The Way to Man's Heart Is through the Stomach

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Abstract

Organ systems do not exist in a vacuum. However, in an era of increasingly specialized medicine, the focus is often on the organ system alone. Many symptoms are associated with differential diagnoses from upper gastrointestinal (GI) and cardiovascular medical and surgical specialties. Furthermore, a large number of rare but deadly conditions cross paths between the upper GI tract and cardiovascular system; a significant proportion of these are iatrogenic injuries from a parallel specialty. These include unusual fistulae, herniae, and embolisms that transcend specialties. This review highlights these conditions and the shared anatomy and embryology of the two organ systems.

Keyword
- anatomy
- aneurysm
- aorta/aortic
- cardiac
- esophageal surgery

Introduction

"The Way to the Heart is Through the Stomach." In an era of increasingly specialized medicine, it is important to be aware of how one's specialty overlaps with others to work efficiently in a multidisciplinary capacity. This is particularly true as diseases that were previously considered untreatable are now frequently treated thanks to advances in pharmacology, minimally invasive techniques, and surgery. This article will highlight how physicians and surgeons of the upper gastrointestinal (GI) tract and of the heart have crossed paths over the years, as each specialty has impacted on the other due to the complications of disease and treatment.

Embryology

The three germ cell layers, the ectoderm, mesoderm, and endoderm, are formed in a process called gastrulation.[1] The heart is the first organ to form in the embryo and begins with cardiogenic mesoderm giving rise to the heart tube.[2] The primitive heart begins to beat at around day 21 and starts pumping blood by days 24 to 25. At this time, the three germ cell layers differentiate to form the primordia of major organ systems including the GI tract and the heart. Cardiac formation involves complex three-dimensional folding that involves the ectoderm, mesoderm, and endoderm.

The primitive gut derives from a simple tube of endoderm, with the muscle and connective tissue originating from the splanchnopleuric mesoderm.[3] The primitive foregut diverticulum develops into the esophagus, stomach, duodenum (derived partly from the midgut), and ampulla, as well as liver, pancreas, and respiratory system. The primitive esophagus lengthens and narrows, while the foregut distal to this dilates into the stomach. Differential growth of the stomach results in the stomach rotating on its long axis.

Anatomy

The heart and the roots of the great vessels are contained in the middle mediastinum.[4] The heart lies within the pericardium, which is fused with the tunica adventitia of the great vessels and the central tendon of the diaphragm. The great vessels cross into the superior mediastinum, and as the aorta arches over the left main bronchus, it continues as the thoracic aorta. The latter descends with the esophagus in the posterior mediastinum, behind the pericardium. The thoracic aorta crosses the diaphragm to become the abdominal aorta; the esophagus descends posteriorly and to the right of the aorta, passing adjacent to the base of the heart, and traverses the hiatus to join the cardia of the stomach at the gastroesophageal junction. The stomach sits in the left hypochondrium, separated from the heart by the pericardium and left dome of the diaphragm.

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Angina

Angina pectoris was first named by William Heberden in 1772 but had been described in ancient medical texts.[5] Its cause remained unclear until the 19th century, and for many years, it was believed to be a primarily gastric disorder. Once angina's relationship to diseased coronary arteries was better understood, operative attempts were made to improve blood flow to the myocardium, including Laurence O'Shaughnessy's 1936 technique of attaching omentum directly to the ischemic myocardial tissue, with impressive results.[6]

Gastric and, in particular, esophageal diseases continue to be important differentials in the diagnosis of chest pain. Indeed, gastroesophageal disease and coronary artery disease often coexist, and it is now believed that a mutual neural connection exists, such that stimulus to the esophageal mucosa may modulate coronary blood flow.[7] The phenomenon of "linked angina" was proposed by Smith and Papp[8] to explain the observation of typical angina-like chest pain upon the instillation of acid into the esophagus[9] or dynamic ischemic electrocardiogram abnormalities occurring during esophageal spasm.[10]

Antiplatelet Therapy and Gastric Ulcer Disease

Perhaps the most common pharmacological interaction between the cardiac and GI systems is the prescription of antiplatelet agents. Aspirin is a cyclooxygenase (COX) inhibitor that is widely prescribed as primary preventative therapy in patients deemed at risk of ischemic heart disease, along with inflammatory conditions such as pericarditis, Kawasaki's disease, and rheumatic fever.[11] In patients with established coronary artery disease, secondary prevention normally consists of aspirin and the coprescription of a second antiplatelet agent for 1 year following an acute coronary syndrome. The most common choices are P2Y12 inhibitors such as clopidogrel and ticagrelor.[12]

Via its COX inhibition, aspirin causes gastric mucosal irritation and increases the risk of peptic ulceration and upper GI bleeding.[13] Combination with other nonsteroidal anti-inflammatory drugs or antiplatelets increases this risk still further. Proton pump inhibitors can mitigate some of the risk, but there has been concern recently regarding an increased rate of myocardial infarction due to their interaction with clopidogrel,[14] though they remain widely prescribed.

Other commonly prescribed medications can also exacerbate upper GI bleeding, such as warfarin, or the direct oral anticoagulants such as rivaroxaban or dabigatran.[15]

Inflammatory Bowel Disease

Crohn's disease can affect the entire digestive tract and is also a multisystem inflammatory disorder. It can present with numerous cardiac manifestations including pericarditis, heart block, aortitis, atrial fibrillation (AF), and coronary artery disease.[16,17] Several meta-analyses have demonstrated that patients with inflammatory bowel disease have an elevated risk of myocardial infarction and all-cause cardiovascular death, especially during periods of disease activity.[18] A link between Takayasu's arteritis and Crohn's disease has also been proposed.[19]

Deglutition Syncope

An association between swallowing and cardiac rhythm disturbance is well described.[20,21] This can include tachyarrhythmias, but bradyarrhythmias are more common. Deglutition syncope describes the loss of consciousness brought on by swallowing. A large proportion of these patients have esophageal pathology such as achalasia, gastroesophageal reflux disease (GERD), or gastric diverticula.[22]

The Atrioesophageal Interaction

The posterior wall of the left atrium and the esophagus are separated by a thin layer of tissue, typically under 5 mm.[23] As a result, it has recently been suggested that a relationship might exist between AF and GERD. Conflicting data exist; there appears to be a correlation, although causation has not been established.[23] Mechanisms might include localized inflammation or mechanical compression of either structure by the other. Intriguingly, the treatment of GERD symptoms in a patient with both diagnoses might actually improve success rates of cardioverting to and maintaining sinus rhythm.[23]

Fistulae between the Upper GI Tract and the Heart

Atrioesophageal Fistula

Radiofrequency catheter ablation (RFA) is an effective treatment for AF. However, as mentioned earlier, the esophagus is only thinly separated from the left atrium, and there is therefore an associated risk of thermal injury to the esophagus following ablation.[24] Atrioesophageal fistula is a rare but deadly consequence of this, with an incidence of 0.05% and mortality of more than 90%. It can present up to 5 weeks following the culpable procedure,[25] and subsequently can be misdiagnosed as infective endocarditis,[26] which may be an associated feature, along with upper GI bleeding, and septic or air cerebral embolism.[27] Less severe but nevertheless debilitating complications of RFA involve injury to the periesophageal nerve complex, resulting in gastric hypomotility and pyloric spasms. Depending on the severity of the thermal injury, patients may be treated with proton pump inhibitors, or urgent imaging and referral to a tertiary center with cardiothoracic and upper GI surgical care.

Aortoesophageal Fistula

Aortoesophageal fistula (AEF) is a rare but deadly condition. Classical presentation is a triad of dysphagia or chest pain, sentinel hematemesis, and fatal hemorrhage.[28] The earliest cases of AEF were reported in the first half of the 19th century, and were caused by the erosion through the esophagus of foreign bodies such as animal bones and dentures, resulting in perforation of the aorta and fatal exsanguination.[29,30] Although most foreign bodies pass through the GI tract

spontaneously,[31] AEF is a rare but frequently fatal complication of foreign body perforation of the esophagus.[32–34] It can also result from iatrogenic injury to the thoracic aorta following endoscopic retrieval of a foreign body.[35]

AEF can be a consequence of esophageal malignancy,[36] as well as the result of radiation therapy for esophageal[37,38] or pulmonary malignancy.[39] It can also be caused by the erosion of stents inserted for obstructing esophageal cancers[40] and benign stenosing conditions of the esophagus,[41] as well as by benign esophageal ulceration[42] and after esophageal surgery.[43]

Two-thirds of AEFs originate from pathology of the aorta, including thoracic aortic aneurysm,[44] aortic dissection,[45] infective causes (including tuberculosis[46] and syphillis[47]), congenital abnormalities,[48] and trauma.[49] Thoracic endovascular stent-graft aortic reconstruction, in use since the early 1990s, is a very successful, minimally invasive technique for treating thoracic aortic aneurysm.[50] However, this too can lead to AEF via erosion of the stent through the esophagus.[51,52]

AEFs have been successfully managed by stents and open surgical repair, with the most successful outcomes from tertiary referral centers, and following minimal delay between presentation and treatment.

Esophagopericardial Fistula and Pericardial Effusions

Foreign body perforation through the esophagus can result in breach of the pericardium. Culprits include dentures and fish or chicken bones, and the resulting stomach contents in the pericardium[53] cause purulent pericarditis[54] and cardiac tamponade.[55]

Pericardial effusion can occur in esophageal malignancy or as a consequence of chemoradiation therapy.[56] Twine et al found it to be present on endoscopic ultrasound (EUS) in 16.3% of patients diagnosed with esophageal cancer, with a pericardial effusion associated with lower survival rates.[57] Prompt drainage via pericardiocentesis or surgery is indicated in patients with clinical tamponade or purulent pericarditis.[58] Rarely, the latter conditions may occur secondary to an esophagopericardial fistula due to esophageal malignancy.[59,60]

Gastroventricular and Gastropericardial Fistulae

It is also possible for a fistula to form between the heart and the stomach. Rana et al[61] reported the case in a 70-year-old man who had previously undergone esophagectomy and esophageal replacement with a gastric tube. He presented with melena, dyspnea, and weakness, and was found to have a deep ulcer with a pulsatile clot in the intrathoracic gastric tube, the result of a fistula between the stomach and the right ventricle. There have also been reports of peptic ulcers fistulating into the heart from hiatus herniae[62] and the abdominal stomach,[63] most commonly after previous esophagogastric surgery,[64] or in the context of comorbidities with pericardial manifestations, such as obliterative pericarditis secondary to rheumatoid arthritis.[63]

Infective Endocarditis, Endoscopy, and Transesophageal Echocardiography

Infective endocarditis, an infection of the cardiac endothelium, is a relatively rare condition, with an incidence of ~1.7 to 6.2 cases per 100,000 patient-years.[65] It can be a consequence of bacteremia following endoscopic procedures. Upper GI endoscopy (esophagogastroduodenoscopy) is associated with a 4% rate of bacteremia. Bacteremia rates are far higher with interventional procedures, such as endoscopic variceal sclerotherapy and laser therapy, and esophageal stricture dilatation. Antimicrobial prophylaxis is currently recommended for the latter procedures, but not for diagnostic endoscopy or for banding of esophageal varices.[66] All of the earlier procedures have been anecdotally associated with endocarditis, apart from banding and laser therapy.[67]

Infective endocarditis has been reported to cause upper GI hemorrhage due to a ruptured superior mesenteric artery aneurysm and duodenal fistula,[68] requiring urgent surgical intervention.

Diagnosis of infective endocarditis often relies on transesophageal echocardiography (TEE), a frequently used diagnostic tool, helpful in assessing cardiovascular pathology and function, and for perioperative monitoring of patients undergoing major surgery. However, TEE itself carries risks of complications, including esophageal perforation,[69] and significant upper GI bleeding.[70]

Radiation Injuries

Radiation therapy is often used as neoadjuvant or adjuvant treatment, or as part of the definitive management of esophageal malignancy. Due to its anatomical position, the heart is often unintentionally irradiated, which can result in injury, leading to congestive heart failure, ischemia, coronary artery disease, valvular disease, or myocardial infarction. This is thought to be caused by microvascular injury and fibrosis leading to atherosclerosis.[71] Multivariate analysis by Gharzai et al of patients who had been treated for esophageal malignancy found radiation therapy to be associated with a higher probability of cardiac death, particularly if the tumor was located lower down in the esophagus.[71] Improvements in radiation delivery techniques have meant that lower doses are now administered to the heart.

Radiation injury to the heart does not appear to be compounded by chemotherapy, as modern chemotherapeutic and biologic agents used for esophageal malignancy no longer have the cardiotoxicity profile of the anthracyclines previously used.[72]

Embolism

Air Embolism

Cardiac embolism, a rare phenomenon, is usually of iatrogenic etiology and is characterized by a "mill wheel" thrill. Clinical presentation of air emboli ranges from being asymptomatic to cardiovascular collapse and death. Cardiac air embolism has been reported most frequently during endoscopic retrograde cholangiopancreatography,[73] but can occur after simple endoscopy. Risk factors include inflammation or a history of trauma, surgery or interventional techniques to the biliary system, as well as peptic ulcer and fistulae.[74] The mechanism of action is thought to be via air moving down a pressure

gradient into damaged vasculature or vascular tissue, such as liver. Successful management requires a high index of suspicion early in the patient's presentation. The causative procedure must be stopped if possible, particularly if nitrous oxide is in use, and the patient should receive high-flow oxygen and high volumes of intravenous saline. The Trendelenburg (feet higher than the head) and left lateral decubitus positions may be beneficial.

Foreign Body Embolism

An unusual iatrogenic injury was described in a case report from 2017.[75] A 53-year-old patient with severe calcified pancreatitis underwent a difficult EUS and fine needle aspiration, which required five needle passes. Six months later, the fractured tip of the EUS needle was incidentally discovered on a chest radiograph, and computed tomography revealed that it had migrated through the duodenal wall, diaphragm, and into left ventricle, eventually migrating to the aortic bifurcation. The needle was retrieved endovascularly via bilateral common femoral artery access and the patient made a full recovery.

Herniation

Herniation describes the protrusion of a viscus from its enclosing cavity. An extremely rare version of this is the herniation of intra-abdominal viscera into the pericardial cavity, secondary to congenital defects of the septum transversum,[76] trauma,[77] or surgical procedures. This has been reported following the formation of a pericardioperitoneal window for drainage of a pericardial effusion.[78–80] Herniation of omentum[81] and stomach[82] into the pericardial cavity has also followed the use of the right gastroepiploic artery for coronary artery bypass grafting.

Interestingly, the use of the right gastroepiploic artery for coronary bypass grafting has also been reported to cause ischemic perforation of the stomach.[83] It can also lead to difficulties with the treatment of metachronous gastric cancers that require gastrectomy.[84,85]

Conclusion

A large number of rare but deadly conditions cross paths between the upper GI tract and cardiovascular system. Some of these conditions are iatrogenic in etiology, and it is vital for specialists to be aware of how treatments they administer may cause injuries to surrounding organs.

Conflict of Interest
None declared.

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