Potential Danger in the Medical Use of *Trichuris suis* for the Treatment of Inflammatory Bowel Disease

To the Editor:

The commentary by Das¹ regarding the paper of Summers et al² on the use of the pig pathogen, *Trichuris suis*, as a treatment of inflammatory bowel disease raises some important questions. We have been aware of this treatment since 1999, when at an AGA meeting, a poster³ prompted one of us to question the safety of it.

Summers et al² have repeatedly spoken of *T. suis* as noninvasive. In their 2003 paper, they state “Embryonated eggs hatch in the proximal small bowel. The larvae migrate aborally and attach to the mucosa of the distal small bowel and proximal colon. After several weeks, they mature and begin to shed eggs.” The claim is made that *T. suis* “fulfills these criteria,” i.e., colonizing the intestine “without invading the host.” Das¹ says the ova colonize the intestine.

The literature indicates otherwise. In the pig intestine, when embryonation is complete, the polar plugs of the ova dissolve away, liberating larvae bearing 5- to 7-μm-long lancet-shaped stylets with which they penetrate the mucosa. They remain for 13 to 16 days, migrating through lamina propria, undergoing 4 molts, and moving deeply to just above the muscularis mucosae and then later working their way back toward the surface. Finally as fifth stage larvae, they protrude their posteriors through to the lumen, progressively growing and extending out of the mucosa, until only esophageal portions remain embedded.⁴,⁵

During this “histotropic” migration, the potential exists for these larvae, with anterior stylets, to find their way into lymphatics or venules. The idea that they are noninvasive is false and all the more troublesome when one recognizes (1) that there is mucosal damage with increased vascularity and often disruption of the muscularis mucosae in inflammatory bowel disease, potentially facilitating deep penetration of larvae into the bowel wall, and (2) that larval parasites in unnatural hosts travel peculiar and often unpredictable paths. The human parasite, *Enterobius vermicularis*, which normally completes its life cycle in the intestinal lumen without even penetrating the mucosa, has on occasion been identified in human liver and lung;⁶ the human pathogen, *Trichuris trichiura*, which like its porcine relative burrows in the mucosa, has been reported intraperitoneally.⁷

There are numerous examples of aberrant migrations of parasites that find themselves in unfamiliar hosts: both *Toxocara canis* and *Dirofilaria immitis* of dogs migrate aberrantly when in human hosts, sometimes with significant clinical consequences. Such “lost” larvae are often stopped at the level of the liver or lung and incorporated into granulomas, but on other occasions the outcome is more serious. For example, larvae of *Baylisascaris procyonis*, the raccoon round worm, cause fatal central nervous system (CNS) disease in abnormal hosts; in humans, they cause retinal disease or encephalitis.⁸

The meningeal worm of the deer, *Paralophostrongylus tenuis*, when lost in the CNS of the moose, causes serious encephalitis and death.⁹ *T. suis* have been found in the renal pelvis of wild boar.¹⁰

There is no predicting where *T. suis* larvae will go in humans, the abnormal host in this controversy. These larvae are invasive, and it can be reasonably expected that their paths of travel will be different in humans than they are in the domestic pig. It may only be a matter of time and numbers of larvae before retinal or CNS disease occurs in a patient “treated” with *T. suis*.

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Progressive Dysphagia Caused by Isolated Esophageal Involvement of Crohn’s Disease

To the Editor:

Crohn’s disease (CD) is characterized by chronic inflammation of the digestive tract, which may be localized at any level from the mouth to the anus. Involvement of the upper gastrointestinal tract is uncommon.¹,² CD of the esophagus is very rare. The prevalence of esophageal CD ranges from 1% to 2% in
adults with CD. The esophageal manifestations of CD may be quite variable. Strictures resembling those from reflux esophagitis or a tumor, fissures, esophagobronchial fistulas, mediastinal abscesses, and aphthoid lesions have been described. Since Franklin and Taylor in 1950 reported the first case of esophageal CD, less than 100 cases have been reported. Isolated esophageal involvement by CD has been previously reported in only 10 cases.

A 33-year-old black woman was admitted to our hospital with a 4-month history of progressive dysphagia and weight loss. She had been in good health until 4 months before admission, when she noted sudden onset of fever, heartburn, chest pain, dysphagia, and odynophagia. The patient was treated with omeprazole (40 mg q.i.d.), but heartburn and dysphagia did not improve. In the following 2 months, the dysphagia progressed from solids to liquids, and weight loss of 20 kg was noted. Esophagoscopy revealed the presence of distal esophageal ulcerations and thickened folds just proximal to the gastroesophageal junction. Biopsies of the distal esophagus revealed nonspecific inflammation. Treatment with omeprazole was continued for 2 months without improvement. Because during this time the patient had an additional weight loss of 15 kg, she was referred to our institution. There was no history of vomiting, melena, hematochezia, regurgitation, abdominal pain, arthralgias, or oral aphthous ulcers. On admission, the patient was cachectic, with the abdomen slightly distended without tenderness. Laboratory data revealed a hemoglobin concentration of 11.2 g/dL (normal range, 13–15.7 g/dL), a hematocrit of 35% (normal range, 38%–46%), albumin concentration of 1.9 g/dL (normal range, 3.5–5 g/dL), and negative HIV serology. Anti-saccharomyces cerevisiae antibody antibodies were positive (IgG, 40 UI; normal range, <20 UI; IgA, 22 UI; normal range, <20 UI) and perinuclear antineutrophil cytoplasmic antibody were negative. A barium-swallow examination showed a long irregular narrowing of the esophagus. A thoracic computed tomography scan revealed a thickened esophageal wall without mediastinal lymph nodes. Upper endoscopy showed a long intrinsic stenosis of the proximal esophagus with “punched out” ulcers, mucosal edema, and friability with normal intervening mucosa. Biopsies of the esophagus revealed focal infiltration with neutrophils, eosinophils, and lymphocytes in the lamina propria, intraepithelial vascular congestion, and granulation tissue. PAS and Ziehl-Nielsen staining were negative. Small bowel follow-through examination with barium and colonoscopy were normal. The patient was on total parenteral nutrition for 3 weeks before a transhiatal esophagectomy with partial gastrectomy. The esophagus surgical specimen measured 10 cm, with a 2.5-cm fibrous wall. A cobblestone appearance of the esophageal mucosa was observed in the distal portion without affection of the stomach (Figs. 1A and B). Histologically, multiple ulcerated lesions with fibrosis and an intense lymphoplasmocytic infiltrate with granuloma formation that extended from the submucosa deep into the serosa were found. Fissures were also detected lined by fibrin and granulation tissue. These pathologic findings were diagnosed as CD of the esophagus. Postoperative evolution was uneventful.

Although CD usually is found in the ileum and/or colorectum, it can be located in the whole gastrointestinal tract. The prevalence of gastric and duodenal CD in adults has been estimated to be 0.5% to 4.0%, and the prevalence of esophageal CD is 1.8%. Esophageal involvement typically is discovered rather late in the course of the CD, when severe dysphagia secondary to strictures or other complications have occurred. Most patients have distal CD involvement that is diagnosed initially and presents later with symptoms suggestive of esophageal disease, but some patients, albeit few, present with isolated esophageal disease. In a review of the literature performed by Ohta et al, in
only 10 of 77 (13%) cases was the esophagus the only organ affected. None of these cases were able to be diagnosed as CD preoperatively. Ileocolic lesions developed after esophageal lesions in only 5 patients (6.5%). In the remaining 62 patients (80.5%), ileocolic synchronous lesions had existed with the esophageal lesions. Differentiation between esophageal CD and gastroesophageal reflux disease, tuberculosis, herpes, Behcet’s disease, mycotic infections, and caustic or drug-induced lesions often is difficult. Initial symptoms include heartburn, odynophagia, and epigastric pain. Severe involvement results in progressive dysphagia, the most common presenting complaint among patients with esophageal CD, as in our case. The endoscopic findings in esophageal CD are nonspecific and include hyperemia, granularity, friability, and nodular thickening of the folds of the middle or distal esophagus. The microscopic diagnosis of esophageal CD is difficult. Although granulomas are generally accepted as histologic proof of CD, in esophageal CD, granulomas are reported in less than 60% of the cases. The most common histologic feature in esophageal CD is the presence of numerous lymphocytes and mast cells in the epithelium and lamina propria. The management of CD of the esophagus is not well established because of the limited number of cases. For inflammatory acute lesions, first-line treatment consists of corticosteroids and antisecretory agents; if ileocolonic involvement is present, therapy with 5-aminosalicylic acid may be useful.2

There are no data on the benefit of prophylactic treatment in patients with isolated CD of the esophagus. Surgical therapy for esophageal CD is limited to case reports. Davidson and Sawyers8 reviewed the literature and identified that 13 of 20 patients with esophageal CD were treated with surgery. All patients underwent esophagectomy. Four patients had esophageal fistula, and 5 patients underwent surgical resection because cancer could not be ruled out by preoperative studies. Postoperative mortality rate was 25%. With the limited literature available, recommendations are difficult to define. It seems reasonable to rule out neoplasm with endoscopic biopsy and to reserve esophagectomy for patients with symptomatic, high-grade obstruction refractory to medical and endoscopic therapy as in this case.

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