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# Crohn's Disease with the Suspicion of Colon Cancer: A Case Report and Literature Review

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Crohn's disease; Colon cancer; Multidisciplinary team (MDT)

**Abbreviations:**

CD: Crohn's Disease; MDT: Multidisciplinary Team; IBD: Inflammatory Bowel Disease; PET-CT: Positron Emission Computed Tomography; CRP: C-Reactive Protein; CEA: Carcinoembryonic Antigen, MRI: Magnetic Resonance Imaging; ASCA: Anti-Saccharomyces Cerevisiae Antibody; ASA: Aminosalicylic Acid; GCS: Glucocorticoids; EPAAC: The European Cooperative Action on Cancer

## 1. Abstract

**1.1. Background:** Crohn's Disease (CD) and colon cancer have many similarities in imaging. However, treatments for the two entities are vastly different, making proper diagnosis critical in the clinic. This case is an atypical Crohn's disease, which was misdiagnosed as colon cancer. We reviewed a lot of related literature and found almost no similar diseases.

**1.2. Method:** We reviewed the patient's clinical symptoms, serum findings, imaging information, and pathology findings, then we conducted a Multidisciplinary Team (MDT). In addition, we studied the relevant literature.

**1.3. Results:** In this case, the patient underwent two colonoscopies and a series of imaging tests. We discovered that while colonoscopic pathology suggested inflammation, imaging revealed a potentially malignant tumor. Which test should we believe in light of this? The surgeon preferred to make the diagnosis of a tumor. Following the surgical removal of the tumor, the pathology indicated inflammatory symptoms, which were then verified by MDT, leading to the ultimate diagnosis of Crohn's disease.

**1.4. Discussion:** The diagnosis of CD cannot be confirmed solely based on radiographic evidence. All clinical tests, serum findings, endoscopy, and histology should be considered in diagnosis. In addition, an MDT discussion and treatment plan is indicated if the clinician is still unable to diagnose the disease. We believe that the MDT model has clear benefits in the diagnosis and treatment of complicated disorders and that each hospital should implement it to the greatest extent possible.

## 2. Introduction

Crohn's Disease (CD) is a form of Inflammatory Bowel Disease (IBD) characterized by chronic, nonspecific granulomatous disease of the gastrointestinal tract that typically persists throughout life. CD is thought to be caused by a complex interaction between genetic predisposition, environmental factors, and altered gut microbiota resulting in dysregulated innate and adaptive immune responses. CD can segmentally affect any part of the gastrointestinal tract from the mouth to the anus and mostly commonly involves

the terminal ileum, followed by the small intestine and colon. Symptoms may correlate to disease severity and site(s); however, some CD patients may have mild or even no clinical symptoms [1].

Colon cancer is one of the most prevalent malignant tumors of the digestive tract. Most colonic malignancies originate in a polyp. Typically, an abnormal crypt progresses to a neoplastic precursor lesion (a polyp) and then, finally to colon cancer over 10−15 years. Colon cancer patients may experience a variety of signs and symptoms, including occult or overt rectal bleeding, changes in bowel habit, anemia, and/or abdominal pain. However, the early stages of colon cancer are largely asymptomatic and undetectable until the cancer has progressed to a relatively advanced stage [2].

In the early stages of both CD and colon cancer, there are no or minimal clinical symptoms. Thus, CD and early colon cancer can be difficult to identify and differentiate. In certain cases, radiological imaging simply shows thickening of the intestinal wall in a similar manner. Here we described a Crohn's disease patient with a suspicion for colon cancer. We also described the role of the Multidisciplinary Team (MDT) in complex cases such as this.

## 3. Case Presentation

On November 18th, a 36-year-old woman complaining of discomfort in the right lower abdomen for 2 months presented to our outpatient clinic. She had no past medical history of diseases including hepatitis, tuberculosis, diabetes, hypertension, or coronary heart disease. She also had no history of surgery, trauma or blood transfusion and no known allergies. Her vaccination history was unknown. Her family history was unremarkable. Physical examination of the patient was unremarkable except for discomfort on examination of the right lower quadrant of her abdomen.

Abdominal ultrasonography was performed. It demonstrated an unevenly thickened segment of intestine in the right lower abdomen. As ascending colon cancer could not be excluded on imaging, endoscopy was recommended. (Figure 1a-c). The first endoscopy showed an ileocecal mass. Intestinal tuberculosis and ileal lymphoid tissue hyperplasia were differential diagnoses. Pathological examination of biopsies taken revealed chronic moderate and severe active mucosal inflammation with lymphoid tissue hyperplasia of the terminal ileum, pieces of granulation tissue and ileocecal ulceration (Figure 2a&b).

Positron Emission Computed Tomography (PET-CT) was then performed in another institution and demonstrated: i) a focal hypermetabolic focus which infiltrated through the serosa and into the surrounding mesentery suggestive of a cecal/ascending colon cancer and ii) multiple enlarged lymph nodes in the mesentery of the ileocecum with slightly increased metabolism, considered lymph node metastasis. The patient was admitted to our hospital one week later for further treatment. Laboratory tests including C-Reactive Protein (CRP), Tuberculosis (TB)-spot test, Carcinoembryonic Antigen (CEA, 1.32 ng/mL), tumor marker of carbohydrate antigen 15-3 (CA15-3, 4.77 U/mL), CA19-9 (0.6 U/mL) and CA-125 (28.07 U/mL), and blood cultures for fungi and bacteria were all within normal limits or negative. Magnetic Resonance Imaging (MRI) and CT were performed to aid in diagnosis. MRI again demonstrated a thickened ascending colon wall forming a mass suggestive of a carcinoma and multiple slightly enlarged lymph nodes around the mass, considered metastatic in nature (Figure 1d-f). Contrast-enhanced CT also showed colon cancer manifested by a malignant appearing lesion of the ileocecal-ascending colon, which likely involved the appendix. Multiple lymph node metastases around the colon were detected as well (Figure 1g-i). No other sites of disease were seen. To confirm the diagnosis, the patient underwent a second endoscopy; however, persistent, chronic and severe active inflammation with erosion in the ileocecal mucosal and lymphoid and granulation tissue hyperplasia with increased plasma cell infiltration was detected (Figure 2c&d).

For definitive diagnosis and treatment, based on the imaging diagnosis of an ascending colon mass without pathological confirmation of cancer, a laparoscopic right hemicolectomy was performed. Postoperative pathology showed local ileocecal and appendiceal intestinal wall erosion with transmural inflammation and ulcers in the right colon. Inflammatory granulation tissue formation was found at the ulcer site without caseous necrosis. Acid-fast stain was negative; however, acid-fast bacilli fluorescent staining found a suspected brevibacterium. All 27 resected lymph nodes were histologically confirmed as inflammatory reactive hyperplastic lymph nodes with no evidence of carcinoma. Thus, differential diagnoses were now inflammatory bowel disease and tuberculosis (Figure 2e&f). Tuberculosis checks were negative three consecutive times at the local Tuberculosis Control Institute after the patient was discharged from our hospital. Thus, tuberculosis was excluded and the ultimate diagnosis was CD.

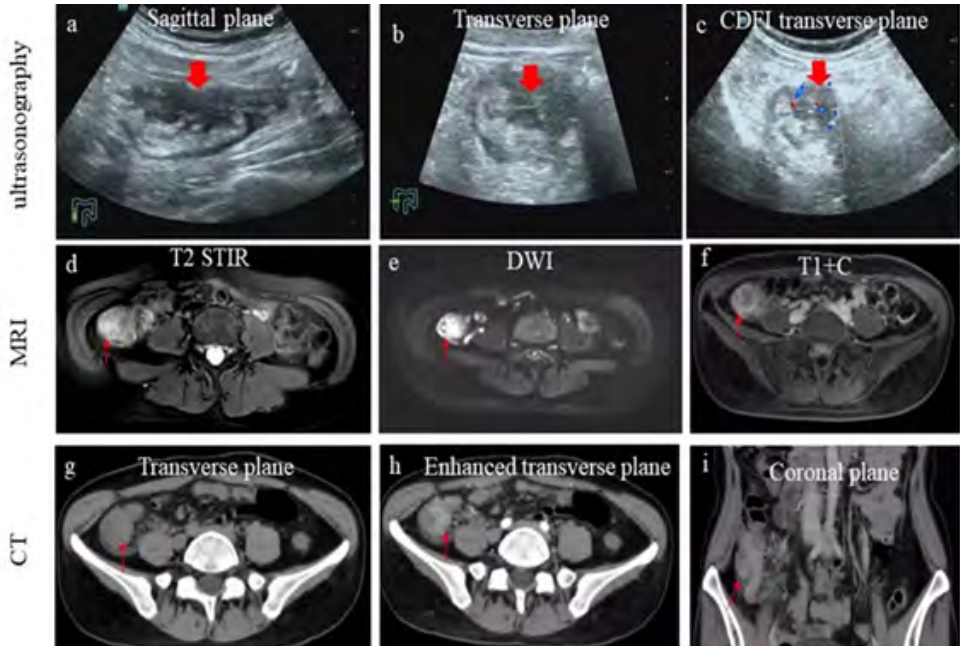


**Figure 1:** Ultrasonography, MR, and CT images before surgery. (a-c) Ultrasonography. (a) Red arrow indicates hypoechoic of the intestinal wall, indicating intestinal wall thickening. (b) Uneven thick of the intestinal wall and narrowing of the intestinal cavity. (c) CDFI shows a few blood flow signals from the intestinal wall. (d-f) MR images. (d) T2 STIR: ascending colon's annular wall was thickened with high signal intensity. (e) DWI showing ileocecal mass with high signal intensity. (f) Enhanced scan showing the irregularly thickened ileocecal-ascending colon wall and a soft tissue mass expanded along the intestinal wall, resulting in an evident narrowing of the local intestinal cavity and contrast-enhanced scan enhancement. (g-i) CT images. (g) The intestinal wall at the beginning of the ascending colon thickened and masses formed. (h) The masses were enhanced. (i) Thickening of the intestinal wall, narrowing of the intestinal cavity, masses formed. Abbreviations: STIR: short TI inversion recovery.

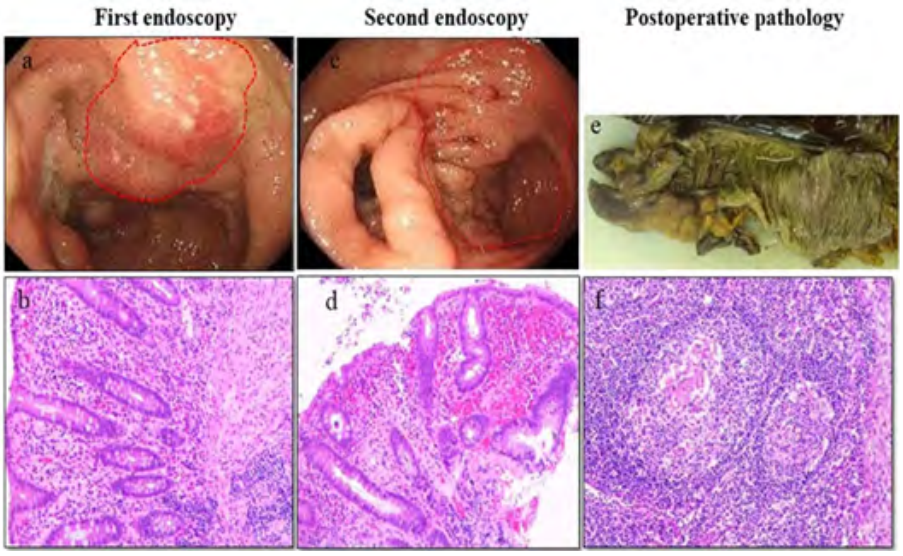


**Figure 2:** Endoscopy, postoperative specimens, and corresponding pathology. (a) The first endoscopy showed an ileocecal mass. (b) H&E staining relative to (a) showing chronic active inflammation of ileocecal mucous membrane with lymph hyperplasia. (c) The second endoscopy showed an ileocecal mass. (d) H&E staining relative to (c) showing chronic severe active inflammation with erosion in ileocecum mucosal, lymphoid, and granulation tissue hyperplasia, with more plasma cell infiltration. (e) Postoperative specimens. (f) Postoperative H&E staining relative to (e) showing local ileocecal and appendiceal intestinal wall erosion, transmural inflammation, and ulcer development in the right colon. Inflammatory granulation tissue formation occurred at the ulcer site. Abbreviation: H&E: hematoxylin-eosin.

## 4. Discussion

The described patient underwent a very detailed examination and diagnostic work up, including ultrasound, CT, MR, PET-CT and two endoscopies which suggested carcinoma; however, no pathological evidence of cancer was found. After surgical resection of the ascending colon, postoperative pathology revealed inflammatory lesions instead of a tumor. After tuberculosis was ruled out, CD was diagnosed. In this case, colonoscopic pathology revealed inflammation, but imaging demonstrated a likely malignant tumor. This raises the question: which test should we believe?

Colonoscopy is the gold standard for the preoperative diagnosis of both CD and colon cancer, particularly when used in combination with an evaluation of clinical symptoms, imaging, endoscopy, and histological examination. Pathological diagnosis either acquired by endoscopic biopsy or surgical resection is confirmatory for both CD and colon cancer [1]. In our case, despite two colonoscopies and histology indicating inflammation, the clinician considered all results, concluded that the biopsies were insufficient and preferred to trust the imaging for diagnosis. However, for early stage CD or colon cancer, thickening and mucosal hyper enhancement with bowel-wall stenosis may be almost indistinguishable, which can pose a great challenge for diagnosis.

Radiological imaging is the most common technique used to better reflect the extent of large and small intestinal involvement and evaluate CD activity and disease severity. This is compared with colonoscopy [1], which is also important for CD but critical for the diagnosis of colon cancer. In CD, the intestinal lumen can be irregularly narrowed due to thickening, which is detectable using several imaging modalities. Enhanced CT scan can reveal an enhancing intestinal wall with circular stratified enhancement in some cases. Increased mesenteric vessels arranged in a comb shape along the intestinal wall around the diseased intestine for CD are known as the "comb sign." The "comb sign" and circular enhancement of the intestinal wall are common signs of active CD. Similar to CT findings, MRI can reveal segmental thickening. It can also detect enhanced T2 weighted imaging signal intensity in the intestinal wall and stenosis of the intestinal lumen [6-8]. Similarly, early imaging observations of colon cancer included thickening of the intestinal wall, mucosal irregularities, varying degrees of narrowing of the intestinal lumen, and a mass in the late stage. The contrast-enhanced CT and MRI can reveal neoplastic lesions, metastasized lymph nodes and local (and distal) organ involvement, which are very useful in determining the location of the colon cancer focus, the extent of invasion, and TNM staging [2, 5, 11]. Furthermore, abdominal ultrasound can reveal segmental or continuous thickening of the intestinal wall, narrowing of the intestinal lumen, hypo echogenicity of the intestinal wall, reduction or disappearance of intestinal peristalsis, and/or an unclear layered structure of the intestinal wall suggesting CD and colon cancer. In the active stage of inflammation, blood flow signals from the intestinal wall are multiple [9, 10]. In this case, the patient did not have a "comb sign," but an only irregular thickening of the intestinal wall and narrowing of the intestinal cavity, which can occur in both diseases. Therefore, these imaging findings could not be used to confirm the diagnosis of CD.

In addition to imaging for diagnosis, Anti-Saccharomyces Cerevisiae Antibody (ASCA) can be tested in the serum to indicate CD; however, it was not tested in this case. Although CRP is a nonspecific inflammatory blood marker that can reflect disease activity, roughly 1/3 of CD patients have normal CRP levels [3, 4]. CEA is the most extensively utilized tumor marker for colon cancer diagnosis. Additionally, CA19-9 and CA242, are significant auxiliary tools for the early detection of tumor patients [2, 5]. Therefore, laboratory tests including molecular diagnostics are crucial in the differential diagnosis of these two illnesses.

CD and colon cancer have many similarities on imaging; however, treatments for the two entities are vastly different, making proper diagnosis critical in the clinic. For CD, pharmacological treatment in the form of oral, topical, intravenous and/or subcutaneous medications are typically used to control acute attacks, promote mucosal healing, maintain remission, reduce disease recurrence, and prevent and treat sequelae. In the mild and moderate active stages of CD, Aminosalicylic Acid (ASA) and Glucocorticoids (GCS) are the drugs of choice. Surgery is indicated when conservative treatment fails or major problems arise (for example, intestinal perforation, persistent or recurrent blockage, intractable bleeding, IBD associated colorectal cancer etc.). The choice of operation should be based on the reason for surgery, patient condition and disease location and behavior [1, 10, 12]. In contrast, radical surgical resection to include surrounding lymph nodes is the main treatment for colon cancer. However, with the introduction of endoscopic therapy and the development of new chemotherapy, targeted therapy, immunotherapy, and neoadjuvant therapy, the field of colorectal cancer treatment is changing [2]. Colorectal surgery causes permanent functional loss that can be potentially avoided in the case of CD. Therefore, an accurate diagnosis of CD versus colon cancer is very important.

Above all, colonoscopic evaluation and biopsy with histopathological examination are essential for diagnosis. The diagnosis of CD should be comprehensive, taking into account all clinical tests needed to make the diagnosis. If, however, after performing all of the necessary tests, the physician is still unable to make a definite conclusion, what should be done next to avoid misdiagnosis and improve diagnostic accuracy?

In this situation, we advise a Multidisciplinary Team (MDT) approach to diagnosis. The MDT diagnosis and treatment approach was developed in the United Kingdom at the end of the twentieth century. Belgium, France, Canada, Australia, and other nations subsequently adopted it [13]. In 2014, The European Cooperative Action on Cancer (EPAAC) declared that major European me-

dical associations had endorsed the MDT model, confirming its importance in the diagnosis and treatment of many complicated diseases. The MDT model is a diagnosis and treatment approach in which experts from several disciplines collaborate to give the best possible care to patients. Experts from surgery, internal medicine, radiology, radiation oncology, medical oncology, pathology, and other disciplines create a treatment team under this strategy. The optimal treatment plan for a patient is presented in the form of regular expert consultation. The treatment plan is then rigidly implemented by the discipline in charge of the patient separately or in cooperation with multiple disciplines. The MDT model has now become an important feature of the tumor diagnosis and treatment systems in Europe and America [14, 15]. We believe that MDT is not only suitable for cancer patients, but also for patients with complex and/or undiagnosed diseases. In this case, the radiologists considered the findings to likely be colon cancer, but the pathologists believed it was an inflammatory disease. However, tumor markers were negative and CRP was elevated. So we recommended an MDT discussion and invite surgeons, oncologists, internal medicine specialists, radiologists, and laboratory physicians to discuss the situation. The MDT model allowed the physicians and pathologists to fully express their opinions and participate in clinical decision-making, diagnosis, and treatment of patients, increasing the accuracy of disease diagnosis.

In conclusion, colonoscopy is critical for the diagnosis of CD. Pathology results should be carefully evaluated. The diagnosis of CD cannot be confirmed solely based on radiographic evidence. All clinical tests, serum findings, endoscopy, and histology should be considered in diagnosis. In addition, an MDT discussion and treatment plan is indicated if the clinician is still unable to diagnose the disease. We believe that the MDT model has clear benefits in the diagnosis and treatment of complicated disorders and that each hospital should implement it to the greatest extent possible.

## 5. Funding

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