Dientamoeba fragilis: A Family Cluster of Disease Associated With Marked Peripheral Eosinophilia

Timothy James Gray,1 Yiu L. Kwan,2 Thuy Phan,1 Graham Robertson,1 Elaine Y. L. Cheong,1 and Thomas Gottlieb1

1Department of Microbiology and Infectious Diseases and 2Department of Haematology, Concord Repatriation General Hospital, Concord, New South Wales, Australia

Dientamoeba fragilis has emerged as an important and underrecognized cause of gastrointestinal illness. We report a familial cluster of D. fragilis associated with marked peripheral eosinophilia and gastrointestinal symptoms. Dientamoeba fragilis infection should be considered in the setting of unexplained eosinophilia. If confirmed, screening of household members should be considered.

Keywords. Dientamoeba fragilis; eosinophilia; diarrhea.

Dientamoeba fragilis is a pathogenic protozoan of the human gastrointestinal tract with a worldwide distribution. In developed countries, D. fragilis is emerging as a more prevalent cause of gastrointestinal disease than Giardia intestinalis [1–3]. The prevalence of D. fragilis is likely to be underreported in many settings because permanent stains of fixed stools may not be routinely performed and when they are, the diagnosis is dependent on the individual expertise of laboratories. More-sensitive molecular diagnostic techniques are still not widely available.

There is now convincing evidence that D. fragilis is an important cause of human disease, although this has not always been appreciated [4]. We report a family cluster of D. fragilis–related illness and asymptomatic carriage, which presented with a marked eosinophilia at levels not previously reported with dientamoebiasis.

CASE REPORTS

A 45-year-old man (case 1) underwent a complete blood count (CBC) because of a 2-week history of mild abdominal distension. He denied abdominal pain, diarrhea, nausea, or vomiting. He was referred to the hematology service with a provisional query of eosinophilic leukemia, with an absolute eosinophil count of 10.9 × 10⁹/L (upper limit of reference range, 0.5 × 10⁹/L). His total white blood cell (WBC) count was 21.5 × 10⁹/L and the blood film did not contain any blast cells. Two years prior on routine blood tests, he had an eosinophil count of 0.09 × 10⁹/L. He underwent a bone marrow biopsy, which excluded malignancy. A stool specimen collected in sodium acetate acetic acid formalin (SAF) and permanently stained using a modified iron-hematoxylin stain revealed Blastocystis hominis, Endolimax nana, Entamoeba hartmanni, and high numbers of D. fragilis. He reported that he and his family frequently consumed raw fish (sashimi).

The patient’s 45-year-old wife (case 2) had no symptoms but was directed to undergo investigations because of the shared diet of raw fish. A CBC revealed an absolute eosinophil count of 5.2 × 10⁹/L (WBC count 12.4 × 10⁹/L). Two years prior she had a normal CBC. She had 2 stool specimens collected in SAF, which on iron-hematoxylin stain revealed B. hominis, E. nana, and large numbers of D. fragilis.

Of 2 daughters living in the household, aged 17 and 19 years, neither presented with any gastrointestinal symptoms. The first daughter (case 3) had an absolute eosinophil count of 0.9 × 10⁹/L (WBC count 9.7 × 10⁹/L), and stool microscopy revealed only D. fragilis. The second daughter (case 4) had an eosinophil count of 0.5 × 10⁹/L (WBC count 6.6 × 10⁹/L), and 6 stool specimens collected over 2 months did not reveal any parasites on microscopy.

One week prior to case 1 developing symptoms, his sister-in-law (case 5), who resided separately but frequently ate at the same residence, had developed severe diarrhea (>6 episodes per day), which was associated with abdominal bloating and discomfort. She recorded a 7-kg (12%) weight loss over a 1-month period. Her primary care provider had arranged for stool microscopy and culture, which revealed no bacterial pathogens and no parasites. However, no SAF fixed specimen was collected. Her symptoms abated after she was treated empirically with 2 g of metronidazole, but she returned 3 days later. She underwent a CBC and fixed stool collection 40 days after the onset of her symptoms. Her absolute eosinophil count was 4.7 × 10⁹/L.
(WBC count 9.4 × 10⁹/L), and her fixed stool specimen revealed *E. nana* and large numbers of *D. fragilis*. Three years prior, a routine CBC had revealed an eosinophil count of 0.1 × 10⁹/L.

All family members had negative *Strongyloides* serology as well as negative *Strongyloides* stool culture by both agar plate and Harada-Mori techniques. All patients were confirmed positive for *D. fragilis* on real-time polymerase chain reaction (PCR) performed on pretreatment specimens, including case 4, who had negative stool microscopy [5]. Family members had not traveled overseas or out of their urban environment in the previous 2 years, there were no pets in the household, and no home-grown or local market food had been consumed.

The 4 cases with *D. fragilis* on microscopy were treated with metronidazole (400 mg 3 times daily for 7 days), with a subsequent fall in eosinophil counts and the complete resolution of symptoms for case 1 and case 5. Doxycycline (100 mg twice daily for 7 days) was prescribed to the 3 cases with persisting *D. fragilis* on stool microscopy, but given the poor response in our cohort, they were subsequently treated with paromomycin (500 mg 3 times daily for 7 days) (Figure 1). Twelve months after completion of treatment, all cases remained symptom free, and the absolute eosinophil count had returned to normal in all cases.

**DISCUSSION**

The transmission of *D. fragilis* is not completely understood, but is presumed to occur via the fecal-oral route at the trophozoite stage [4]. Although foodborne or waterborne outbreaks have not been described, *D. fragilis* has been reported to occur in family groups [6]. In the cluster presented here, *D. fragilis* was the only consistent finding in all family members with gastrointestinal symptoms and/or peripheral eosinophilia. The coexistence of nonpathogenic parasites including *B. hominis*, *E. nana*, and *E. hartmanni* in the stool of cases 1, 2, and 5 reflects the similar mode of transmission and suggests consumption of food or water contaminated with human feces as the mode of transmission. A point source for the family outbreak would seem likely, as the 2 symptomatic members of the family had onset of symptoms within 1 week. We were unable to identify an environmental risk factor that would have promoted fecal-oral transmission, such as consumption of market or home-grown vegetables or untreated water. The contamination of raw

---

**Figure 1.** Outline of the temporal relationship between the 5 cases of *Dientamoeba fragilis* within the cluster, including absolute eosinophil counts and response to therapy. *Eosinophil count for case 1 and 5 had normalized to 0.2 × 10⁹/L 12 months after completion of treatment.*
fish purchased at local markets was considered as the possible source of the enteric parasites, although the cases could not be confidently linked to this exposure.

*Dientamoeba fragilis* has been reported as an occasional cause of mild peripheral eosinophilia, more commonly in children [7,8]. In a recent series of symptomatic adults diagnosed with *D. fragilis*, only 3 of 22 were reported to have a peripheral eosinophilia [3]. The nonpathogenic protozoa identified in the cases have not been described to cause eosinophilia [9]. The peripheral eosinophilia seen in the cases presented here was high, with the symptomatic cases having higher levels (50.7% and 50.0% of the WBC count), compared with the asymptomatic cases (range, 7.6%–41.9%). The natural history of *D. fragilis* infection is not well described, so we can only postulate that the high range of eosinophilia seen in this cluster was related to the heavy burden of organisms. Other causes of eosinophilia were considered but were excluded given the negative serological workup, negative Harada-Mori and agar plate cultures for *Strongyloides*, and the completion of 43 fixed stool specimens (range, 6–11 per family member). A familial tendency to eosinophilia was considered unlikely as previous CBCs were normal and cases 1 and 2 denied consanguinity.

*Dientamoeba fragilis* is most readily identified among the intestinal parasites by its characteristic binucleate form seen on permanently stained fixed stool specimens. Characteristic motility of the advancing leaf-like pseudopodia may occasionally be observed when unfixed specimens are rapidly processed using an iodine or saline preparation. However, this technique has poor sensitivity because of the morphological deterioration that rapidly occurs in the aerobic environment [4]. This is highlighted by case 5, where the opportunity to make an early diagnosis of this family cluster was missed, presumably because a stool fixative was not used. However, even optimal fixation and staining of specimens only detects one-third of *D. fragilis* cases otherwise identified using a more-sensitive, but not widely available, PCR technique [10, 11]. The clinical significance of PCR identification of *D. fragilis* in asymptomatic cases with negative microscopy may be questionable, as evidenced by case 4, who, despite a positive PCR test, was never symptomatic nor treated with any antiparasitic therapy on the basis of 6 negative fixed stool microscopy specimens.

Recent surveys have reported *D. fragilis* to be the most frequently isolated pathogenic parasite in stools of patients with gastrointestinal symptoms, with the most common associated symptoms being diarrhea, abdominal pain, or bloating [1–4]. Although there is no consensus as to the best therapy to treat *D. fragilis*, there is substantial evidence that treatment of this organism resolves gastrointestinal symptoms [4, 12]. In observational studies, metronidazole may be associated with higher rates of treatment failure (range, 11%–35%) when compared with paromomycin, which in a recent retrospective analysis was shown to eradicate *D. fragilis* in 60 of 61 (98%) cases [13]. Other drugs that have been observed to resolve symptoms and eradicate *D. fragilis* include doxycycline, erythromycin, clioquinol, and the nitroimidazole derivatives including tinidazole, ornidazole, and secnidazole [3, 4, 12]. We saw a clear response to metronidazole when given as a prolonged course (7 days) with the rapid resolution of symptoms (case 1 and case 5), and a marked reduction in the peripheral eosinophilia in all cases. Of the 4 treated cases, only case 5 cleared carriage of *D. fragilis* with metronidazole; 1 of the other 3 cases cleared with an additional course of doxycycline, and for 2 of the 3 cases, paromomycin was subsequently required to eliminate *D. fragilis* carriage (Figure 1).

This familial cluster of dientamoebiasis highlights the clinical spectrum from asymptomatic carriage to severe gastrointestinal symptoms. The tendency to peripheral eosinophilia in this infection has been demonstrated, even in the absence of symptoms. The use of stool fixative and staining should be emphasized to laboratories considering this diagnosis, although PCR may become the definitive diagnostic test in the future. When *D. fragilis* is identified in an individual, consideration should be given to screening other members of the household, irrespective of symptoms.

**Note**

**Potential conflicts of interest.** All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

**References**


