POEM for Chagas Disease-Induced Achalasia

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Introduction

Chagas disease is a relatively uncommon but fascinating cause of esophageal dysmotility. While the GI manifestations of Chagas have been studied for many years, there is relatively little data available to guide the use of Peroral Endoscopic Myotomy (POEM) in this disease. In this chapter, the pathophysiology and treatment of Chagas are reviewed.

Chagas Disease: Pathology, Epidemiology, and Manifestations

Chagas disease is the systemic manifestation of *Trypanosoma cruzi* infection and is also referred to as American Trypanosomiasis. First described by the Brazilian Dr. Carlos Chagas in 1909, the disease was increasingly recognized as an important pathogen in Central and South America in the 1960s. It remains endemic in many countries from Mexico to Argentina and is estimated to cause more than 10,000 deaths per year worldwide [1]. Because of the potentially long interval between infection and presentation with symptoms, patients infected in endemic regions can emigrate and later present for care in communities around the world (Fig. 10.1).

Transmission of the parasitic protozoa occurs mostly via hematophagous insects of the Triatominae subfamily, also known as "kissing bugs." While vector-borne transmission typically occurs in endemic areas, other forms of blood-borne transmission have occurred through transfusion, organ transplantation, etc. Several other methods of infection have been identified; including vertical transmission from mother to child, rare cases of consumption of uncooked food contaminated with feces from infected bugs, and accidental laboratory exposure.

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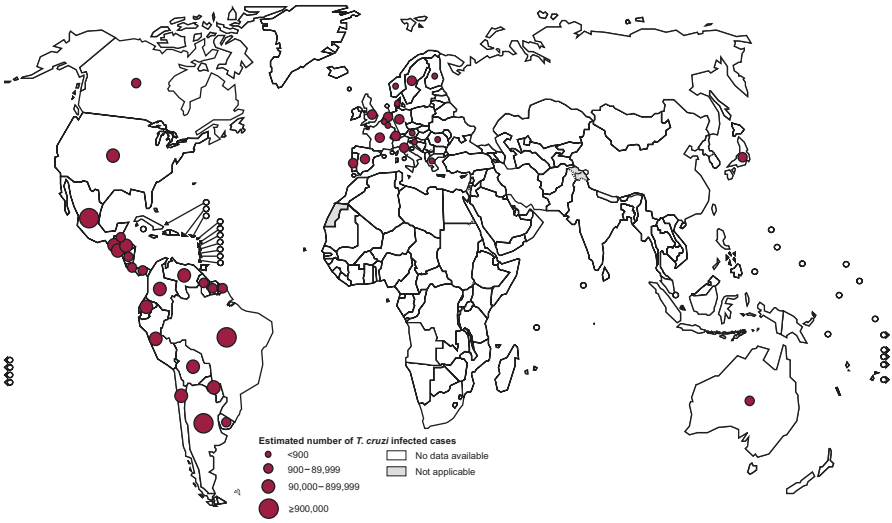

Fig. 10.1 Global distribution of cases of Chagas disease, based on official estimates, 2006–2010. Image ©World Health Organization, 2010

Once infected, the disease in humans can unfold in several patterns. An acute illness sometimes occurs in the weeks or months after infection—producing fevers, myalgias, headache, or nonspecific GI symptoms. Physical signs can include lymphadenopathy, rash, hepatosplenomegaly, or local induration at the site of the bite. It is common for acute Chagas to go unnoticed, with minimal symptoms and rapid improvement over a several weeks.

After infection, Chagas can progress to a chronic form of the disease. This occurs in approximately one third of patients, and treatment of the acute illness does not necessarily prevent chronic disease. The manifestations of Chagas can take decades to appear and are often irreversible once discovered.

Chronic Chagas disease primarily affects the heart, GI system, and rarely the central nervous system. Cardiomyopathy and conduction abnormalities are frequently seen (~20–30%). GI manifestations are also common and thought to be related to destruction of both excitatory and inhibitory pathways in the enteric plexus and damage to the interstitial cells of Cajal.

Gastrointestinal manifestations of Chagas can include any of the following: sialorrhea, achalasia with or without massive esophageal dilation, delayed gastric emptying and impaired receptive relaxation of the stomach, prolonged small bowel transit times, colonic dysmotility with massive dilation leading to megacolon, or biliary dilation and cholelithiasis.

Esophageal Manifestations: Chagasic Achalasia

Dysphagia, chest pain, or weight loss may be the initial presenting symptoms of chronic achalasia. A high level of suspicion is required to differentiate the disease from other forms of esophageal dysmotility. Further investigation is required to

differentiate chagasic from idiopathic achalasia. As previously described, chronic *Trypanosoma cruzi* infection can lead to profound esophageal disease that is quite similar to idiopathic achalasia.

Symptoms of Chagas-related esophageal disease may include dysphagia, active and passive regurgitation, chest pain, odynophagia, cough, aspiration, sialorrhea, and weight loss. Megaesophagus is frequently seen in later stages of the disease.

Manometric differences between idiopathic achalasia and Chagas related have been debated [2–4]. Some have reported resting pressures in the lower esophageal sphincter (LES) that are lower than normal [1, 5], due to the destruction of both excitatory and inhibitory neuronal pathways. In contrast, patients with idiopathic achalasia often have increased basal LES pressures [6, 7]. A spectrum of other manometric findings is seen, including the typical progression of discoordination, failure of appropriate LES relaxation, and aperistalsis [8, 9].

Diagnostic Workup

Patients may present with any combination of organ systems affected, and a careful history is critical when considering an intervention for achalasia secondary to Chagas disease. Investigations should be focused on describing esophageal motility and function, testing for Chagas disease, and evaluating for extra-esophageal disease.

A large number of serologic tests have been used to detect Chagas disease in its chronic form by identifying formed antibodies to the parasite. Patients at risk for Chagas (from areas with endemic disease, etc.) should be tested with at least two different serologic assays to secure the diagnosis [10]. Additional testing to rule out other intestinal parasites may be useful including the detection of trypomastigotes in blood via microscopy following initial infection. Labs to assess for protein-calorie and micronutrient deficiencies may be indicated.

Cardiac evaluation should be performed before any surgical intervention in those with confirmed Chagas disease, including ECG and chest radiographs. Dysrhythmias can present during surgery, especially during esophagectomy [10–12]. Patients with chronic aspiration may also require pulmonary testing.

Workup of esophageal disease in patient with Chagas proceeds similarly to those with idiopathic achalasia. Routine tests should include barium esophagram and esophageal manometry [11]. Radiographic appearance of the esophagus can range from normal to a massively dilated, tortuous esophagus. Manometry is a key component of the workup, and several patterns may be identified as described earlier in this chapter. However, there is a typical finding of incomplete or absent LES relaxation in advanced Chagas disease as well as aperistalsis in its final stages with megaesophagus [8]. Endoscopy should always be performed, as it is helpful in evaluating the quality of mucosa, assessing presence of candidiasis, clearance of foreign bodies or food, ruling out alternative diagnoses, and as a therapeutic intervention.

Stage at Presentation

The timeline of progression of chronic Chagas to symptomatic and then aperistaltic megaesophagus is variable, but can often take decades. Further, patients may come from resource-limited environments with poor access to care. When discovered early, treatment is quite similar to that of idiopathic achalasia. However, there are many series of patients described in the literature (mostly from endemic regions) who present with end-stage disease and a nonfunctional esophagus. The published experiences of these centers are critically important in understanding the spectrum of disease management in Chagas achalasia, but should not necessarily be extrapolated to populations where the disease is likely to be discovered much earlier (Fig. 10.2).

Treatment

Occasionally, patients will present with acute esophageal obstruction or complications requiring immediate endoscopic intervention. However in the vast majority of patients, treatment begins after appropriate workup including serologic testing, treatment of systemic infection, evaluation for extra-esophageal disease, nutritional evaluation, and examination of the esophagus with the testing described above.

As is the case for idiopathic achalasia, therapy for Chagas-related disease is palliative rather than curative. Dysmotility is usually progressive, and thus the goal of therapy is to produce a useful conduit (for oral nutrition, to reduce symptoms, and prevent complications such as aspiration) rather than to restore truly normal function.

The general approach to a patient with Chagas is similar to that in idiopathic achalasia. Patients with unacceptable perioperative risk may be considered for botulinum toxin injection of the LES or systemic therapy with nitrates or calcium channel blockers [6]. For the vast majority of patients, more definitive therapy is preferable.

The debate over the role of pneumatic dilation as a first-line therapy is beyond the scope of this chapter [6, 15]. The authors of this chapter prefer myotomy for most patients with acceptable perioperative risk. A small early study comparing pneumatic dilation to bouginage in Brazilian patients with Chagas megaesophagus demonstrated sustained normalization of LES pressures 1 year after pneumatic dilation, but no change in pressure and a return of symptoms after bougie dilation [16]. There have been multiple series examining the effectiveness of dilation in Chagas patients, including patients with megaesophagus [17]. Overall results are good, but equivalent or inferior to minimally invasive esophageal myotomy.

The adoption of minimally invasive techniques has significantly increased the popularity of surgical therapy [18, 19]. Laparoscopic Heller myotomy has become the standard first-line therapy for patients without megaesophagus. A large body of literature has demonstrated excellent symptomatic improvement, low rates of complications, and long-term durability of this operation in patients with idiopathic and chagasic achalasia and a non-dilated esophagus.

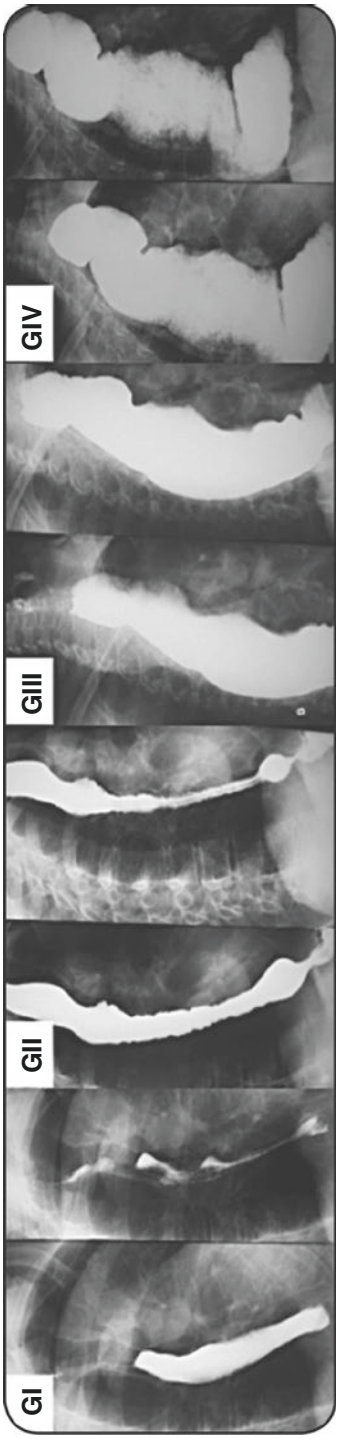

Fig. 10.2 Classic grouping (I–IV) of progressive esophageal findings with Chagas, as described by Rezende et al. [13]. Image from de Souza et al. [14]

POEM is now a well-established and increasingly common procedure. Like the Heller myotomy, POEM results in complete division of the circular muscle fibers of the LES. There have been unpublished presentations on POEM for the treatment of achalasia caused by Chagas. However, there are currently no published series or trials evaluating the use of POEM in patients with Chagas disease. It may be a good approach for patients without significant esophageal dilation, but further study is needed.

To perform POEM, it is necessary to navigate through the submucosal space. Thus, the creation of the submucosal tunnel might be more challenging when compared to idiopathic achalasia since fibrosis and chronic inflammation may be present. During the acute phase of Chagas, tissue damage occurs as a result of both parasitemia and direct tissue parasitism. An immunologic response follows, which is important in controlling acute infection, but may result in further tissue inflammation. This has been confirmed by histologic studies of many organ systems [20–23]. Esophageal parasitism and inflammation can involve both smooth muscle and the Meissner and Auerbach nerve plexuses. This can lead to neuronal death, fibrosis, and lymphocytic infiltration. At the same time, the muscularis mucosa may hypertrophy. All of these could potentially contribute to differences in the POEM submucosal dissection plane.

For patients with significant esophageal dilation and megaesophagus, decision-making is more complicated. A determination must be made as to whether the esophagus will function well as a conduit. If not, up-front esophagectomy can be considered. Patients with Chagas often present with late-stage disease, and esophagectomy became popular in the 1970s and 1980s in Brazil. Despite advances in minimally invasive esophagectomy in the 1990s and 2000s, many surgeons have embraced Heller myotomy as a first-line therapy for massively dilated esophagus [24–26].

The results for Heller myotomy in this setting are generally good, with low perioperative risk [24]. However, published case series are small and have short follow-up. These results could potentially translate to the use of POEM, but further study is needed. In particular, the risk and difficulty of creating a submucosal tunnel in a massively dilated esophagus is a critical issue that requires further investigation before the procedure is widely adopted.

Other innovative operations such as esophageal mucosectomy with endomuscular pull-through, sleeve esophagectomy and myotomy, and partial resection with Roux-en-y diversion have also been developed for patients with massive esophageal dilation [3]. There is no clear consensus on the management of this problem, and these patients should be evaluated by an experienced foregut surgeon when possible.

Patients with failed dilation or myotomy can be difficult to manage. In those with megaesophagus, esophagectomy is indicated and commonly performed. For patients with more favorable anatomy and reassuring manometry, repeat myotomy could be considered. This is another potential area of interest for the application of POEM. However, this has not yet been described in the literature and should only be performed within a clinical trial at this time.

Conclusions

Esophageal manifestations of Chagas disease are a significant cause of morbidity, particularly in areas with endemic disease. Although reversal of the disease is impossible, there is a long history of endoscopic and surgical interventions that can provide excellent palliation. Some patients with megaesophagus may require esophagectomy, but there is clearly a role for esophageal myotomy in both late-stage and especially in early-stage disease. While described, no cases of POEM have yet been published in the literature, and the role of POEM in the management of Chagas achalasia has not yet been determined. Patients with Chagas disease should undergo multidisciplinary evaluation, and consultation with an experienced foregut surgeon is advisable.

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