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Case Report Open Access

Anemia: A Diagnostic Dilemma

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Abstract

This case report describes a four decade old history of iron deficiency anemia in a female. Iron deficiency anemia is one of the most common symptoms in the female population and despite a straight forward workup it can become protracted if there is loss to follow up, unavailability of advanced equipment to assess the entire gastrointestinal tract and if the physician does not exclude every possible cause if symptoms persist. This case highlights the importance of screening the entire gastrointestinal tract by endoscopies supplemented by radio-imaging. At the same time, it is important to not keep an open mind to the possibility of more than one cause of anemia in a single patient as was seen in this case.

Keywords: Anemia; Iron deficiency; Crohns; Celiac; Ulcerative; Jejunitis

Introduction

Chronic ulcerative enteritis was first described by Nyman in 1949 [1]. It is characterized by multiple ulcerations of the small intestine, mainly the jejunum; resulting in abdominal pain, diarrhea and malabsorption [2], including iron deficiency. It can present acutely as a surgical emergency or with chronic symptoms. It remains a diagnosis of exclusion and should be considered when a patient presents with any of the above symptoms which do not conform to a conventional diagnosis. It can arise in isolation or in a background of a chronic condition like celiac disease [3].

Case Report

A 61-year-old female with no co-morbids had a long standing history of iron deficiency anemia. She initially presented during her first pregnancy when she was 23 years of age. At that time her hemoglobin was 8.0 mg/dl and she was transfused one pint of red cell concentrate. Her anemia was attributed to pregnancy and dietary deficiency. Then during her third and fourth pregnancies within the next 10 years-she had chronic diarrhea in each of her last trimesters. She was managed symptomatically each time but with poor relief of symptoms and no definite diagnosis was clinched. Following delivery her symptoms self-subsided.

Her next visit to hospital was 3 years after her fourth and last pregnancy in 1991. This time she again had severe watery loose motions. Stool microscopy revealed hookworm infection and this time she was transfused two pints of red cell concentrates along with antihelminthic therapy.

She remained alright for some time but then 5-6 years later she developed exertional shortness of breath and had documented anemia requiring multiple transfusions. Around this time she had developed second and third degree hemorrhoids as well. This was considered as the cause of her anemia and she underwent hemorrhoidectomy in 2003. Even though her fresh bleeding per rectum settled, she again developed iron deficiency anemia within a year. She was managed with parentral and oral iron replacement. Despite her compliance to replacement therapy she continued to remain anemic. She underwent hysterectomy for fibroids in 2004 since menorrhagia was suspected to be the cause of her persistent anemia.

She; however, continued to have low hemoglobin and had her lowest reading at 4 mg/dl in 2007. This time a complete workup was done. Hemoglobin electrophoresis was normal, there was documented iron deficiency and one of her samples for stool for occult blood was positive. USG abdomen was unremarkable. Autoimmune and thyroid profiles were normal. She underwent upper and lower gastrointestinal endoscopy then in 2008; both turned out to be normal. This was followed by RBC labeled GIT Bleeding Studies; the study was negative for active GI bleeding. She was again managed symptomatically with transfusions and iron replacement.

Soon afterwards she started having abdominal pain on off as well. It was nonspecific; not related to food intake, with no particular relieving or exacerbating factors. She had irregular follow ups in medical outpatient department and no conclusive diagnosis was reached. She started taking anti-spasmodics regularly and remained on oral replacement. She started taking homeopathic and hakeemic medications for a few months as well in an attempt to cure her chronic anemia. During this interval she required multiple parentral iron replacements whenever she became symptomatic.

In December 2016 her abdominal pain became more severe and she underwent upper and lower gastrointestinal endoscopy again. This time again gross inspection revealed no abnormality. However, microscopy showed inflammation in antral mucosa and mild distal gastritis; intact villous architecture with increased intraepithelial lymphocytes in samples taken from distal duodenum. No dysplasia, malignancy or giardiasis was seen. Immunohistochemical staining with CD3 highlighted increased intraepithelial lymphocytes.

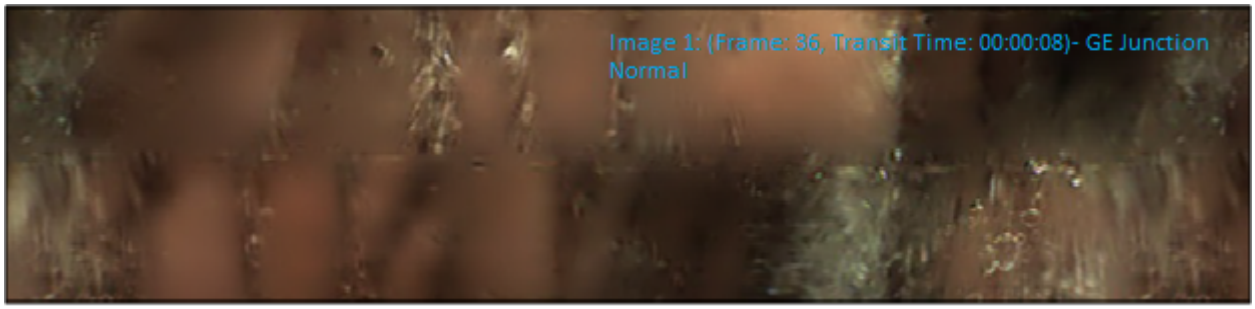

Figure 1: GE junction normal–Frame 36

Since bowel was already prepared and the surveillance endoscopies did not show any gross finding which was against the physician's expectation it was decided to do capsule endoscopy (Image 1, 6, 7 and 22- select pictures chosen here from the collection of images captured during capsule transit inside the small bowel) while awaiting biopsy report–especially before the patient is lost to follow up again for some more time. This time ulcerations involving widespread areas of jejunum and ileum were identified.

Based on the findings of above investigations-Celiac disease was the main differential diagnosis. Patient was advised a trial of gluten free diet. Celiac serology was negative; thyroid profile was within normal limit. Plan was a three months trial; however, by the end of two months patient started complaining of generalized weakness, fatigue and persistent abdominal pain. Her complete blood picture was done which revealed a fall of hemoglobin level to 7.5 mg/dl from 10.1 mg/dl which was at the start of trail period. Her trial was stopped prematurely.

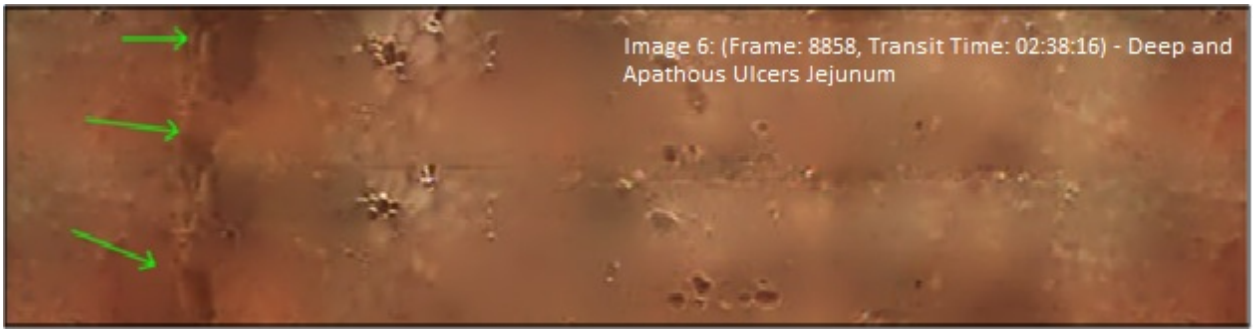

Figure 2: Deep and apathous ulcers jejunum–Frame 8858

Patient again lost follow-up after the poor response to therapy and difficulty in reaching a definite diagnosis. During 2017 she remained on oral and parentral iron replacement. At this time stool for calprotectin was sent as well which was raised (119.1 ug/g; normal <43.2 ug/g).

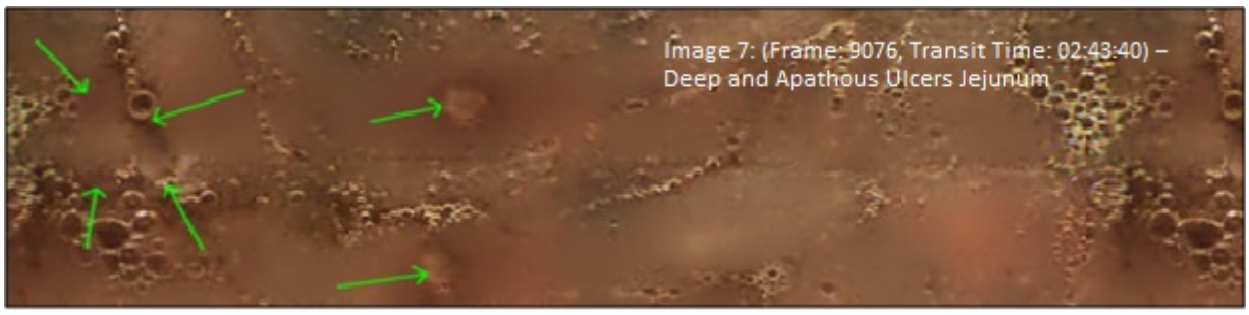

Figure 3: Deep and apathous ulcers jejunum - Frame 9076

After recurrent episodes of injection site reactions during iron sucrose transfusions and worsening abdominal pain; patient visited her physician again in 2018 and was advised double balloon enteroscopy to biopsy the lesions seen on capsule endoscopy. She relented. During the procedure a developing stricture was found in terminal ileum-it was dilated and biopsy samples were taken from ulceration sites. Microscopy and histochemical analysis did not reveal any evidence of significant pathology, ruling out any dysplasia or malignancy and chronic infections like tuberculosis. There were no cryptitis, crypt abscess, basal plasmacytosis. Magnetic Resonance Enteroscopy was done as well to assess the anatomy of the rest of the bowel. It revealed multifocal involvement of distal ileum and ileocecal valves showing wall thickening and edema with skip areas and, mesenteric stranding.

There was a mild focally stenotic segment involving 2.5 cm segment in ileum without any pre stenotic dilatation (Figures 1-4).

Following the biopsy report diagnosis of idiopathic chronic jejunitoilitis was made. She was started on high dose steroids and Azathipurine (Figure 5). After two month her steroids were tapered, Azathiopurine dose was increased and she was advised to follow up with complete blood picture. Patient presently is improved; her hemoglobin is at a steady level. Her response to treatment is being assessed by hemoglobin trend and regular liver function tests.

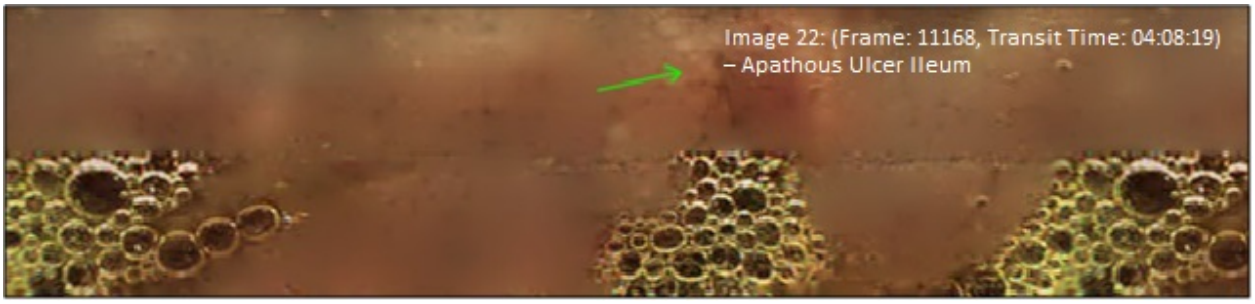

Figure 4: Apathous ulcer ileum-Frame 11168

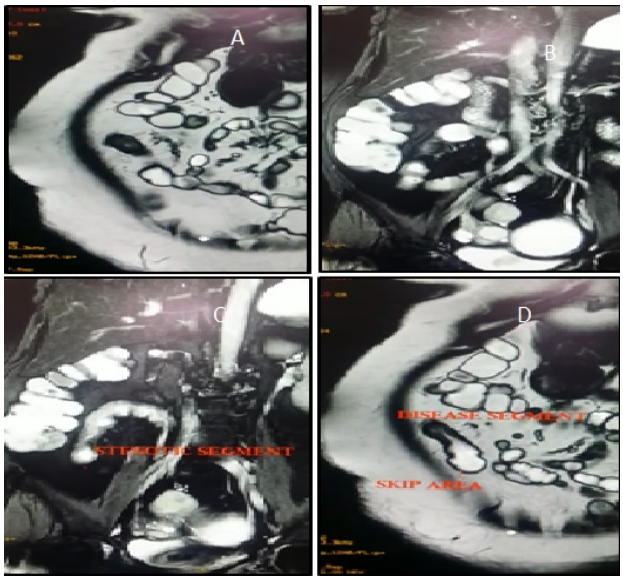

Figure 5 (a-d): Magnetic resonance enteroscopy

Discussion

Iron deficiency anemia is one of the most common hematology issue faced in clinical practice [4].

It is also one of the more straight forward cases diagnostically and usually patients respond to treatment quickly and effectively. However on rare occasions the clinical scenario does not fit the conventional diagnoses–exposing patient and doctor to new and difficult to treat conditions. With advances in diagnostic approaches there is a rise in such situations.

Idiopathic ulcerative enteritis is one such condition-a rare entity and is currently a diagnosis of exclusion- with poorly understood pathophysiology and no guidelines for management. It is usually suspected when a patient with a clinical picture suggestive of Celiac disease fails to respond to gluten free diet. It is defined by ulcerations in the small bowel after excluding infectious, inflammatory, metabolic and medicinal causes. It is present with different names in literature e.g. ulcerative jejunitis, ulcerative jejunoilietis, non-granulomatous ulcerative jejunoileitis [2]. It presents in a similar manner to Celiac disease- with blood loss, malabsorption and abdominal pain in addition to ulcerations [5]. However in contrast to Celiac disease patients are refractory to gluten free diet and frequently require surgical intervention for strictures and perforations. Jejunum or ileum and/ or both are affected by ulcerations leading to blood loss, stricture formation and perforations- latter due to ulcerations involving the entire thickness of the bowel wall. Malabsorption is due to mucosal atrophy along with ulcerations. Besides features of malabsorption patients can present with pain due to stricture formation-initially mild but later it can become colicky due to advancing obstruction.

Due to its varied presentation and pathological findings it has been categorized by some studies into four divisions: those with established celiac disease, those unresponsive to gluten free diet despite having villous atrophy, those with normal intestinal mucosa- morphologically and histologically, and lastly those with malignant histiocytosis [6].

According to surgical pathological criteria of Stanford Medicine it is diagnosed when there are multiple transversely located ulcerations of varying depth involving the jejunem and/or ileum; presence of heterogenous cellular infilterate, absence of granulomas, stricture formation, and villous atrophy. It is suspected when a patient labeled as

Celiac disease fails to respond to gluten free diet; and it can herald onset of T cell Lymphoma [7].

There is no established treatment for this condition [6]. A trial of gluten free diet is given, but response to treatment is variable. In addition, elemental diets have been tried. Antibiotics are given if there is evidence of bacterial overload. Response to steroids is again mixed. In presence of strictures and perforation surgical intervention is inevitable. There have been trials with varying success for new therapies including Infliximab [8] but again so far no definite treatment has been proposed for this entity.

The patient in the above case report had presented repeatedly with iron deficiency anemia, each time it was attributed to some other coexistent cause. However despite correcting every obvious cause patient remained symptomatic suggesting a concurrent occult cause. After ruling out any obvious cause of anemia, Celiac and Crohns were the main contending diagnoses. It was decided to give a trail of gluten free diet in 2016 after her second upper gastrointestinal endoscopy as the biopsy report favored this diagnosis and Celiac is more common than Crohn's by a factor of 100 [9]. After failure of gluten free trial Crohn's was the leading differential [10,11]. During double balloon enteroscoy in 2018 the stricture raised the possibility of malignancy and tuberculosis as well; both were less likely though based on the chronicity of symptoms and relatively stable condition of the patient during the years. However nonconlcusive biopsy report eventually drove the diagnosis in the favor of idiopathic ulcerative enteritis. Based on patient's history of hakeemic and homeopathic medications a case of drug induced ulcerative enteritis was also considered [12]. However the occurrence of symptoms preceded her intake of these medications and in the last year leading upto double balloon enteroscopy she had given up on these as well due to lack of improvement in her condition-ruling out this possibility. Since patient did not have any overt hemorrhage or perforation plan was to treat with steroids and immunosuppressants rather than surgery-usually considered first line in this condition [13]. Her stricture formation was in the initial phases and successfully dilated during endoscopy. Infliximab was not instituted because it has established efficacy in fistulating disease which the patient did not have and in view of the high cost it was decided to try oral therapy first.

Delay in diagnosis in this case was due to involvement of the part of small intestine not approached by standard endoscopes. Without the availability of capsule endoscopy and double-balloon enteroscopy this patient would have probably remained without a diagnosis [14]. This case report highlights not only the importance of investigating small bowel in difficult to diagnose cases but also keeping an open mind for new and unknown pathologies.

Disclosure

All the information related to the patient given in this article was mentioned after taking consent and explaining the implication of this article.

References

1. Nyman E (1949) Ulcerous jejuno-ileitis with symptomatic sprue. Acta Med Scand. 134: 275-283.
2. Biagi F, Lorenzini P, Corazza GR (2000) Literature review on the clinical relationship between ulcerative jejunoileitis, coeliac disease, and enteropathy-associated T-cell lymphoma. Scand J Gastroenterol 35: 785–790.
3. O'Mahony S, Howdle PD, Losowsky MS (1996) Review article: Management of patients with non-responsive coeliac disease. Aliment Pharmacol Ther 10: 671-680.
4. Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L (2015) Iron deficiency anaemia Lancet 387: 907-916.
5. Kane SP, Parkins RA (1979) Chronic ulcerative jejunitis without symptoms. Postgrad Med J 55: 215-7.
6. Jewell DP (1983) Ulcerative enteritis Br Med J (Clin Res Ed) 287: 1740-1741.
7. Surgical Pathological Criteria (2009) Stanford Medicine. Ulcerative Jejunoileitis.
8. Seven G, Assaad A, Biehl T, Kozarek RA (2012) Use of anti-tumor necrosis factor-alpha monoclonal antibody for ulcerative jejunoileitis. World J Gastroenterol. 18: 5135-5137.
9. Virginia P, Romina DC, Natalia LP, Andrés B, Luz MM, et al. (2014) Inflammatory bowel disease and celiac disease: Overlaps and differences. World J Gastroenterol 20: 4846–4856.
10. Hapke RJ, Corless C, Katon RM (1997) Isolated jejunal Crohn's disease in a young woman presenting with malabsorption syndrome and abdominal pain. Am J Gastroenterol 2: 1916-1919.
11. Lonardo A, Tondelli E, Selmi I, Bagni I, Della Casa G, et al. (1998) Isolated jejunal Crohn's disease in a young adult presenting as fever of unknown origin. Am J Gastroenterol 93: 2285-2287.
12. Sutton CD, White SA, Marshall LJ, Dennison AR, Thomas WM (2002) Idiopathic chronic ulcerative enteritis--the role of radical surgical resection. Dig Surg 19: 406–408.
13. Chen Y, Ma WQ, Chen JM, Cai JT (2010) Multiple chronic non-specific ulcer of small intestine characterized by anemia and hypoalbuminemia. World J Gastroenterol 16: 782–784.
14. Zhi FC, Yue H, Jiang B, Xu ZM, Bai Y, et al. (2007) Diagnostic value of double balloon enteroscopy for small-intestinal disease: Experience from China. Gastrointest Endosc 66: S19–S21.