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Atypical Presentation of Crohn's Disease: Diagnostic Challenges in a Clinical Case

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Abstract

Introduction: Crohn's Disease (CD) is a chronic inflammatory disorder with a heterogeneous presentation. While diarrhea, abdominal pain, and weight loss are hallmarks, atypical manifestations can obscure the diagnosis. This report highlights an unusual presentation of CD to emphasize the need for comprehensive diagnostic strategies. **Case Report**: A 25-year-old male presented with peripheral edema, anorexia, and abdominal distension but lacked classic gastrointestinal (GI) symptoms. Laboratory findings included microcytic anemia and hypoalbuminemia, while imaging revealed ascites and bowel wall thickening. Elevated fecal calprotectin and positive Anti-Saccharomyces cerevisiae antibodies (ASCA) supported the diagnosis. Endoscopy confirmed ileocolic Crohn's Disease (L3 + L4). Infliximab therapy resulted in marked clinical improvement. **Discussion**: This case underscores the complexity of atypical CD presentations. Early use of serological markers, imaging, and endoscopy guided the diagnosis. Recognition of CD's diverse manifestations is critical for timely intervention. **Conclusion**: Atypical CD presentations require heightened clinical suspicion and a multidisciplinary approach to reduce diagnostic delays and improve patient outcomes.

Keywords

Crohn's Disease, Atypical Presentation, Diagnostic Challenges, Inflammatory Markers, Infliximab, Imaging

1. Introduction

Crohn's Disease (CD) is a chronic, relapsing inflammatory bowel disease (IBD) that affects various segments of the gastrointestinal tract. Although it is most frequently associated with diarrhea, abdominal pain, and weight loss, CD exhibits

significant heterogeneity in its clinical course and manifestations. Atypical presentations, particularly those devoid of hallmark GI symptoms, remain a diagnostic challenge and often result in delayed treatment, increasing morbidity and compromising prognosis [1] [2].

Recent data highlight a rise in CD incidence globally, particularly in regions undergoing rapid industrialization. This shift is associated with environmental factors such as dietary changes, reduced microbial diversity, and urbanization, superimposed on genetic predisposition [3]. The prevalence of CD ranges between 3 and 20 per 100,000 person-years, with increasing diagnoses in younger populations [2]. Genetic susceptibility, notably variations in **NOD2/CARD15** and autophagy-related genes, has been implicated in disease pathogenesis, particularly in familial cases [4].

While classic CD symptoms dominate the clinical narrative, atypical manifestations—including isolated extraintestinal symptoms such as peripheral edema, ascites, or dermatological findings—complicate the diagnostic process. This case report aims to elucidate the challenges posed by such presentations and emphasize the value of integrating family history, advanced biomarkers, and imaging techniques into diagnostic algorithms.

2. Case Report

2.1. Atypical Manifestations of Crohn's Disease

Atypical presentations, such as peripheral edema, ascites, or systemic inflammatory syndromes, are less commonly recognized but may precede or entirely replace classic GI symptoms. Ascites, hypoalbuminemia, and unexplained systemic inflammation in young adults should prompt consideration of IBD as a differential diagnóstico, particularly when accompanied by suggestive serological markers [1] [5]. Extraintestinal manifestations (EIMs), including dermatological, ocular, and joint disorders, are reported in up to 30% of CD cases and may represent the initial presentation in some patients [3].

In this patient, the presence of ascites, hypoalbuminemia, and peripheral edema initially directed diagnostic efforts toward hepatic or nephrotic syndromes. These were excluded via cytological, microbiological, and electrophoretic analyses. Elevated fecal calprotectin and ASCA positivity ultimately shifted diagnostic focus to IBD [6].

2.2. Role of Biomarkers in Diagnosis

Fecal calprotectin has emerged as a reliable, non-invasive marker of intestinal inflammation. Elevated levels, as observed in this case, are highly sensitive for active mucosal inflammation and correlate with endoscopic findings [7]. ASCA, while lacking diagnostic specificity, remains a valuable adjunct in differentiating CD from ulcerative colitis. Advances in serological profiling, including the use of anti-glycan antibodies, further enhance diagnostic accuracy [7].

2.3. Imaging and Endoscopy

The combination of imaging modalities, such as contrast-enhanced MRI and CT, with endoscopy provides a robust framework for diagnosing atypical CD. Cross-sectional imaging delineates bowel wall inflammation and evaluates complications such as strictures, fistulas, and abscesses. Endoscopy remains the gold standard, offering visual and histological confirmation [2]. The Montreal Classification used here (L3 + L4) enables precise disease characterization, guiding therapeutic decisions [7].

3. Therapeutic Advances

3.1. Infliximab: Mechanism and Role in Crohn's Disease

Infliximab, a monoclonal antibody targeting tumor necrosis factor-alpha (TNF-α), is one of the most established biological therapies for Crohn's Disease (CD). TNF-α is a central cytokine in the inflammatory cascade of CD, promoting immune cell infiltration, tissue damage, and mucosal remodeling. By neutralizing this cytokine, infliximab reduces inflammation, promotes mucosal healing, and alleviates clinical symptoms [4] [5].

In this case, the patient presented with moderate-to-severe CD characterized by significant nutritional impairment and active inflammation, as evidenced by elevated fecal calprotectin levels and positive ASCA. These features justified the initiation of infliximab to induce remission and control inflammatory activity. Treatment with infliximab led to notable clinical improvement, including resolution of peripheral edema, reduction in abdominal distension, and progressive normalization of laboratory markers such as albumin and hemoglobin.

3.2. Therapeutic Regimen

Infliximab is administered intravenously, typically following an induction schedule (doses at weeks 0, 2, and 6) and maintenance therapy every 8 weeks thereafter. The standard dose is 5 mg/kg, though it may be escalated to 10 mg/kg in refractory cases [7]. Adherence to the therapeutic schedule and careful monitoring are essential to prevent complications such as immunogenicity and loss of response.

3.3. Monitoring Treatment Response

Assessing the effectiveness of infliximab requires a multidimensional approach involving clinical, laboratory, endoscopic, and imaging parameters. Biomarkers play a key role in this process:

1) Fecal Calprotectin

- One of the most reliable non-invasive markers for monitoring treatment response. A significant reduction in levels (typically below 250 μg/g) correlates with clinical improvement and mucosal healing [6].
- In this patient, initial fecal calprotectin levels exceeding 2000 μg/g markedly decreased after infliximab initiation, reflecting effective inflammation control.

2) C-reactive Protein (CRP)

- A systemic inflammatory marker. Decreasing CRP levels during therapy often indicate treatment success [8].

3) Serum Infliximab Levels and Antidrug Antibodies (ADA)

- Measuring serum infliximab levels helps optimize dosing strategies. Subtherapeutic levels or the presence of antidrug antibodies (ADA) may require dose adjustment or a switch to alternative biologics, such as vedolizumab or ustekinumab [8].

4) Endoscopic Evaluation

- Endoscopic assessment of mucosal healing remains the gold standard for evaluating long-term efficacy. Patients achieving mucosal healing have better prognoses and lower risks of complications [9].

5) Emerging Biomarkers

- Recent research highlights the potential of cytokine profiling (e.g., IL-6, IL-22) and transcriptomics-based tests to predict response to infliximab and other biologics [10].

3.4. Safety and Tolerability

While infliximab is highly effective, it is associated with potential adverse effects, including infusion reactions, opportunistic infections (such as reactivated tuberculosis), and, in rare cases, lymphoma. Rigorous monitoring is essential, particularly for patients with predisposing factors such as malnutrition, as seen in this patient.

3.5. Prognosis with Infliximab

In this case, the rapid clinical and laboratory improvement following infliximab initiation highlights the effectiveness of this treatment for atypical CD presentations. Continued monitoring with biomarkers such as fecal calprotectin and CRP, combined with scheduled endoscopic evaluations, will be crucial to confirm sustained remission and adapt therapy as needed.

4. Conclusion

This case highlights the diagnostic complexities of Crohn's Disease with atypical presentations, emphasizing the critical role of advanced serological, imaging, and endoscopic modalities in achieving timely and accurate diagnoses. Clinicians should maintain vigilance for CD in patients with unexplained systemic symptoms, particularly when accompanied by family history or inflammatory markers. Prompt recognition and early initiation of biologic therapies can mitigate disease progression, reduce morbidity, and improve quality of life [2] [4].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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