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Original Article

Evaluation of Gastrointestinal Cause in Cases of Unexplained Anemia in Adults - A Study from Tertiary Care Center

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Abstract

Background: Anemia is the most common illness, the human being is suffering even on today. About 50% of Indian population suffer from this disease. Evaluation of anemia is the most important step in the management. Blood loss from gastrointestinal (GI) tract is one of the common causes of anemia in adults, but its evaluation is expensive and multistep procedures. On the contrary, if there is delay in evaluation, it may be too late to offer the optimal therapy.

Aims and Objective: The aim of this study is to evaluate the profile of GI disorders in unexplained anemia in adult patients and need of its evaluation.

Materials and Methods: A total of 146 patients with the unexplained anemia attaining Clinical Haematology Department of SCB Medical College, Cuttack, from January 2014 to January 2017 were taken in the study. A detailed GI evaluation was done in all cases. All the analyses were done in SPSS 17 software.

Results: A total of 46 cases responded to treatment after addressing to known primary etiology. A total of 100 cases did not respond to treatment and underwent further evaluation in the present study. The mean age was 50 years (range 15-72 years). Male-to-female ratio was 1.086. The mean duration of the illness was 8 months, and the mean hemoglobin was 7.2 g/dl (range 4.5-9 g/dl). Among 100 patients not responding to treatment, GI causes for anemia found in 50 (50%) patients, 10 (10%) patients had a disease outside GI tract, and in 40 (40%) patients no cause for anemia established. GI malignancy was the most common finding (26%) followed by chronic duodenal ulcer and ileocecal tuberculosis.

Conclusions: GI disorders are the leading cause of unexplained anemia in adults (50%). Malignancy was identifying as the most common cause with colon and stomach being the frequent sites of involvement, followed by benign etiology with chronic duodenal ulcer and ileocecal tuberculosis. We strongly recommend a thorough GI evaluation in this subset of unexplained anemia of adult patients.

Key words: Adults, Etiology, Gastrointestinal, Unexplained anemia

INTRODUCTION

Anemia is the most common disease in the world including India affecting 50% of general population. The evaluation of anemia is a complex time-consuming and expensive process.[1] Thus, a scientific, multistep, and rational evaluation is important by considering the relevance of clinical settings and cost-effective ratio. Evaluation of entire gastrointestinal (GI) tract is itself a multistep process and expensive which includes gastroscopy, colonoscopy, and capsule endoscopy; computed tomography (CT) scans of abdomen and CT angiography, among other things. Most of the clinicians do not recommend that these procedures routinely and a significant proportion of patients are also reluctant to undergo such procedures. On the contrary,

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if diagnosis is delayed, it may be too late to catch these lesions at early stage to offer the optimal curative options. There is no recommendation or guideline for indication of such procedures in anemic patients, leaving it entirely to the clinical judgment. Moreover, there is paucity of studies involving large series in this context. Thus, the present study was taken up to evaluate GI causes in these types of cases and the need for such evaluation routinely in such subset of adult patients of unexplained anemia.

MATERIAL AND METHODS

All patients in between 15 and 75 years of age presenting with anemia who were admitted in the Department of Clinical Haematology, SCB Medical College, Cuttack from January 2014 to January 2017 were enrolled for this prospective study. All the patients had undergone some investigations earlier by local physicians but failed to find a definitive cause for their anemia.

Unexplained anemia is defined in the present study as persistent anemia (Hemoglobin <11 g%) with no evidence of hemoglobinopathy, immunodeficiency, vitamin B12 and folic acid deficiency, autoimmune hemolytic anemia, bone marrow failure syndromes, leukemia, multiple myeloma, lymphoma, etc.

Patients were excluded from the study if they had a known cause of blood loss or had been taking nonsteroidal anti-inflammatory drugs regularly or had an established reason for anemia such as nutritional deficiency (iron, folic acid, and cobalamin), hemoglobinopathies, autoimmune hemolytic anemia, bone marrow failure syndromes, thyroid disorders, drugs causing bone marrow suppression, etc. Patients with liver, renal, pulmonary, and cardiac dysfunctions were excluded from the study. Pregnant ladies and lactating mothers were not included in this study.

GI symptoms were grouped into upper and lower GI symptoms. Upper GI symptoms which consisted of anorexia, nausea and vomiting, and upper abdominal pain that was related to food or relieved by antacid or H2 blocker. Lower GI symptoms comprised changed bowel habit, lower abdominal pain diarrhea, and constipation that was colicky or associated with altered bowel habit or relieved by the passage of stool or flatus. The finding of an epigastric mass or hepatosplenomegaly suggested that they were related to upper GI disease while a mass in the right iliac fossa pointed to lower GI disease as the cause. As GI symptoms or signs may be nonspecific, two or more features related to either the upper or lower tract were considered necessary to suggest the site of possible disease.

Anemia was assessed by estimating hemoglobin concentration and other parameters by 5-part automated cell counter (sysmex pocH-100i). Serum ferritin concentration, serum iron concentration, total iron binding capacity, transferrin saturation, bone marrow aspiration, hemoglobin electrophoresis, reticulocyte count, osmotic fragility test, Coombs test, liver function tests, kidney function tests, thyroid function tests, tuberculin test, and X-ray chest were performed in all the cases to exclude any known cause for anemia. Serum electrophoresis for M band, biopsy of lymph nodes was done whenever needed.

The GI investigations comprised endoscopy of upper GI tract, duodenal (D2) biopsy, barium follow through X-ray examination of the small gut, capsule endoscopy, sigmoidoscopy, colonoscopy, ultrasound examination of the abdomen, CT of the abdomen with CT angiography, and fecal occult blood test were performed when considered appropriate. Diagnostic laparoscopy or laparotomy was done when clinically indicated.

All the analyses were done in SPSS 17 software.

Ethical clearance was obtained from the institutional ethical review board. Informed consent was filled in respective cases.

RESULTS

A total of 146 patients were included in this study, 46 cases responded to treatment after addressing to known primary etiology. A total of 100 cases did not respond to treatment and underwent further evaluation in the present study. The mean age of the study group was 48.2 years (range 15-72 years). A total of 76 patients were male; remaining 70 were female. The mean duration of the illness was 8 months and the mean hemoglobin was 7.2 g/dl (range 4.5-9 g/dl). Among 100 patients, GI causes for anemia were found in 50 patients. A total of 10 patients had a disease outside GI tract; in 40 patients, no cause for anemia could be established.

Table 1a shows the number of identifiable malignant GI cases of unexplained anemia. The most common cause of malignancy was colon in 13 patients followed by gastric malignancy in 9 patients. Totally, 3 patients were found to be small intestinal malignancy while 1 case found to have ampullary growth.

Table 1b shows GI diseases other than malignancy associated with anemia in 24 patients. Among them, 11 patients presented with chronic duodenal ulcer. A total of 6 patients presented with tuberculosis involving GI tract.

Five of the 6 patients with GI tuberculosis had involvement of the terminal ileum and cecum, and 1 had colonic tuberculosis. Colonoscopy with biopsy allowed a definitive diagnosis of GI tuberculosis in 5 patients; in one patient, biopsy was not conclusive, but presumptive diagnosis of GI tuberculosis was made on the colonoscopic appearance of cecal ulceration and response to antitubercular therapy. A total of 4 patients had celiac sprue on duodenal biopsy which had raised anti-tissue transglutaminase antibody titer after revaluation. Despite the absence of symptoms lesions were found in 1 case of Crohn's disease. 2 patients had angiodysplasia of colon diagnosed after CT angiography. Totally, 10 patients had a disease outside GI tract accounting for anemia (Table 2). Among them, 8 cases had gynecological cause. A total of 2 patients had malignancy outside GI tract, i.e., malignancy of unknown primary site which was diagnosed by laparoscopy and biopsy of peritoneal seeding.

DISCUSSION

This study was conducted in 100 patients of unexplained anemia with or without GI symptoms who did not respond to treatment and were evaluated to find out a GI cause. GI malignancy was the most common finding. Colorectal cancer and Carcinoma of stomach accounted for 13 cases (13%) and 9 cases (9%), respectively, in this series. Different series have estimated that carcinoma of colon accounts for 11-14% and carcinoma of stomach accounts for 1-5% of iron deficiency anemia in Western countries.[2,3] Anemia was the only presenting manifestation in patients of duodenal adenocarcinoma, ampullary carcinoma, and ileal adenocarcinoma. Few literatures have demonstrated the extreme latency of these tumors and the necessity for detailed GI investigations in patients presenting with isolated iron deficiency anemia by performing endoscopic examination of upper GI tract, duodenoscopy, and endoscopic retrograde cholangiopancreatography.[4,5]

Table 1a: Malignant gastrointestinal cases of unexplained anemia (*n*=26)

Cases	Number
Colonic malignancy	13
Gastric malignancy	9
Small intestinal malignancy	3
Ampullary growth	1

Table 1b: Non-malignant gastrointestinal cases of unexplained anemia (*n*=24)

Cases	Number
Chronic duodenal ulcer	11
Ileocaecal tuberculosis	5
Celiac sprue	4
Colonic tuberculosis	1
Crohn's disease	1
Angiodysplasia of colon	2

Table 2: Diseases outside gastrointestinal tract associated with unexplained anemia (*n*=10)

Cases	Number
Gynaecological cause	
Carcinoma cervix	6
Cervical polyp	2
Malignancy outside GI tract	2

GI: Gastrointestinal

Next to malignancy, chronic duodenal ulcers were the most frequent cause of anemia in the present study. It reflects higher prevalence of Helicobacter pylori infection in our population.[6] GI tuberculosis was the next frequent cause of anemia in our study. Anemia in GI tuberculosis may result from occult GI bleeding from ulceration or malabsorption of dietary iron or as a part of anemia of chronic disease.[7] Tuberculosis is common in our country. Sign and symptoms of GI tuberculosis are nonspecific; a high index of suspicion should be maintained to ensure a timely diagnosis. In the present study, 4 patients had celiac sprue that had only presented with anemia but without any GI complaints, and 10 (10%) patients had a disease outside GI tract as the cause for anemia. One previous study reported 2% patients had a systemic disease without coexisting GI disease during evaluation of patients with iron deficiency anemia.[2] This finding suggests that some patients presenting with anemia and GI symptoms may have disease outside the GI tract. Gynecological evaluation should be considered during evaluation of female patients with anemia.

There were 40 (40%) patients in whom no cause for the anemia could be ascertained in the present study. Some earlier studies have shown similar finding in patients with iron deficiency anemia.[8-10] Follow-up data were not available in these patients. Most of these patients were asymptomatic. Conditions such as unreported menstrual losses or insufficient dietary intake of iron in the context of the prevalent poor socioeconomic status in our country may have been responsible for occult iron deficiency. Alternatively, ulcerations or benign lesions might have caused blood loss in the past but then healed and thus were not detected. Moreover, abnormalities such as polyps or vascular ectasia might have been missed during the endoscopic examination or their anemia was associated with undiagnosed chronic disease such as rheumatoid arthritis. Up to 5% of patients with anemia result from recurrent GI bleed who remain undiagnosed in spite of upper GI endoscopy and colonoscopy, with the presumed source of

bleeding being the small bowel.[11] Recently, various methods, including push enteroscopy, two-way enteroscopy, and capsule endoscopy, have been employed to detect and manage small bowel lesions.[12] Several studies showed that capsule endoscopy is highly effective in detecting small-bowel lesions, with an overall diagnostic yield superior to that of push enteroscopy or radiologic imaging.[13-16] Capsule endoscopy is being recommended as the primary initial investigation in occult GI bleeding by two international guidelines, with double balloon enteroscopy at present reserved for therapeutic action.[17-19] Capsule endoscopy, double balloon enteroscopy, mesenteric angiography are now available in our set up which resulted in diagnosis of one case of Angiodysplasia.

This study also reflects that age is an important factor determining the cause of anemia. Malignancy particularly of GI tract origin contributing to anemia was found in middle aged people 46 years and above, whereas hematological causes or other systemic illness or no identified cause was found in younger people between 15 and 45 years. Some earlier studies have found evidence of such differences.[8] Investigations for anemia should be tailored to the patient's age and the clinical setting.

CONCLUSION

This study was conducted on a selected group of patients presenting to a specialized unit of a tertiary care hospital. The sample size was also not big. Despite these limitations, findings of this study suggest the need of routine evaluation of GI tract in adult patients of unexplained anemia to identify the GI lesions and offer optimal treatment.

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