Trichuris trichiura Incidentally Detected by Colonoscopy and Identified by a Genetic Analysis: A Case Report

Yuto Ishizaki¹, Kazumasa Kawashima¹, Naohiko Gunji¹, Michio Onizawa¹, Takuto Hikichi², Mitsuko Hasegawa³,⁴ and Hiromasa Ohira¹

Abstract:
Although trichuriasis, a zoonotic disease, has recently become rare in Japan due to improved environmental hygiene, we herein report a 79-year-old man in whom a worm was incidentally found in the ascending colon during colonoscopy for positive fecal occult blood and was endoscopically removed. A genetic analysis identified the worm as Trichuris trichiura possessing mixed sequences from non-human primate and human origins. Despite controversy regarding Trichuris trichiura infection originating from Japanese macaques, according to some studies, it originates primarily from humans. This report suggests the efficacy of a genetic analysis for identifying infection sources.

Key words: Colonoscopy, Genetic analysis, Trichuriasis, Trichuris trichiura, Zoonosis

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Introduction
Trichuriasis is a significant soil-transmitted helminth infection common in tropical and subtropical regions. In 2017, the World Health Organization reported that approximately 460 million people worldwide were infected with Trichuris trichiura (1). However, the incidence of trichuriasis in Japan has decreased in recent years due to improvements in environmental hygiene (2).

In the present case, the patient was referred for colonoscopy after positive fecal occult blood. A worm was found incidentally in the ascending colon and removed with grasping forceps. The worm was identified as T. trichiura through genetic and histological analyses. However, the infection source could not be determined based on the patient’s life history and interviews and was ultimately determined via a genetic analysis.

In this report, we discuss the infection source of a rare case of trichuriasis in Japan and include a brief discussion of the current literature.

Case Report
A 79-year-old man underwent colonoscopy for positive fecal occult blood at our hospital. He had experienced an acute myocardial infarction a month previously. At that time, he underwent treatment with a drug-eluting stent, two additional antiplatelet agents, and an anticoagulant for paroxysmal atrial fibrillation. He had no other medical complaints.

A blood examination showed slight anemia (hemoglobin, 12.2 mg/dL) and eosinophilia (white blood cell, 4,500/μL; eosinophil, 7%). The liver and renal functions were normal, and the C-reactive protein (0.11 mg/dL) level was not elevated. Regarding his life history, he had used organic fertilizers for a long time while growing vegetables outside his house; however, he had never used feces as fertilizer. He had no history of overseas travel, pets, or livestock.

Colonoscopy revealed a white, linear worm 10 mm in diameter that was burrowing into the ascending colon and was carefully removed with grasping forceps (Fig. 1). In addition, three small polyps and slight telangiectasia were observed in the rectum, which might have caused the positive
Figure 1. A white worm, approximately 10 mm in diameter, had penetrated the colon mucosa and was active in the ascending colon.

Figure 2. Histological specimen of the nematode (Hematoxylin and Eosin staining). (a) The marked areas are shown enlarged in b (dotted line boxed area) and c (solid line boxed area). (b) A series of basophilic cells (stichosomes) observed in the anterior part of the worm body. (c) Numerous eggs that were found at the posterior end of the worm body and the plug-like structure observed in the eggs.

Fecal occult blood. A histological specimen of the nematode showed that the anterior end was thin, and the posterior end was thickened (Fig. 2a). Large spherical cells known as stichocytes, which form a digestive tract called the stichosome, were found at the anterior end of the worm (Fig. 2b). In addition, numerous barrel-shaped eggs were found at the posterior end of the worm; the eggs showed the presence of a polar mucoid plug at each extreme (Fig. 2c). These histological findings were typical of a T. trichiura infection, and we identified the nematode as a female T. trichiura.

The eosinophilia improved three weeks after worm removal. Fecal ova tests at three weeks and two months after worm removal were both negative. In addition, a fecal ova test performed on the patient’s daughter, who lived with him, was negative. We suspected that this case was likely that of a single-worm infection; therefore, we decided to observe the patient and not administer anthelmintic medication. A third fecal ova test after 6 months revealed a negative result.

A genetic analysis was performed with polymerase chain reaction (PCR) to identify the infection source. Hotspots have been reported in the literature where sequences differ between infection from Japanese macaques and infection from humans (3). Four out of five of these hotspots in this patient showed a Japanese macaque origin, while one showed a human origin (Table 1, Fig. 3). Based on 18S rRNA sequence data, the nematode was genetically identified as T. trichiura. The results suggested that it had mixed sequences of T. trichiura from humans and Japanese macaques. The two nucleotide sequences obtained in this study have been deposited in the DDBJ/EMBL/GenBank database as an adult T. trichiura under accession numbers LC596912 and LC596913.

Discussion

In tropical and subtropical regions where environmental hygiene is inadequate, trichuriasis remains a major disease.
Table 1. Nucleotide Sequence Alignment in 18S Ribosomal RNA of Trichurus Trichiura.

|               | 8  | 88 | 96 | 777 | 1,153 | 1,318 | 1,369 | 1,709 |
|---------------|----|----|----|-----|-------|-------|-------|-------|
| Japanese patients\(^a\)(11) | C  | G  | A/T| T   | C     | G     | C     | T     |
| Japanese macaques\(^b\)(11)   | T  | T  | T  | C   | T     | T     | T     | *     |
| Present case               | T  | T  | T  | *   | *     | G     | T     | *     |

\(^a\)T. trichiura from two Japanese patients (AB699090)
\(^b\)T. trichiura from Japanese macaques (AB699092)

*: could not be sequenced

Comparison of 18S ribosomal RNA sequences obtained from T. trichiura from Japanese patients and Japanese macaques and the present case. This shows five of eight locations where the sequences differed between the patients and Japanese macaques. In the present case, four of these five locations were consistent with the Japanese macaque origin, and only the 1,318th nucleotide sequence was consistent with the human origin.

![Nucleotide Sequence Alignment](image)

Figure 3. Direct sequencing results of the 18S ribosomal RNA of the removed nematode from the patient. Only the 1,318th nucleotide sequence contained a guanine (G) of human origin (arrow). A: adenine, C: cytosine, T: thymine

However, the incidence of trichuriasis in Japan is low owing to improvements in environmental hygiene. In the present case, we incidentally found T. trichiura in the ascending colon, which we removed endoscopically. The fecal ova test was negative at all three follow-ups, suggesting that the patient was cured without administration of anthelmintics. There was no history of overseas travel, pets, or livestock, and he was suspected of having been infected through ingestion of his home-grown organic vegetables. A PCR gene analysis suggested that the patient might have ingested vegetables contaminated with feces of Japanese macaques, which may have subsequently caused the T. trichiura infection.

In a report published in 2013, Wang et al. stated that T. trichiura was found in 10.6% of patients who underwent colonoscopy in mainland China (4). In contrast, by 1984, the Ministry of Health and Welfare in Japan reported that the prevalence of trichuriasis was only 0.57%, lower than that reported by other countries (5). In 2020, Hasegawa et al. conducted a sensitive PCR test on the feces of 682 children 2-14 years old living in an area that had had a high rate of roundworm infections in 1966 (2). They reported that none of the recently tested children were found to have current T. trichiura infections (2). This indicates that trichuriasis is an extremely rare disease in Japan.

T. trichiura infection is considered to be primarily due to the ingestion of embryonated eggs from soil or food (6). When the ingested eggs reach the small intestine, they hatch and become larvae, which invade the crypt of the small intestine where they grow into adult nematodes. Adult T. trichiura mainly inhabits the cecum, which allows the ante-
Aerekul et al. reported tables with animal feces and ingestion of inadequately washed raw vegetables. Aerekul et al. reported that the 18S ribosomal RNA sequences of *T. trichiura* found in humans differed slightly from those found in Japanese macaques (3). A PCR genetic analysis was performed for the present case, and the results showed that the gene sequence was highly homologous to that of *T. trichiura* from Japanese macaques. However, a complete sequence was not obtained. The formalin used to fix the worm may have damaged the DNA. Notably, Japanese macaques inhabit the area where the patient lives, so we suspect that he became infected by ingesting inadequately washed vegetables that had been contaminated with macaque feces containing *T. trichiura* eggs.

To our knowledge, 19 cases were reported in Japan from 1990 to 2021 in which *T. trichiura* was endoscopically diagnosed (12-24). Table 2 summarizes these 19 cases. Most of the cases were single infections in the right-side colon; therefore, a differential diagnosis of trichuriasis and colonic anisakiasis by colonoscopy should be carefully performed. According to Table 2, whipworms were often found endoscopically in the right colon, and colonic anisakiasis was also found in the right-side colon (61%) as well as in the transverse colon (20%), descending colon (7%), sigmoid colon (5%), and rectum (5%) (25). The differential diagnosis of trichuriasis and anisakiasis at the infected site of the large intestine is difficult, but there are some differences in endoscopic appearance. *T. trichiura* has a whip-like shape, becoming thicker towards the posterior end, and the anterior end is long and slender, penetrating the mucosa. Furthermore, the length of the adult worms varies from 30 to 50 mm (26). The Anisakis body, on the other hand, is almost constant in thickness, ranging from 10 to 29 mm in length, which is smaller than that of *T. trichiura* (27). These endoscopic findings can help distinguish between *T. trichiura* and anisakiasis.

In conclusion, trichuriasis has the potential to become

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**Table 2.** Literatures of Endoscopically Removed *Trichuris Trichiura* in Japan during 1990-2021.

| Case No | Year | Age, Sex | Chief complaints | Detection site | Treatments | References |
|---------|------|----------|------------------|---------------|------------|-----------|
| 1       | 1991 | 56, F    | abdominal pain   | cecum         | removed endoscopically+mebendazole | (12)     |
| 2       | 1993 | 68, F    | occult blood     | cecum         | removed endoscopically+mebendazole | (13)     |
| 3       | 1993 | 75, F    | no complaint     | cecum         | removed endoscopically             | (14)     |
| 4       | 1996 | 60, M    | no complaint     | cecum         | removed endoscopically             | (15)     |
| 5       | 1996 | 65, F    | abdominal pain   | cecum         | removed endoscopically+mebendazole | (16)     |
| 6       | 2000 | 25, F    | abdominal pain   | cecum         | removed endoscopically+mebendazole | (17)     |
| 7       | 2005 | 64, F    | occult blood     | descending colon | mebendazole | (18)     |
| 8       | 2006 | 67, M    | no complaint     | cecum         | removed endoscopically             | (19)     |
| 9       | 2006 | 63, M    | no complaint     | cecum         | removed endoscopically             | (19)     |
| 10      | 2009 | 56, F    | constipation     | cecum         | removed endoscopically             | (20)     |
| 11      | 2009 | 44, M    | anal pain, diarrhea | rectum | removed endoscopically             | (21)     |
| 12      | 2015 | 73, M    | no data          | no data       | no data                             | (22)     |
| 13      | 2015 | 60-69, M | no data          | no data       | no data                             | (22)     |
| 14      | 2015 | 67, F    | no data          | no data       | no data                             | (22)     |
| 15      | 2015 | 75, F    | abdominal pain   | cecum         | no data                             | (22)     |
| 16      | 2015 | 45, F    | occult blood     | ascending colon | removed endoscopically+mebendazole | (22)     |
| 17      | 2018 | 73, F    | constipation, diarrhea | cecum | no data                             | (23)     |
| 18      | 2020 | 64, M    | no complaint     | transverse colon | removed endoscopically             | (24)     |
| 19      | 2021 | 79, M    | occult blood     | ascending colon | removed endoscopically             | current report     |
more prevalent in the future due to increased consumption of organic vegetables and an increase in overseas travel. This report showed for the first time a case of *T. trichiura* infection in a human with a possible origin from Japanese macaques detected through a genetic analysis.

The authors state that they have no Conflict of Interest (COI).

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