



## Elevated Cobalamin as Initial Presentation of Colon Cancer: Case Report

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### Abstract

**Introduction:** Globally, colorectal cancer (CRC) is the third-most common type of cancer. It is imperative to find early markers for the prompt detection of CRC, as the prognosis is highly dependent on the stage at which the cancer is identified. Hypercobalaminemia, or high serum levels of Vitamin B12, is a frequently underestimated abnormality in clinical practice. A potential correlation between high vitamin B12 levels and tumorigenesis has been reported. This article reports an additional case where isolated elevation of cobalamin leads to the subsequent diagnosis of colorectal cancer.

**Case:** 42-year-old Lebanese female with no past medical or surgical history presenting for a regular checkup and was found to have incidental elevated vitamin b12 on general health maintenance laboratory examination. Further investigations lead to the early diagnosis of colon cancer and to favorable outcomes post resection.

**Discussion:** Despite the existence of effective screening techniques, nearly 2 million cases were reported in 2022, with more than 900,000 deaths per year. Vitamin B12 is essential in homocysteine metabolism, acting as a cofactor of the methionine synthetase enzyme. Due to its significant involvement in DNA methylation, this enzyme may promote tumorigenesis in colorectal cancer and might be a potential non-invasive screening marker as reflected by this case.

**Conclusion:** Colorectal cancer can present with multiple symptoms, most commonly weight loss, altered bowel habits, or rectal bleeding. Less frequently, it can present as an isolated elevation in vitamin B12 or cobalamin. Clinicians should therefore suspect malignancy, especially CRC, in cases presenting with elevated cobalamin.

**Keywords:** Cobalamin; Vitamin B12; Colon Cancer

## Introduction

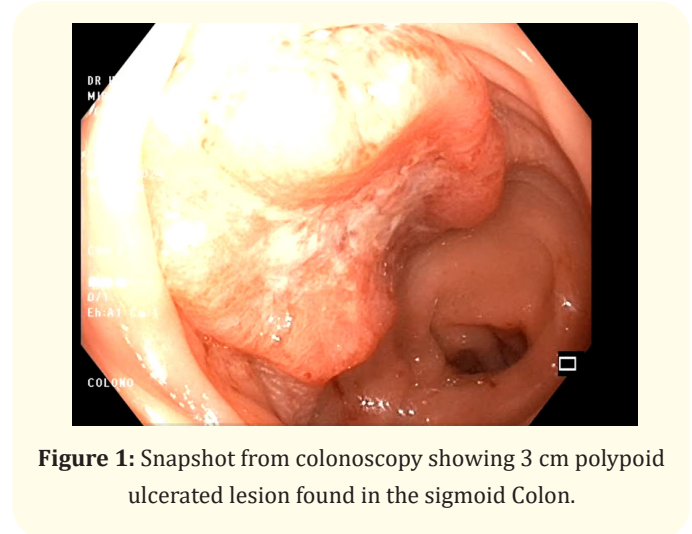
Globally, colorectal cancer (CRC) is the third-most common type of cancer [1]. According to the American Cancer Society, individuals 45 years of age and older, with no risk factors or family history of CRC, must undergo colorectal screening using either stool-based tests like the fecal immunochemical test (FIT) or visual exams like colonoscopy. It is therefore imperative to find early markers for the prompt detection of CRC, as the prognosis is highly dependent on the stage at which the cancer is identified. Stage 4 CRC has a 5-year survival rate of 10% only compared to 90% in stage 1. Cobalamin or Vitamin B12 (B12), is an essential water-soluble vitamin used for DNA synthesis and for the maintenance of neurological functions. Hypercobalaminemia, or high serum levels of Vitamin B12, is a frequently underestimated abnormality in clinical practice. Several studies have pointed out the potential correlation of high vitamin B12 levels with tumorigenesis. In the 1970s, the first cases of markedly increased serum levels of B12, in relation to solid tumors like CRC were reported [3,4]. Other conditions associated with high serum levels of B12 include hematological malignancies and liver diseases [5]. This article reports an additional case where isolated elevation of cobalamin leads to the subsequent diagnosis of colorectal cancer.

## Case

This case pertains to a 42-year-old Lebanese female with no past medical or surgical history presenting for a regular checkup. The patient did not report any concerning complaints about including dizziness, fatigue, altered bowel habits or weight loss. The patient does not use tobacco, alcohol, or have any family history of malignancies. She takes no regular medications or any vitamins supplements. Her physical exam was not pertinent for any findings.

General health maintenance laboratory tests results were only pertinent for elevated vitamin B12 levels of 1290 pg/ml. Other parameters were normal including complete blood count, folic acid, liver and kidney function tests. Abdominal ultrasound was done and was negative for any abnormalities. In addition, due to this isolated finding, a fecal immunochemical test (FIT) was ordered and turned out to be positive. Other additional testing included carcinoembryonic antigen (CEA) level which was at 0.67 ng/ml (reference range is <4 ng/ml), and Cancer Antigen 19-9 (CA 19-9) level which was at 13 U/ml (reference range is <34 U/ml).

Due to high suspicion, colonoscopy was done and revealed a 3 cm ulcerated polypoid lesion in the sigmoid colon as seen in figure 1, from which biopsies were obtained.



**Figure 1:** Snapshot from colonoscopy showing 3 cm polypoid ulcerated lesion found in the sigmoid Colon.

Histopathology showed a moderately differentiated invasive adenocarcinoma made of columnar basophilic cells disclosing a dark and irregular nucleus, arranged in tubules, tubule-papillary, and polyadenoid structures. Further staging, with a CT scan chest abdomen pelvis as well as PET scan did not show any metastasis. Patient was referred to oncology for appropriate management and later had partial colectomy with good outcomes at 1 year post op follow up.

## Discussion

We reported a case of 42-year-old women who presented with an incidental elevated vitamin B12, revealing later on an underlying diagnosis of colorectal cancer. Despite the existence of effective screening techniques, nearly 2 million cases were reported in 2022, with more than 900,000 deaths per year [6]. CRC begins with the proliferation of epithelial glandular cells into polyps; of those, only 10% can progress to invasive cancer known as adenocarcinoma, which constitutes 96% of total CRC. Risk factors associated with CRC include family history, smoking, alcohol, obesity, IBD, and diet [7]. Concerning serum markers, CEA and CA19-9 are most tested despite being non-specific and can be increased in other gastrointestinal diseases like pancreatitis. Both CEA and CA19-9 were found to be ineffective for screening and are not universally elevat-

ed in all CRC patients; rather, they are recommended for prognosis and recurrence [8]. This fact was reflected in this case, where both CEA and CA 19-9 were at normal levels.

Vitamin B12, or cobalamin, is an essential water-soluble vitamin with a major role in red blood cell hematopoiesis, DNA synthesis, and the myelination and proper functioning of the central nervous system. The differential for elevated cobalamin includes exogenous intake (enteral or parenteral), liver and kidney disorders, solid tumors (primary and secondary liver tumors, colon cancer, gastric cancer, breast and pancreatic tumors), as well as blood disorders such as acute leukemias, chronic myelomonocytic leukemia, primary hypereosinophilic syndrome, and myelodysplastic syndromes [9]. Vitamin B12 contributes to the pathogenesis of CRC through several mechanisms. First off, the colorectal mucosa has a high rate of cell turnover, which makes it sensitive to variations in nutrient quantities such as vitamin B12. Vitamin B12 is essential in homocysteine metabolism, acting as a cofactor of the methionine synthetase enzyme. Due to its significant involvement in DNA methylation, this enzyme may promote tumorigenesis in colorectal cancer. A study found that elevated vitamin B12 levels are associated with LINE1 hypomethylation, which is typically found in CRC [10]. Moreover, methylation of tumor suppression genes like cyclin dependent kinase inhibitor 2A (p16) and DNA repairing protein like methylguanine methyltransferase (MGMT) was found to be associated with elevated vitamin B12 levels [11-13].

All this data supports the possible use of cobalamin as a predictive marker for CRC. Values of greater than 1000 ng/L (or pg/ml) were found by a study to raise the likelihood of an underlying solid tumor of the esophagus, pancreas, stomach, colon, or rectum. More specifically, an association between cobalamin and solid tumors was stronger when its values were between 1250 and 1749 ng/L [14]. This patient falls specifically into this category with a vitamin B12 level of 1290 ng/l. The pathophysiology behind the increased cobalamin levels is not well explained. Arondet, *et al.* suggested an alteration in cobalamin metabolism by tumor cells as an underlying factor leading to B12 accumulation [15]. Another suggested mechanism is the antitumor immune response secondary to inflammation leads to the release of cobalamin transporter protein (haptocorrin) [16].

## Conclusion

Colorectal cancer can present with multiple symptoms, most commonly weight loss, altered bowel habits, or rectal bleeding. Less frequently, it can present as an isolated elevation in vitamin B12 or cobalamin. Clinicians should therefore suspect malignancy, especially CRC, in cases of elevated cobalamin. This fact warrants further studies to assess the significance of cobalamin as a potential tumour marker for CRC.

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## Conflicts of Interest

The authors declare that they do not have any conflicts of interest.

## Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the case.

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

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