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Etiology of Non-variceal Bleeding of upper Gastrointestinal System: A Brief Review

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Authors' contributions

This work was carried out in collaboration between both authors. Author MG designed the study and wrote the first draft of the manuscript. Author GA managed the literature searches and wrote the paper. Both authors read and approved the final manuscript.

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ABSTRACT

Upper gastrointestinal bleeding (UGB) has important morbidity and mortality risk and these risk increases when co-morbidities exist. Nonsteroidal anti-inflammatory drugs use and Helicobacter Pylori infection are risk factors for peptic ulcer bleeding. Peptic ulcer disease is the most common cause of non variceal UGB. However, other rare causes should be responsible for UGB especially in treatment resistant cases.

Keywords: Upper gastrointestinal bleeding; peptic ulcer; nonsteroidal anti-inflammatory drug; helicobacter pylori infection.

1. INTRODUCTION

Gastrointestinal bleeding originated from the proximal of Treitz ligament is classified as upper gastrointestinal bleeding (UGB). It carries a high risk of morbidity and mortality and despite clinical advancement; there is no significant change in its mortality risk. General risk of mortality in UGB is

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around 7-10%, however, it reaches as high as 33% when comorbidities exist [1]. UGB risk in men is double the risk of in women [2].

Four of each five non variceal UGB resolves spontaneously [3]. However, rebleeding causes important morbidity and mortality in these patients [4]. Mortality risk of the disease has not changed although there have been important advancement achieved in endoscopic treatment options [5]. Possible causes for that are improvement in life expectancy and therefore increase in the rate of comorbidities, widely use of nonsteroidal anti-inflammatory drugs (NSAID) and bleeding disorders that accompany the disease.

2. ETIOLOGY

The most common cause of UGB is peptic ulcer disease. Half of the patients with UGB have peptic ulcer. Bleeding risk of duodenal ulcer is double of the risk of gastric ulcer. NSAID use and Helicobacter Pylori (HP) infection increase the risk of bleeding in peptic ulcer. Mortality risk of peptic ulcer bleeding is about 6-10%. Other causes are mucosal erosions, Mallory-Weiss tear, gastric antral vascular ectasy (watermelon stomach), angiodisplasia, tumors and dieulafoy lesions.

Hemobilia, aortoenteric fistula, and vasculitis are rare causes of nonvariceal UGB.

2.1 Peptic Ulcer Disease

Peptic ulcer bleeding is the most important cause of life threatening major nonvariceal UGB. Erosion of the artery on the ulcer base causes bleeding. Severity of the bleeding is determined by the diameter of the artery and the degree of the damage on the artery wall. Patients usually do not have dyspeptic complaints but the history of the patient is usually positive for aspirin or NSAID use [6,7].

A study in 2003 reported that peptic ulcer was responsible for 50% of nonvariceal UGB cases, erosive diseases for 25%, Mallory-Weiss tear for 8%, and rare causes (hemobilia, neoplasms, angiodisplasias) for 1-5% [8]. HP infection and NSAID use are two major risk factors for peptic ulcer disease; which is the most common cause of UGB. Studies in literature reported increased ulcer bleeding risk in patients with NSAID use [9,10]. This risk increases with use of classic NSAIDs instead of cox-2 inhibitors, with comorbidities, with use of steroids or anticoagulant drugs, with advanced age, and with former ulcer bleeding related complications history [11,12]. A meta-analysis reported that either NSAID use and HP infection are independent risk factors for ulcer bleeding and they might be synergistic when coexisted [13].

Aspirin or NSAID use increase the risk of ulcer bleeding dose dependently [14]. Ulcer bleeding risk is increased even with low dose aspirin (e.g 75 mg) [15]. Similarly, anticoagulant therapy may induce ulcer bleeding [16]. Steroids and bisphosphonates (e.g. alendronate) may increase the ulcer bleeding risk when used alone or combination with NSAIDS [17,18].

2.2 Mallory-Weiss Tear

Severe vomiting episodes which are triggered by alcohol compsumption, drugs, renal insufficiency or neoplastic disease may cause mucosal tears in gastroeosophageal junction; so called Mallory-Weiss syndrome. Mallory Weiss bleeding usually resolves spontaneously and need for endoscopic treatment is very uncommon [7].

2.3 Eosophagitis

Bleeding caused by eosophagitis usually occur in elderly with coffee ground vomiting. It is usually a mild bleeding that can be treated with supportive care and a proton pump inhibitor [7].

2.4 Erosive Disease

Gastroduodenal erosions usually occur due to NSAID use and HP infection and treated easily with supportive care, eradication of HP and stopping the use of NSAIDs [7].

2.5 Other Causes

Vascular abnormalities may cause gastrointestinal bleeding. Arteriovenous malformations may be accompanied by iron deficiency anemia and occasionally, they may cause major bleeding. Sporadic cases are seen usually in the elderly, however, occasionally, younger population might be affected whom had hereditary hemorrhagic telengiectasia [7].

Tumors of the eosophagogatric region are very rare causes of nonvariceal UGB. While gastrointestinal stromal tumors cause UGB, carcinomas and gastric lymphomas usually cause iron deficiency anemia or complaints other than bleeding [7].

Aortoenteric fistula should be kept in mind in a patient with massive bleeding who had a history of aortic grafting operation or pancreatitis.

Angiodysplasias are important causes of occult blood loss from gastrointestinal system. Mild obstruction of the submucosal veins during tresspassing muscular layer results angiodysplasia formation. They are common in patients with chronic renal failure and aortic stenosis. Isolated gastric angiodysplasia usually located on great curve of corpus [19]. Osler-Weber-Rendu syndrome is characterized with angiodysplastic lesions on skin, mucosa and all over the body. Epistaxis, iron deficiency anemia, and gastrointestinal bleeding are common in this syndrome. Lesions of Osler Weber Rendu syndrome are difficult to differentiate from other angiodysplasias endoscopically but they are tend to be more widespread than classic angiodysplasias [19]. Radiation toxicity may cause angiodysplastic lesions in gastrointestinal system which may cause UGB [19].

A rare cause of UGB is Dieulafoy lesion. It is described as a large vessel which has a submucosal tortuous course [20]. Characteristically, lesion protrudes through a small mucosal defect which base contained fibrinoid necrosis [21]. Arteries are usually 1-3 mm diameter and the mucosal defect is usually 2-5mm. They are hard to detect endoscopically due to its small nature. Etiology of Dieulafoy lesion is unknown but it is common in elderly. Although the lesion is common in smaller curve it may be seen in all parts of the stomach. It is hard to detect by upper endoscopy and can be treated either with sclerotherapy with adrenalin injection, electrocoagulation with heater probe or band ligation [19]. It can also be treated by surgical resection or angiography and embolisation [22]. Another treatment option is hemoclips.

Gastric antral vascular ectasy (watermelon stomach) is a rare cause of UGB. Evident vascular columns longitudinally trespass the stomach and a watermelon image occurs. Clear mucosal and submucosal thickness can be detected with endoscopic ultrasound. They usually occur in elderly women. Ninety percent of the patients with watermelon stomach are diagnosed during evaluation of treatment resistant iron deficiency anemia. Half of the patients have concomitant autoimmune disease; CREST (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome or pernicious anemia. It can be misdiagnosed as portal hypertensive gastropathy. Histopathological examination of the lesions reveals reactive fibromuscular hyperplasia, dilatation and thrombosis in the capillaries of lamina propria. Endoscopic laser and heater probe are successful in treatment. Steroids and 5- hydroxy triptamin antagonists are medical treatment options [23]. Diagnosis of these lesions are important because they could be misdiagnosed as antral gastritis by inexperinced endoscopists [19].

Cameron erosions are chronic linear erosions located on herniated folds of patients with hiatal hernia [19].

Hemobilia described as bleeding from biliary tract into gastrointestinal channel. It is difficult to diagnose. Side vision endoscopy is needed to diagnose it. The most common cause of hemobilia is external or operative trauma (55%). Other reasons include systemic infections, gallbladder stone, and aneurysm. Classic triad of the disease (pain, jaundice, melanea) only seen in 40% [19].

3. CONCLUSION

Peptic ulcer disease is by far the most common cause of nonvariceal UGB. However, other rare causes should be kept in mind especially in resistant or recurrent bleeding cases.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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