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Endoscopic imaging of parasites in the human digestive tract

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ABSTRACT

There are various diagnostic approaches for parasitic infections, including microscopic identification of parasites in the stool or biopsy samples from the intestinal mucosa, antigen testing of feces or serum, polymerase chain reaction (PCR) testing, and serology. Endoscopy is sometimes used for direct confirmation of parasite infection and as a therapeutic option for removal. In recent years, innovations in endoscopy have advanced remarkably with regards to endoscopic devices as well as diagnostic and therapeutic endoscopical methods. Several new endoscopic devices are now used for diagnostic and therapeutic approaches to parasitic infections. In the present article, we have focused on in vivo imaging of parasitic infections. In vivo images of parasites were obtained using various endoscopic methods such as high-definition endoscopy, super-magnifying endoscopy, and video capsule endoscopy.

1. Introduction

The incidence and prevalence of parasitic infection remain high worldwide [1–4]. In developing countries, controlling parasitic infection is crucial for public health. There are various diagnostic approaches for parasitic infections, including microscopic identification of parasites in the stool or biopsy samples from the intestinal mucosa, antigen testing of feces or serum, polymerase chain reaction (PCR) testing, and serology. Endoscopy is sometimes used for direct confirmation of parasite infection and as a therapeutic option for removal.

In recent years, innovations in endoscopy have advanced remarkably with regards to endoscopic devices as well as diagnostic and therapeutic endoscopical methods. Several new endoscopic devices are now used for diagnostic and therapeutic approaches to parasitic infections.

In the present article, we have focused on in vivo imaging of parasitic infections. In vivo images of parasites were obtained by various endoscopic tools, ranging from conventional to newly developed devices. We have also discussed and described endoscopic innovations.

2. *Anisakis* visualized and removed by endoscopy

Anisakiasis is a common parasitic disease that is caused by *Anisakis* larvae. Anisakiasis patients have a typical history of consumption of raw fish and present with epigastric pain, nausea, and vomiting. Diagnosis of anisakiasis is usually made by identifying *Anisakis* larvae. Endoscopy is mainly used for diagnosing gastric anisakiasis [5–11], while computed tomography (CT) is mainly used for intestinal anisakiasis [12,13]. Another option is serological testing [14,15]. Endoscopy can be used to directly diagnose anisakiasis as well as to subsequently remove the larvae by using biopsy forceps (Fig. 1). Many case reports have illustrated gastric anisakiasis [5–11], a few reports have highlighted esophageal anisakiasis [16,17], and colonic cases are relatively rare [13,18–23]. Only one case report has described enteric anisakiasis detected using video capsule endoscopy (VCE). Celestino et al. [6] reported a case of anisakiasis observed using a magnifying endoscope. Nakagawa et al. [24] compared magnified endoscopic images between hookworm and *Anisakis*. A magnifying endoscope (GIF-H260Z, Olympus Medical Systems, Tokyo) can obtain high-definition images with 85× magnification and is mainly used to distinguish between malignant and benign mucosa [25,26].

High-definition endoscopic images of our case of Anisakiasis are shown in Fig. 1. An *Anisakis* larva sticking to the edematous gastric wall is shown in Fig. 1a. The *Anisakis* larva could be removed by biopsy forceps.

3. *Entamoeba histolytica* visualized using super-magnifying endoscopy

Amoebic colitis is distributed worldwide, and is known to be a sexually transmitted disease [27]. Some cases of amoebic colitis that exhibit chronic symptoms are misdiagnosed as ulcerative colitis and treated with corticosteroids [28]. Importantly, the usage of corticosteroids is detrimental in such cases. Therefore, it is essential that the diagnosis of amoebic colitis is made promptly and accurately in order to prevent fulminant worsening of the disease. Accurate diagnosis of amoebic colitis

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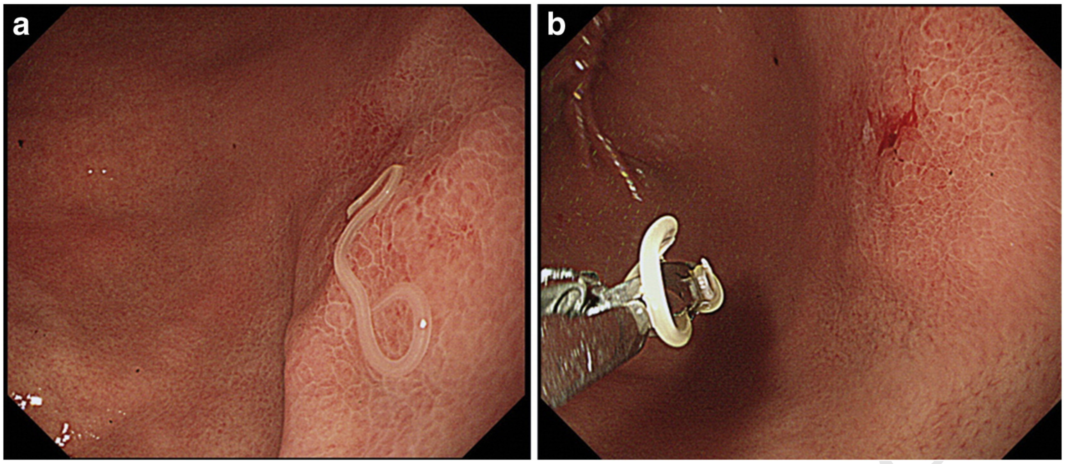

Fig. 1. Endoscopic view of an *Anisakis* larva. (1a) The *Anisakis* larva was seen sticking to the gastric wall. (1b) The *Anisakis* larva could be removed with forceps.

relies on the microscopic identification of amoebic trophozoites in the stool or colonic mucosa of patients. Moreover, there are a variety of laboratory tests that use antigen testing of feces or serum, PCR, and serology. However, these are neither sensitive nor specific, even in combination with a patient's history, endoscopic findings, and other laboratory tests. Thus, it is necessary to develop better diagnostic tools for amoebic colitis.

Recently, super-magnifying endoscopes have been developed, which allow us to obtain images at the cellular level. Currently, there are two devices available that have the ability to allow in vivo microscopic inspection: confocal laser endomicroscopy (CLE) (Pentax, Tokyo) [29] and an endocytoscopy system (ECS) with a high magnification light microscopy device (Olympus Medical Systems, Tokyo) [30–32]. CLE based on tissue fluorescence uses local and/or intravenous contrast agents to generate images. The ECS is based on the principle of contact light microscopy [33–35]. ECS observation also requires pre-treatment with methylene blue or toluidine blue staining [36]. Most clinical studies reported to date have used CLE integrated into the distal tip of a conventional upper endoscope (iCLE: EG-3870CIK, Pentax, Tokyo) or colonoscope (EC-3870CILK, Pentax) [37]. A smaller number of studies have used probe-based CLE (pCLE) (Mauna Kea Technologies, Paris, France) inserted through the accessory channel of a traditional endoscope [37]. Similarly, the ECS is classified as a probe-based ECS (pECS) or an integrated-scope type ECS (iECS) (Fig. 2) [38–40].

In the field of ophthalmology, confocal laser microscopy (Heidelberg Retina Tomograph 2, Rostock Cornea Module, Heidelberg Engineering GmbH, Dossenheim, Germany) has been used to diagnose *Acanthamoeba* keratitis [41–45]. On the other hand, the ECS has been used to obtain real-time in vivo histology for cancer [30–32,46–48]. Previously, we reported the utility of the ECS for predicting the histopathological activity of ulcerative colitis and its usefulness as a real-time diagnostic tool for amoebic colitis [49].

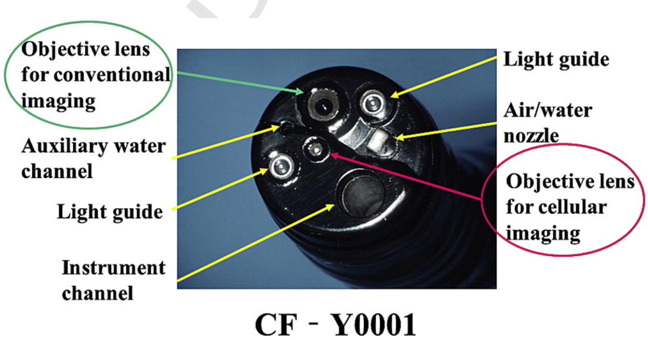

Fig. 2. Integrated-scope type endocytoscope (CF-Y0001).

4. ECS procedures for detecting *E. histolytica* trophozoites

We use an iECS (ECS, CF-Y0001, Olympus Medical Systems, Tokyo) to detect amoebic trophozoites; this system is shown in Fig. 2. This scope can be switched easily from conventional view to a super-magnifying view (×450) by using a button located at the top of the endoscope. A conventional colonoscopic image of amoebic colitis is shown in Fig. 3a. Irregular shallow ulcers with marginal redness, edema, and mucus exudates are seen in the rectum. Subsequently, we changed the conventional view to a super-magnifying view (Fig. 3b). The observation area of the epithelial surface is 400 μm × 400 μm, and the bar represents 100 μm (Fig. 3b). Without methylene blue staining, *E. histolytica* trophozoites were hardly detectable. In order to better visualize *E. histolytica* trophozoites, the lesions were stained with 1.0% methylene blue for 2 min, followed by a few washes with dimethicone solution. As shown in Fig. 3b, following staining, we were clearly able to visualize the body of amoebic trophozoites in the mucus surrounding the lesions. Numerous bluish amoebic trophozoites with a characteristic round shape (white arrows) were easily found in one field of view. We noticed that the size of *E. histolytica* trophozoites detected by the ECS were appreciably smaller relative to the trophozoites detected by traditional hematoxylin and eosin staining. We found that methylene blue staining could make the cytoplasm collapse, resulting in the observation of nuclei that were smaller in size. Biopsy samples were obtained from the lesion, and histological findings corresponded with those of the ECS. Interestingly, in one case only, non-stained *E. histolytica* trophozoites with amoeboid movement were clearly visualized using the ECS (Fig. 3c). An amorphous amoeba was also seen on the surface of the aphthous lesion. The small spots are red blood cells, and amoebic trophozoite phagocytosis of floating red blood cells could be observed.

5. Tapeworm visualized by VCE

Tapeworms are classified as fish tapeworms (*Diphyllobothrium latum*), pork tapeworms (*Taenia solium*), and beef tapeworms (*T. saginata*). Fish tapeworms are prevalent in Europe and East Asia, in countries where raw or undercooked freshwater fish is consumed. In Japan, the main pathogenic tapeworm is the fish tapeworm *D. nihonkaiense*, which is considered as a separate species from *D. latum*. On the other hand, in Europe, *D. latum* is the most common fish tapeworm [50]. Several reports [51–54] have shown in vivo imaging of tapeworms detected by conventional colonoscopy. In addition, we have successfully detected

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