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Hypercalcemia as Initial Presentation of Duodenal Adenocarcinoma: A Case Report and Review of the Literature

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Abstract

Duodenal cancer is a rare form of gastrointestinal cancer, accounting for 0.3%-1% of all gastrointestinal cancer incidences. It predominantly occurs in the periampullary sector of the duodenum and is often diagnosed late due to symptomatic manifestations. Hypercalcemia, a condition that can arise from various causes, is often a consequence of osseous metastases or the secretion of paraneoplastic substances like Parathyroid Hormone-related Protein (PTHrP) or 1,25-dihydroxyvitamin D, often in conjunction with compromised renal excretion of calcium. This condition is predominantly linked with oncogenic processes and is infrequently observed in benign pathologies. A case report from the Indian Subcontinent reveals the first instance of primary duodenal adenocarcinoma presenting with hypercalcemia mediated by PTHrP, underlining its exceptional rarity. It is crucial for clinicians to incorporate duodenal adenocarcinoma within the differential diagnostic framework for patients demonstrating duodenal thickening upon upper gastrointestinal endoscopy and hypercalcemia, especially in the face of such rare clinical presentations.

1. Introduction

Primary duodenal adenocarcinoma is recognized as a remarkably rare entity, with its incidence documented between 2.9 and 4.3 cases per million individuals annually [1]. The disease's initial clinical manifestations lack specificity, contributing to a significant delay in diagnosis. This delay persists until the carcinoma progresses to a stage where it either locally invades and elicits obstructive symptoms or disseminates to distant organs. The association of hypercalcemia with duodenal

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adenocarcinoma is exceedingly infrequent, with literature review revealing a solitary case reported prior to this. In this context, we present a distinctive case involving a 65-year-old male who exhibited nonspecific clinical symptoms alongside hypercalcemia and cholestatic jaundice, marking the onset of duodenal adenocarcinoma without detectable metastatic dissemination. Despite the administration of chemotherapy, the patient's life was claimed within two months post-diagnosis, attributed to the severe complications arising from malignancy-induced hypercalcemia and cachexia associated with the tumor burden. This case emphasizes the imperative consideration of duodenal adenocarcinoma in the differential diagnosis for patients presenting with duodenal thickening in conjunction with hypercalcem.

2. Case Presentation

A 65-year-old male patient was admitted to the emergency department, presenting with symptoms that had progressively worsened over a three-week period, including intractable vomiting, nausea, anorexia, and significant weight loss. The patient further reported experiencing fatigue, generalized weakness, and constipation, while negating the presence of palpitations, chest pain, syncope, lightheadedness, dyspnea, cough, melena, fever, night sweats, or hematochezia.

Upon initial physical evaluation, the patient exhibited pallor. Chest auscultation did not reveal any abnormal respiratory sounds. Abdominal examination showed distension accompanied by a positive fluid thrill and shifting dullness, indicative of ascites. Deep palpation of the epigastric region elicited tenderness, although no guarding, rigidity, or rebound tenderness was observed. Auscultation confirmed the presence of bowel sounds in all four quadrants of the abdomen, with no evidence of hepatomegaly or splenomegaly. Comprehensive examination of other systems yielded no noteworthy findings. The laboratory findings upon admission are summarized in TABLE 1.

TABLE 1. **Laboratory Results at Admission.**

Investigation	Results	Reference	Units
Hemoglobin	7.2	12.0 to 17.0	gm/dL
Hematocrit	24%	45.0 to 55.0	%
Calcium	14.8	8.6 to 10.2	mg/dL
Corrected calcium	15.63	8.6 to 10.2	mg/dL
Bilirubin	1.42	0.0 to 1.2	mg/dL
Direct bilirubin	1.16	0.0 to 0.3	mg/dL
Aspartate Transaminase	148	0.0 to 40.0	U/L
Alanine Transaminase	38	0.0 to 41.0	U/L
Alkaline Phosphatase	172	38.0 to 136.0	U/L
Vitamin D3	13.72	>30	ng/mL
Alpha-fetoprotein	1.97	0.0 to 9.0	IU/mL

The ascitic fluid analysis depicted lymphocytes, foamy macrophages, and mesothelial cells against a backdrop of erythrocytes, with an absence of malignant cells. Computed tomography scans of the chest, abdomen, and pelvis revealed heterogeneously enhancing, circumferential, and asymmetrical thickening in the proximal portion of the duodenum, without metastatic indications. Subsequent to these findings, the patient was hospitalized, initiated on intravenous hydration, calcitonin, and pamidronate treatments, and received a transfusion of two units of packed red blood cells. Diagnostic upper esophagogastroduodenoscopy identified a 2 cm × 2 cm mass within the duodenum's second segment, impeding the pancreaticoduodenal junction yet without luminal stenosis (FIG. 1). Multiple tissue biopsies were procured. Pathological analysis identified the mass as a poorly differentiated adenocarcinoma, with immunohistochemical staining corroborating this diagnosis.

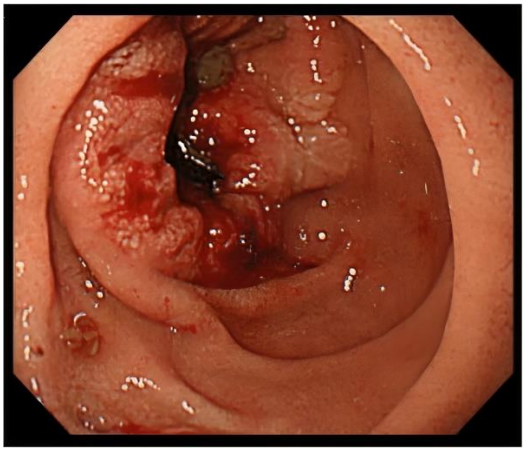

FIG. 1. **Upper Gastro-intestinal Endoscopy depicting mass in the second part of duodenum.**

The patient's corrected serum calcium concentration demonstrated a reduction to 12.6 mg/dL by the third day of admission. Investigations for primary hyperparathyroidism yielded negative results, with a parathyroid hormone (PTH) level recorded at 5.17 pg/mL (reference range: 15.0 to 65.0 pg/mL). Further evaluation for the etiology of the hypercalcemia, with a PTH-related peptide (PTHrP) level measured at 9.2 pmol/L (reference range: 0.02 to 4.0 pmol/L), attributed the condition to humoral hypercalcemia of malignancy.

Based on these clinical and laboratory findings, chemotherapy was initiated. Despite undergoing several rounds of chemotherapy, the patient was rehospitalized multiple times and unfortunately succumbed to complications associated with malignancy-induced hypercalcemia and cachexia within two months of the initial diagnosis.

3. Discussion

Duodenal cancer, a notably rare condition, manifests at a frequency of between 2.9 and 4.3 individuals per million [1]. Primary duodenal adenocarcinoma, which represents a mere 0.3% to 1% of all gastrointestinal malignancies, highlights the rarity of this disease [2]. Within the spectrum of small intestinal cancers, neuroendocrine tumors are the most prevalent, followed by

adenocarcinomas and lymphomas [3]. It's particularly noteworthy that primary duodenal adenocarcinomas commonly occur in the periampullary region, specifically in the second part of the duodenum [4,5].

The diagnosis of duodenal adenocarcinoma frequently faces delays, largely due to the late presentation of symptoms, which emerge once the tumor has reached a significant size [6]. The symptoms associated with this condition, such as abdominal pain, nausea, vomiting, fatigue, weakness, and weight loss, are generally nonspecific, complicating early diagnosis [7]. Advanced stages of the disease may present more severe symptoms, including anemia, gastrointestinal obstruction, and jaundice, further complicating treatment due to the tumor's advanced local and distant spread [8,9].

Hypercalcemia, a condition that can arise from a variety of causes, is most commonly linked to primary hyperparathyroidism or cancer. Distinguishing between these two primary causes is crucial for accurate diagnosis. In the context of cancer, hypercalcemia can result from the metastasis to bone or from the production of substances like PTHrP or 1,25-dihydroxyvitamin D, leading to excessive bone resorption and a diminished capacity of the kidneys to excrete excess calcium [10,11].

Interestingly, hypercalcemia caused by PTHrP is predominantly seen in cases of malignant tumors and is rare in benign tumors. For instance, a study conducted in Queensland, Australia, involving 138 patients with PTHrP-mediated hypercalcemia identified only one case of duodenal adenocarcinoma [12].

Our case is unique as it is the first reported case of primary duodenal adenocarcinoma from the Indian Subcontinent. Uniquely, this case initially presented with hypercalcemia and cholestatic jaundice, an uncommon combination of symptoms. This rarity emphasizes the importance of considering duodenal adenocarcinoma as a differential diagnosis in patients exhibiting duodenal thickening on upper GI endoscopy, particularly when accompanied by hypercalcemia.

Moreover, our case presented initially with hypercalcemia and cholestatic jaundice, which is an uncommon presentation. This makes our case unique in the sense that it is a rare presentation of a rare tumor itself. The hypercalcemia was due to humoral hypercalcemia of malignancy; hence, it becomes essential to consider duodenal adenocarcinoma as a differential diagnosis in patients with duodenal thickening on upper GI endoscopy along with hypercalcemia.

4. Conclusions

In conclusion, while hypercalcemia associated with parathyroid hormone-related protein (PTHrP) is a well-documented occurrence in various malignant conditions, our case underscores the importance of considering less common etiologies in the context of secondary hypercalcemia attributed to PTHrP. Notably, our patient's presentation featured a benign tumor, which is infrequently reported as a cause of hypercalcemia, such as in the case of Duodenal Adenocarcinoma. Therefore, when encountering a case of secondary hypercalcemia linked to PTHrP, clinicians should consider duodenal adenocarcinoma as a differential diagnosis.

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