Open Journal of
Clinical & Medical
Case Reports

Volume 12 (2026)
Issue 2

Case Report ISSN: 2379-1039

Unexpected symptom, uncommon diagnosis: Hypercalcemia as the first manifestation of cholangiocarcinoma

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Abstract

Malignant hypercalcemia is a rare condition, with an estimated annual prevalence for all cancers ranging from 1.5% to 3% [1]. Here, we present the case of a 79-year-old woman admitted to the Emergency Department with general clinical signs and symptoms, subsequently diagnosed with moderate hypercalcemia. Further investigations revealed multiple lytic lesions and a large hepatic mass. Biopsies confirmed the diagnosis of Intrahepatic Cholangiocarcinoma (ICC), at a stage too advanced for curative treatment. This case emphasizes the crucial association between hypercalcemia and an underlying oncologic diagnosis, highlighting the necessity for a comprehensive medical history and diagnostic evaluation, especially when faced with nonspecific symptoms and analytical alterations. It sheds light on the uncommon manifestation of intrahepatic cholangiocarcinoma through hypercalcemia and underscores the challenges in providing appropriate care for patients with advanced disease.

Keywords: Malignant hypercalcemia; Cholangiocarcinoma; Cancer; Liver; Oncology.

Introduction

Malignant hypercalcemia is a serious medical condition characterized by an abnormally high level of calcium in the blood, typically exceeding 10.5 mg/dL. It is a potentially life-threatening electrolyte disturbance associated with a range of malignant tumors and its prevalence varies depending on the tumor type. It is more frequently observed in patients with advanced malignancies, particularly those with solid tumors. Those include breast cancer (10% to 30% in advanced stages), lung cancer (5% to 30%), renal cell carcinoma (20% to 30%) and certain hematologic malignancies like multiple myeloma (10% to 30%) and T- cell lymphoma [1-4].

Clinical manifestations of hypercalcemia range from mild symptoms to severe ones that include skin pruritus, neuromuscular symptoms such as fatigue, corneal calcification, muscle weakness and altered

mental status, gastrointestinal manifestations including constipation, anorexia, nausea and rarely peptic ulcer disease, renal involvement marked by polyuria and the formation of kidney stones, cardiovascular complications such as arrythmias and hypertension and skeletal symptoms mainly represented by bone pain underscoring the consequences of dysregulated calcium metabolism on the musculoskeletal system.

Early recognition and prompt management of malignant hypercalcemia are crucial to prevent potentially life-threatening complications which include cardiac arrythmias that can lead to cardiac arrest, renal failure, comatose status and severe dehydration secondary to gastrointestinal losses. Treatment strategies focus on addressing the underlying cause, restoring calcium balance, and alleviating symptoms. This typically involves a combination of hydration, diuretics and bisphosphonates. In vitamin D-mediated hypercalcemia, glucocorticoids can be used as a treatment because they reduce vitamin D synthesis. Calcitonin may also be used in acute severe symptomatic hypercalcemia [5]. The prophylactic use of bisphosphonates or denosumab in patients with bone metastases appears to be having a positive impact, leading to a decrease in the prevalence of cancer-associated hypercalcemia [4].

The prevalence of malignant hypercalcemia in the setting of cholangiocarcinoma is not well- documented in the literature. Intrahepatic Cholangiocarcinoma (ICC) is a rare type of primary liver cancer that develops in the bile ducts inside the liver [6]. It accounts for less than 1% of all cancers worldwide and approximately 10-20% of all cases of primary liver cancer. This malignancy is more frequently seen in older individuals, with a mean age at diagnosis between 60 and 70 years. Risk factors for developing ICC include chronic liver disease caused by alcohol or viral infection (hepatitis B or C), primary sclerosing cholangitis, and non-alcoholic fatty liver disease. Additionally, exposure to certain chemicals and toxins, such as thorium dioxide and asbestos, has also been associated with ICC [6,7].

ICC is often diagnosed at an advanced stage due to the nonspecific nature of its symptoms, such as abdominal pain, weight loss, and jaundice. Imaging techniques, namely Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), can help identify the location and extent of the tumor once ICC is suspected. Confirmation of diagnosis is done through biopsy and histological examination of the tissue. Localized ICC might be treated by surgical resection. When cancer has spread or surgical removal is not possible, treatment options may include chemotherapy, radiation therapy, or liver transplantation. The use of chemotherapy following surgical resection has been shown to improve survival rates in patients with ICC. Despite that, prognosis is generally poor, with a 5-year survival rate of less than 20% [6].

Clinical Case

We report the case of a 79-year-old female patient with a medical history of arterial hypertension, chronic hepatic alcoholic disease, gout, and osteoarticular degenerative disease. Prescribed medications included 20 mg pantoprazole, 100 mg irbesartan, 40 mg furosemide, 300 mg allopurinol, and 5 mg diazepam as needed for sleeping difficulties. The patient had a Katz index of C due to ambulation difficulties. She presented to the emergency department with a three-week history of generalized pain, as well as nausea and vomiting over the last 24 hours. There was no reported localized abdominal pain or changes in bowel habits. Physical examination was normal except for important pain at palpation of limbs and thoracic

region. Additionally, a mass was identified above the left eye and on the top of the head. Initial laboratory testing was significant for mild hypercalcemia (total calcium of 11.2 mg/dL) with diminished levels of phosphate, parathyroid hormone and vitamin D. Additionally there was leukocytosis of 14000/mm^3, elevated C-reactive protein (3 mg/dl) and erythrocyte sedimentation rate (32 mm/h). To better characterize the cranial mass visualized on physical exam, a cranioencephalic CT scan was performed, which revealed multiple lytic lesions involving the skull and first and second cervical vertebrae, some of which presented an infiltrative component. The largest lesion extended into the cavernous sinus, the posterior wall of the sphenoid sinus with involvement of the ipsilateral carotid canal, and completed disrupted the internal and external tables at the level of the anterior temporal squama, posterior parietal, and the cranial vault of high convexity as showed in Figure 1.

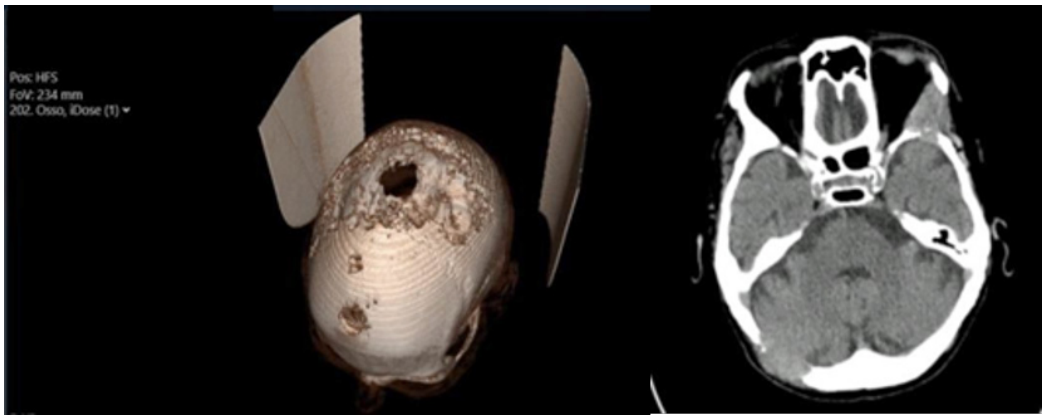

Figure 1: (A and B) – Head CT scan showing extensive and infiltrative lytic lesion – tridimensional reconstitution and transverse plane respectively.

Given these findings, a complete body scan was performed, which showed a 9.3 cm heterogenous hepatic mass with hypervascularity areas and bilateral pleural effusion, with associated pleural carcinomatosis as showed in Figure 2.

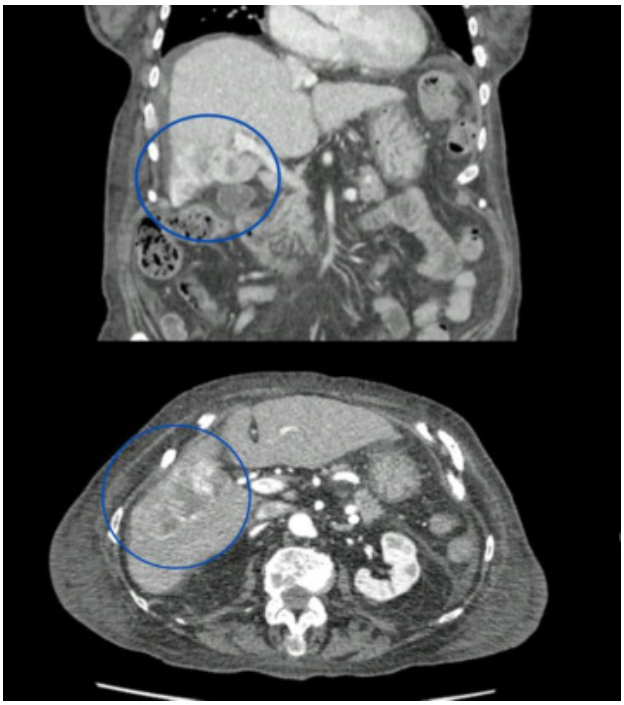

Figure 2: (A and B) – Abdominal CT scan showing hepatic mass – coronal and transverse plane respectively.

Further diagnostic testing excluded multiple myeloma (no monoclonal spike in protein electrophoresis and a normal light chain ratio) and a normal alpha-fetoprotein made hepatocellular carcinoma less likely [8]. Flow cytometry of the lytic lesion and also blood excluded hematologic disease. Biopsies of the hepatic tissue (Figure 3) and larger lytic lesion (Figure 4) showed histologic and anatomopathological features consistent with carcinoma originating from the digestive tract, including the bile ducts, stomach, pancreas or small intestine but excluding hepatocellular carcinoma. Given the location and aspect of the mass within the liver and the absence of other masses or imagiologic findings, the diagnosis of intrahepatic cholangiocarcinoma was made.

Due to the patient's initial physical and cognitive status, as well as weight loss and loss of motor function during hospitalization, she was not a candidate for chemotherapy or surgical intervention. Palliative care, mainly pain management, was initiated. The patient was transferred to a nursing home and referred to palliative outpatient care, with the goal of optimizing her quality of life in the remaining years.

Discussion/Conclusion

This case highlights the intricate clinical challenges associated with diagnosing severe conditions, particularly those presenting initially with vague and nonspecific symptoms, signs, and analytical alterations. In this specific instance, the patient exhibited the rare condition of malignant hypercalcemia, a manifestation associated with various disturbances and diseases, of which cancer is just one possibility. Notably, Intrahepatic Cholangiocarcinoma (ICC) is infrequently linked with hypercalcemia as its initial presentation, further complicating the diagnostic process. This case is also remarkable, particularly due to the considerable size of the largest cranial lesion, which protruded noticeably and was especially discernible during the physical examination.

A structured and comprehensive diagnostic approach to both clinical and analytical alterations prove indispensable in instances featuring atypical presentations, enabling a swift diagnosis and subsequent patient management. The delayed diagnosis of ICC with metastatic dissemination underscores the paramount importance of early detection and timely intervention. In situations where curative treatment proves unattainable, the decision to transition to palliative care becomes a nuanced consideration. Despite its complexities, palliative care extends an opportunity for patients to experience the highest possible quality of life during their final days.

In conclusion, this case serves to emphasize the complexities of diagnosing uncommon diseases and advocates for a patient-centered approach to care.

Declarations

Informed consent statement: Because this work describes a single patient case, it did not require institutional approval. Informed consent for publication could not be obtained as the patient passed away prior to the preparation of this manuscript. All efforts have been made to protect the patient's identity and ensure that no identifiable information is included in this report.

Funding statement: No funding was received for the preparation of this article.

Conflict of interest statement: The authors declare that they have no conflicts of interest related to this publication.

References

1. Goldner W. Cancer-related hypercalcemia. J Oncol Pract. 2016; 12: 426–32.

2. Ramos REO, Perez Mak M, Alves MFS, Piotto GHM, Takahashi TK, Gomes da Fonseca L, Silvino MCM, Hoff PM, de Castro G Jr. Malignancy-related hypercalcemia in advanced solid tumors: survival outcomes. J Glob Oncol. 2017; 3: 728–33.

3. Guise TA, Wysolmerski JJ. Cancer-associated hypercalcemia. N Engl J Med. 2022; 386: 1443–51.

4. Oyajobi BO. Multiple myeloma/hypercalcemia. Arthritis Res Ther. 2007; 9: S4.

5. Carroll MF, Schade DS. A practical approach to hypercalcemia. Am Fam Physician. 2003; 67: 1959–66.

6. Bridgewater J, Galle PR, Khan SA, et al. Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. J Hepatol. 2014; 60: 1268–89.

7. Massarweh NN, El-Serag HB. Epidemiology of hepatocellular carcinoma and intrahepatic cholangiocarcinoma. Cancer Control. 2017; 24: 1073274817729245.

8. Tao LY, Cai L, He XD, Liu W, Qu Q. Comparison of serum tumor markers for intrahepatic cholangiocarcinoma and hepatocellular carcinoma. Am Surg. 2010; 76: 1210–3.

Manuscript Information: Received: January 20, 2026; Accepted: March 03, 2026; Published: March 10, 2026

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Citation: Soares I, Lima R, Salvado C, Santos L, Fidalgo M. Unexpected symptom, uncommon diagnosis: Hypercalcemia as the first manifestation of cholangiocarcinoma. Open J Clin Med Case Rep. 2026; 2406.