

Case Report

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Bowel Angiodysplasia and Myocardial Infarction secondary to an ischaemic imbalance: a case report

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Abstract: Angiodysplasia, defined as a vascular ectasia or arteriovenous malformation, is the most frequent cause of occult bleeding in patients older than 60 years and a significant association with several cardiac condition is described. Patients with anemia and negative findings on upper endoscopy and colonoscopy should be referred for further investigation of the small bowel. The investigation of choice, when available, is wireless capsule endoscopy. Several therapeutic options are available in this cases, as we reviewed in this report. We report a case of 78-year old man admitted to our Intensive Coronary Unit for dyspnea and chest pain. A diagnosis of non-ST-segment elevation acute coronary syndrome was made and a concomitant, significant anemia was found (hemoglobin 8.2 g/dl).

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#Deceased. Paper written in memory

No coronary disease was found by an angiography though the past medical history revealed systemic hypertension, chronic kidney disease (KDOQY stage III), and diabetes mellitus type II on insuline therapy. A Wireless Video capsule examination was positive for jejunum angiodysplasia and an argon plasma coagulation was chosen as therapeutic option. No subsequent supportive therapy and interventions were required in subsequent one year of follow-up.

Keywords: Angiodisplasya, Miocardial Infarction, Ischemia, Bowel

1 Introduction

Bowel angiodysplasia is defined as a vascular ectasia or arteriovenous malformation, frequently associated to occult bleeding [1]. This condition occurs in elderly patients (>60 years) with significant association with several conditons such as cardiovascular diseases, kidney impairment and coagulopathies [1-2]. Myocardial infarction secondary to an ischaemic imbalance is defined as a necrosis where a condition other than coronary artery disease contributes to an imbalance between myocardial oxygen supply and/or demand. Occult bleeding is a not visible bleeding often manifested as a positive fecal occult blood test (FOBT) or iron deficiency anemia with or without a positive FOBT. When an iron deficiency anemia is found, most recent guidelines recommend patients should undergo both upper endoscopy and colonoscopy. Patients with negative findings on upper endoscopy and colonoscopy with anemia should be referred for further investigation of the small bowel and colon [3-8]. Thus, the diagnosis and treatment of small bowel angiodysplasia remains difficult, as these regions are often beyond the reach of conventional endoscopy. Wireless Video Capsule Endoscopy is actually the “gold standard” tecnique to diagnose this condition. Despite contradictory results *hormonal therapy* has been widely used in treatment of

obscure gastrointestinal bleeding. Surgical or endoscopic therapy has proven useful to arrest bleeding from angiodysplasia, but a high risk of rebleeding has been noticed after both procedures. Because of its low cost and its easy application, argon plasma coagulation is the most common and successful method in treatment of angiodysplasia.

2 Case Report

A 78-year old caucasian man was admitted to our Intensive Coronary Unit because of dyspnea and chest pain. Physical examination revealed a sinus tachycardia (120 beats/min) and tachypnea (26 breaths/min); blood pressure was 100/70 mmHg. High sensitivity T Cardiac Troponine (TnT) was elevated (2 mcg/l); a severe anemia was found (hemoglobin 8.2 g/dl). No coronary disease was evidenced by an angiography performed in the Emergency setting. The past medical history revealed systemic hypertension, chronic kidney disease KDOQY stage III, Diabetes Mellitus type II on insulin therapy. He never smoked or used alcohol (EtOH) or drugs. He lived with his family. On the top of optimal medical therapy, in the emergency setting two blood transfusions were performed, to reach of clinical stability. After a week the patient was dismissed with a diagnosis of Non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS). At discharge his hemoglobin was 11 g/dl. After two weeks of his discharge his hemoglobin was 8.5 g/dl, so he was admitted to our tertiary care center, where an hypochromic microcytic anemia was confirmed. Because iron and serum ferritin were reduced, and a fecal occult blood test was positive, an iron deficiency anemia was suspected. An upper endoscopy and a colonoscopy in a first attempt were performed to find the bleeding lesion. None bleeding lesion was found. However, a jejunal angiodysplasia was found in a wireless video capsule endoscopy. Because of its low cost and its easy application, an argon plasma coagulation was chosen as therapeutic option.

The procedure was successful and well tolerated by the patient. No subsequent endoscopic or surgical intervention was required for durable hemostasis. After a week, the patient was discharged in good clinical condition. Actually, after a year follow-up, no blood transfusion neither hospitalization was required.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Discussion

Angiodysplasia, defined as a vascular ectasia or arteriovenous malformation, is the most frequent cause in patients older than 60 years and one of the most usual causes of over obscure Gastrointestinal bleeding (GIB) in patients older than 40 years [1,2]. Gastrointestinal bleeding could be classified as overt, obscure or occult [3]. While overt GIB is visible (e.g. hematemesis, hematochezia or melena), obscure GIB is a persistent and recurrent bleeding in which an upper endoscopy and colonoscopy and/or small bowel radiography cannot find the bleeding source [4]. Occult bleeding is a not visible bleeding often manifested as a positive fecal occult blood test (FOBT) or iron deficiency anemia with or without a positive FOBT. Obscure GIB comprises about 5% of all GIB and in about 75% of cases the bleeding source is located in the small bowel [5]. When an iron deficiency anemia is found, most recent guidelines recommend our patients should undergo both upper endoscopy and colonoscopy [6,9]. While patients with negative findings on upper endoscopy and colonoscopy without anemia do not require further investigations, those with anemia should be referred for further investigation of the small bowel. The initial small bowel investigation of choice, when available, is wireless capsule endoscopy. A meta-analysis of 14 studies demonstrated that the diagnostic yield of capsule endoscopy was superior to push enteroscopy (63% vs 28%) and barium studies (42% vs 6%) [10]. Angiodysplasia could be congenital or associated with hereditary syndromes. Most of the angiodysplasias are acquired. Because of a high number of angiodysplasias are found in part of bowel where the wall tension is higher (e.g. right colon), some authors attribute its pathogenesis to a chronic venous obstruction. Bowel obstruction or chronic constipation could determine mucosal chronic ischemia, determining angiodysplasia. In patient with heart, vascular or lung chronic disease [11], a local ischemia determining angiodysplasia development, could be determined by haemodynamic abnormalities. Other cardiovascular disorders involving extracellular matrix compounds could be associated with abnormal GIB [12,13]. In 1958, E.C. Heyde described an association between aortic-valve stenosis and GIB. Pathogenesis proposed was that fragmentation of high-molecular-weight multimers of von Willebrand factor on the stenotic valve led to acquired von Willebrand's

disease [14]. Of note, GIB is a major adverse consequence of implantation of left ventricular assist devices. A recent study has shown a clinical picture similar to Heyde Syndrome in patients with continuous-flow left ventricular assist devices, including angiodysplastic bleeding, acquired von Willebrand factor deficiency, and impaired platelet aggregation [15]. In this case, because of correlation between pulse pressure and pulsatile shear stress, and due to promotion operated by shear stress on release of preformed von Willebrand factor from endothelial cells, the authors conclude that pulse pressure could be correlated with levels of von Willebrand factor. So the narrow pulse pressure could be explanation for both clinical setting. Therapeutic approach includes several possible treatments:

3.1 Pharmacological options

Despite contradictory results [16], *hormonal therapy*, as in other clinical settings [17-21], has been widely used in treatment of obscure GIB. Junquera and colleagues, in a multicenter, randomized controlled trial of hormonal therapy in the prevention of rebleeding from gastrointestinal angiodysplasia [22] involving seventy-two noncirrhotic patients, demonstrated that continuous estrogen-progesterone treatment is not useful in the prevention of rebleeding from gastrointestinal angiodysplasia. Due to inhibition of angiogenesis and endothelial related growth factors, somatostatin analogs have shown efficacy in acute and chronic GIB. Bon C and colleagues demonstrated that long-acting somatostatin analogues treatment decreased transfusion needs in patients with refractory bleeding from gastrointestinal angiodysplasias [23]. Further, based on data from a total of 62 patients, a recent meta-analysis observed that 76% of patients responded to this therapy, achieving a significant reduction in transfusion requirements [24]. Recently, a study conducted on 98 patients suggests that long acting release-octreotide could be used as rescue therapy to control bleeding due to gastrointestinal angiodysplasias in patients not suitable for endoscopic or surgical treatments [25].

3.1.1 Beta-blockers

Non selective beta-blockers (i.e propranolol and nadolol) are used in portal hypertension, to reduce splanchnic flow, pulse and cardiac output. In GIB they are used in association with octreotide or monotherapy.

3.1.2 Thalidomide

Although thalidomide is less prescribed due to its teratogenic effects, recently thalidomide has shown anti-inflammatory effects and angiogenic activity. In 2011 Ge and colleagues showed that thalidomide is an effective and relatively safe treatment for patients with refractory bleeding from gastrointestinal vascular malformations [26]. Rates of response in the thalidomide and control groups were 71.4% and 3.7%, respectively. No severe adverse effects were observed. Recently, Draper and colleagues shown the utility of thalidomide in patients with left ventricular assist device related angiodysplasia [27]. For this treatment, exclusion criteria include thromboembolic disease without anti-coagulation, major wounds, symptomatic autonomic neuropathy, peripheral neuropathy, bradycardia, and concurrent radiotherapy. Small wounds, constipation, risk of falls, a history of seizures were considered relative exclusion criteria. Women must be counseled to avoid pregnancy, and men must be counseled regarding prophylactic use of condom.

3.1.3 Antifibrinolytics

Due to of their prothrombotic activity, tranexamic acid and epsilon-aminocaproic acid should be used for GIB.

3.2 Endoscopic therapy

3.2.1 Argon plasma coagulation

Because argon plasma coagulation is relatively cheap and easy to perform, it is the most common and successful method in treatment of angiodysplasia. To protect against deep wall injury, saline injection prior to treatment could be used. Long-term follow-up data show a clear increase in hemoglobin levels and reduced blood transfusion requirements after argon plasma coagulation [28].

Electrocoagulation: Bipolar or heater probe was shown to be effective when angiodysplasia is located in colon or upper gastrointestinal tract. Electrocoagulation is less effective when bleeding lesion is in the small bowel, beyond the duodeno. Monopolar coagulation is associated with an increased rate of complications.

Mechanical haemostasis: Mechanical hemostatic methods (i.e. endoscopic clips) are preferred in patients taking antiplatelet agents and/or anticoagulants. Detachable mini-loop ligation is an effective and

safe modality for endoscopic treatment of bleeding gastroduodenal angiodysplasia [29] Band Ligation could be considered as alternative to argon plasma coagulation in bleeding small bowel vascular lesions [30]. Endoscopic band ligation achieved hemostasis in a single session in all the study patients. Mortality was null, and no patient required further blood transfusion.

3.3 Angiography

Actually, there are different angiographic approaches, used when medical and/or endoscopic therapy fails and the patients is considered at high risk to try surgical treatment. First of these methods is vasoactive drugs infusion (vasopressin); in second method, it is possible to mechanically occlude the vascular supply of the bleeding lesion with the delivery particular agents (embolization). Due to its vasoconstrictive action on vessel walls, vasopressin should be used with caution in patients with heart disease and/or severe vascular diseases (e.g. coronary artery disease or peripheral vascular disease). Biodegradable gelatin sponge, polyvinyl alcohol particles, liquid agents and metallic coils are used for embolization. Microcoils have become the preferred agents. Hematomas, arterial thrombosis or dissection, embolism, pseudoaneurysm formation and bowel infarction are the possible complications of this procedure. Cherian and colleagues shown that, despite an high rate of complications, embolization with microcoils may be more successful than vasopressin infusion [31-34].

3.4 Surgery

Surgical therapy is reserved for patients with haemodynamic instability that does not allow to complete the diagnostic algorithm or in patients with increasing transfusion requirements or life-threatening bleedings from clearly identified origins.

3.5 Future perspectives

Cardiovascular diseases can be also approached by cell based therapy overcoming the limitations related to surgical treatment, catheter methods and therapies using different drugs [35-40]. Endothelial progenitor cells (EPCs) could be injected and utilizing several Ca^{2+} mediated mechanisms restore the vascular network in vivo [41-50].

4 Conclusions

Bowel Angiodysplasia is a clinical condition associated with occult bleeding that occurs in elderly patient. It is often associated with several conditions such as cardiovascular and kidney diseases. Surgical or endoscopic therapy should be used in this condition. In our case argon plasma coagulation was used because of it is relatively cheap and easy to perform. In our opinion it is the most successful method in treatment of angiodysplasia.

Conflict of interest statement: Authors state no conflict of interest

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