analysis.

Laboratory test	Values	Reference range
White blood cell	9500/uL	4300–11,000/uL
Hemoglobin	13.2 g/dL	12–16 g/dL
Platelet	247,000/uL	150,000–3,375,000/uL
Sodium	140 mmol/L	135–145 mmol/L
Potassium	4.2 mmol/L	3.6–5.2 mmol/L
Chloride	106 mmol/L	98–108 mmol/L
Creatinine	1.9 mg/dL	0.6–1.3 mg/dL
Blood urea nitrogen	37 mg/dL	4–22 mg/dL
Calcium	13.2 mg/dL	8.5–10.5 mg/dL
Albumin	4.7 g/dL	3.4–5 g/dL
Parathyroid hormone	21.4 pg/mL	7.5–87 pg/mL
Parathyroid hormone related peptide	<2 pmol/L	<2 pmol/L
1,25 dihydroxyvitamin D	105 pg/mL	24.8–81.5 pg/mL
Tumor marker factor-alpha	1.650 ng/mL	<7.51 ng/mL
CA 19-9	26 U/mL	0–35 U/mL

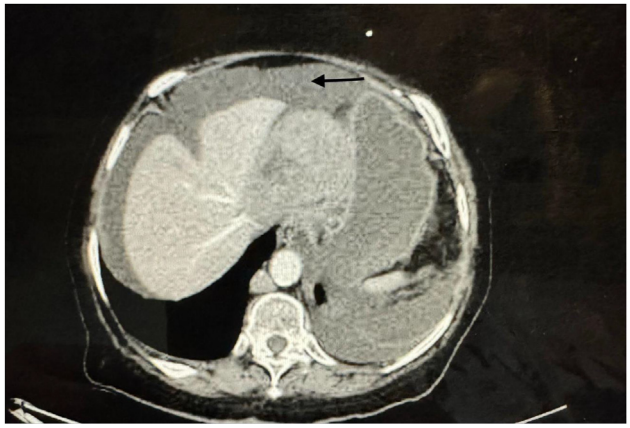

Fig. 2. An image showing the presence of a large amount of ascites (black arrow).

with the hematology-oncology service, the family decided to choose palliative care due to the patient's preference and dismal functional status. Unfortunately, the patient passed away a few weeks later. This case highlights the complexity of diagnosing and managing calcitriol-mediated hypercalcemia, especially in the context of an unusual presentation of primary pancreatic lymphoma. It emphasizes the importance of a multidisciplinary approach in dealing with such complex cases.

3. Discussion

Hypercalcemia, a disruption in calcium homeostasis resulting in elevated calcium levels, is regulated by hormones such as parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (calcitriol), involving organs like kidneys, liver, and bones. Severity is categorized as mild (10.5–11.9 mg/dL), moderate (12–13.9 mg/dL), and severe (14 mg/dL or above).[1,2] It presents with neurocognitive changes, volume depletion, and acute renal failure. In malignancy, hypercalcemia signifies a poor prognosis, with the most common cause being humoral hypercalcemia of malignancy (HHM), primarily mediated by parathyroid hormone-related peptide (80%) production or bony metastasis.[2]

Calcitriol-mediated hypercalcemia is infrequently reported and is often associated with granulomatous diseases like sarcoidosis and certain infections, including disseminated candidiasis and tuberculosis. Calcitriol production, constituting only 1% of HHM, causes a similar pathogenesis as in sarcoidosis with the production of 1, alpha hydroxylase enzyme causing activation of 1,25 dihydroxy vitamin D from the macrophages and lymphocytes, which causes hypercalcemia.[2,3] It has also been found that the presence of hypercalcemia due to calcitriol marks a poor prognostic factor in terms of survival in patients with cancer.[4]

This case report describes a rare cause of hypercalcemia in pancreatic lymphoma caused by calcitriol. At first, the patient was incorrectly diagnosed with sarcoidosis, as the oncological tests came out negative. However, the patient responded well to low-dose prednisone and cinacalcet. Later, the patient was identified as having pancreatic B-cell lymphoma with peritoneal metastasis, which is an unusual condition.

Primary Pancreatic Lymphoma (PPL), comprising 0.5–1% of extranodal malignant lymphomas, is predominantly a diffuse B-cell lymphoma.[5,6] Its presentation, often confused with pancreatic cancer, includes abdominal pain, jaundice, and acute pancreatitis.[7] Radiologically, PPL differs from pancreatic cancer, displaying a clean shadow edge and absence of pancreatic duct dilation.[8,9] The immunohistochemistry and the radiological features favored the PPL diagnosis in our patient.

Hypercalcemia of malignancy is typically treated with zoledronate, denosumab, or intravenous hydration, while cinacalcet, a calcimimetic that activates the calcium-sensing receptors, has shown efficacy in select cases. The first case was of a renal cell carcinoma, where the patient was resistant to denozumab and zoledronate and was treated with cinacalcet 60 mg daily with a response seen in 10 weeks.[3,10] Our case is one of the very few cases of hypercalcemia of malignancy successfully treated with cinacalcet, normalizing calcium levels over several weeks. Cinacalcet is efficacious; it is well tolerated orally and has been shown to normalize calcium levels while targeting the treatment for cancer.[11,12]

4. Conclusion

This case highlights the difficulty in diagnosing calcitriol-mediated hypercalcemia in the context of pancreatic lymphoma. The patient's recurrent hypercalcemia was initially attributed to sarcoidosis but was eventually linked to pancreatic B-cell lymphoma. The case emphasizes the importance of considering unusual causes of hypercalcemia, using advanced imaging techniques, and exploring novel therapeutic strategies. In this case, the successful use of cinacalcet adds to the limited literature on its efficacy in treating calcitriol-induced hypercalcemia in malignancy. The report underscores the need for continued vigilance and comprehensive diagnostic approaches in the realm of hypercalcemia secondary to malignancies.

Funding

All co-authors have seen and agree with the contents of manuscript and there is no financial relationship to declare.

Conflict of interest

The authors have no conflict of interest to declare.

References

1. Chukir T, Liu Y, Hoffman K, Bilezikian JP, Farooki A. Calcitriol elevation is associated with a higher risk of refractory hypercalcemia of malignancy in solid tumors. *J Clin Endocrinol Metab*. 2020;105(4):e1115−e1123. https://doi.org/10.1210/clinem/dgz278.
2. Goldner W. Cancer-related hypercalcemia. *J Oncol Pract*. 2016;12(5):426−432. https://doi.org/10.1200/JOP.2016.011155.
3. Asonitis N, Angelousi A, Zafeiris C, Lambrou GI, Dontas I, Kassi E. Diagnosis, pathophysiology and management of hypercalcemia in malignancy: a review of the literature. *Horm Metab Res*. 2019;51(12):770−778. https://doi.org/10.1055/a-1049-0647.
4. Kallas M, Green F, Hewison M, White C, Kline G. Rare causes of calcitriol-mediated hypercalcemia: a case report and literature review. *J Clin Endocrinol Metab*. 2010;95(7):3111−3117. https://doi.org/10.1210/jc.2009-2673.
5. Abaroa-Salvatierra A, Shaikh B, Deshmukh M, Alweis R, Patel A. Calcitriol-mediated hypercalcemia in a patient with bilateral adrenal non-Hodgkin's B-cell lymphoma case report. *J Community Hosp Intern Med Perspect*. 2016;6(2):30381. https://doi.org/10.3402/jchimp.v6.30381.
6. Zheng SM, Zhou DJ, Chen YH, et al. Pancreatic T/histiocyte-rich large B-cell lymphoma: a case report and review of literature. *World J Gastroenterol*. 2017;23(24):4467. https://doi.org/10.3748/wjg.v23.i24.4467.
7. Shi L, Wang J, Wei L, Ma Z, Liu X. Pancreatic diffuse large B-cell lymphoma: a case report and literature review. *Front Oncol*. 2023;13:1294385. https://doi.org/10.3389/fonc.2023.1294385.
8. Merkle EM, Bender GN, Brambs HJ. Imaging findings in pancreatic lymphoma: differential aspects. *Am J Roentgenol*. 2000;174(3):671−675. https://doi.org/10.2214/ajr.174.3.1740671.
9. Hughes B, Habib N, Chuang KY. The computed tomography "sandwich sign" for primary pancreatic lymphoma. *ACG Case Rep J*. 2019;6(10):e00230. https://doi.org/10.14309/crj.0000000000000230.
10. Glezerman IG, Sternlicht H. Hypercalcemia of malignancy and new treatment options. *Therapeut Clin Risk Manag*. December 2015:1779. https://doi.org/10.2147/TCRM.S83681. Published online.
11. O'Callaghan S, Yau H. Treatment of malignancy-associated hypercalcemia with cinacalcet: a paradigm shift. *Endocr Connect*. 2021;10(1):R13−R24. https://doi.org/10.1530/EC-20-0487.
12. Fuss M, Pepersack T, Gillet C, Karmali R, Corvilain J. Calcium and vitamin D metabolism in granulomatous diseases. *Clin Rheumatol*. 1992;11(1):28−36. https://doi.org/10.1007/BF02207080.