

# Blastocystis hominis Infection Inducing Gut Microbiome Dysbiosis and Aggravating Parkinson's Disease Symptoms: A Case Report

Emanuel-Youssef Dib<sup>1</sup>, Karam Karam<sup>1</sup>, Lama Al Akel<sup>1</sup>, Loulewa Al Sayed<sup>1</sup>, Tala Charafeddine<sup>1</sup>, Laila Al Akel<sup>1</sup>, Serena Khoury<sup>1</sup>, and Walid Abdel Khalek<sup>1</sup>

<sup>1</sup>University of Balamand

July 16, 2024

## **Blastocystis hominis Infection Inducing Gut Microbiome Dysbiosis and Aggravating Parkinson's Disease Symptoms: A Case Report**

Emanuel-Youssef Dib<sup>1</sup>, Karam Karam<sup>2</sup>, Lama Al Akel<sup>3</sup>, Loulewa Al Sayed<sup>4</sup>, Tala Charafeddine<sup>5</sup>, Laila Al Akel<sup>6</sup>, Serena Khoury<sup>7</sup>, Walid Abdel Khalek<sup>8\*</sup>

**[1] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** emanueleyoussef.dib@std.balamand.edu.lb

**[2] Department of Gastroenterology, University of Balamand, Beirut, Lebanon. Email:** Karamek7@gmail.com

**[3] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** lama.akel@std.balamand.edu.lb

**[4] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** loulewa.sayed@std.balamand.edu.lb

**[5] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** tala.charafeddine@std.balamand.edu.lb

**[6] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** laila.akel@std.balamand.edu.lb

**[7] Department of Internal Medicine, University of Balamand, Beirut, Lebanon. Email:** serena.khoury@std.balamand.edu.lb

**[8] Associate professor, University of Balamand, Department of Gastroenterology, Dekweneh, Lebanon. Email:** walid\_ak33@hotmail.com

**\*CORRESPONDING AUTHOR**

### **Key Clinical Message:**

Blastocystis hominis infection in Parkinson's disease patients may exacerbate gut microbiota dysbiosis, potentially worsening neurological symptoms. Targeted interventions to restore gut microbial balance could mitigate disease progression and improve patient outcomes.

### **Funding Information**

None.

## Conflict of interest statement

None.

**Consent:** The patient in this manuscript has given written informed consent to publication of their case details.

**Keywords:** Blastocystis hominis, gut microbiota dysbiosis, Parkinson’s disease, neurological symptoms, therapeutic intervention

## Introduction:

Blastocystis is a genetically diverse unicellular parasite that colonizes the intestines of humans and a wide range of animals. The organism’s basic biology is poorly understood, and controversy surrounds its taxonomy and pathogenicity. Although just three morphological forms—vacuolar, granular, and ameboid—have been identified, recent research has discovered more forms—cyst, avacuolar, and multivacuolar [1].

The organism is categorized as a stramenopile based on molecular evidence, similar to diatoms, chrysophytes, water molds, and slime nets [2].

It is customary to refer to Blastocystis organisms isolated from humans as *B. hominis*. However, due to low host specificity and significant genetic variation, the name Blastocystis species is thought to be more suitable. The subtype (ST), if genetic typing is performed, should also be recorded. Among the nine STs identified in humans, the four most common are ST1, ST2, ST3, and ST4. Several other STs might be connected to zoonotic transmission [2].

Infections occur worldwide in both immunocompetent and immunodeficient individuals. Blastocystis may be transmitted through food, water, or contact with human or animal feces. It is more common among people who live in or travel to developing countries and those who work with animals. *B. hominis* infection typically causes non-specific symptoms such as watery diarrhea, nausea, abdominal pain, bloating, excessive gas, loss of appetite, weight loss, anal itching, and fatigue. Metronidazole is advised as the antibiotic of choice if therapy seems necessary, despite reports of its inability to completely eradicate the organism [1].

Case reports have suggested a pathogenic role of *B. hominis* in causing intestinal inflammation and linking it to irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) [3].

This case report explores the relationship between Blastocystis hominis and its potential exacerbation of Parkinson’s disease symptoms through gut microbiota dysbiosis. By examining the case of an elderly male with Parkinson’s disease who developed severe gastrointestinal symptoms alongside worsening motor function, we aim to shed light on how microbial disturbances in the gut may influence neurological conditions, offering insights into potential therapeutic avenues.

## Case History/Examination

An 86-year-old male presented to the ER with severe watery diarrhea, up to 6 episodes per day, of 1 month duration. The patient’s diarrhea was non-bloody and non-mucoid. He denied fever, nausea, vomiting, abdominal pain, bloating, loss of appetite, or anal itching. There was no history of weight loss, fatigue, or systemic symptoms.

The patient reported that his Parkinson’s disease symptoms, including tremors and motor function, had worsened over the past month concurrent with the onset of diarrhea. Despite taking a full course of ciprofloxacin and metronidazole 1 week prior to presentation, there was no improvement in his symptoms. The diarrhea was also unresponsive to loperamide.

The patient had several comorbidities, including hypertension, diabetes mellitus, Parkinson’s disease, benign prostatic hyperplasia, and coronary artery disease (s/p 7 stents), managed with medications including amlodipine, irbesartan, moxonidine, carvedilol, methyldopa, carbidopa-levodopa, pramipexole, insulin glargine, tamsulosin, and clopidogrel.

Physical examination revealed a soft, non-tender, non-distended abdomen with positive bowel sounds in all four quadrants. The rest of the physical exam was unremarkable with regular heart sounds and good bilateral air entry in the lungs.

### Methods:

Routine laboratory findings on admission showed normal WBC, low hemoglobin, low sodium, low bicarbonate, elevated CRP, and normal liver function tests. A stool sample was examined microscopically using normal saline, revealing *Blastocystis hominis* cysts and a rare WBC count. The sample was concentrated using acetylacetate and ether.

### Conclusion and Results:

The patient was started on IV ciprofloxacin and metronidazole, resulting in an improvement in diarrhea consistency and frequency until the resolution of symptoms within 4 days of initiating IV therapy.

This case report sheds light on the clinical presentation, diagnostic process, and therapeutic approach for a patient with diarrhea associated with *Blastocystis hominis* infection. It is crucial to consider parasitic infections in the differential diagnosis of chronic diarrhea. The identification of *B. hominis* cysts underscores the need for careful clinical consideration. The successful treatment of this case with appropriate antimicrobial therapy demonstrates symptom resolution and highlights the necessity for continued investigation into the pathogenic role of *B. hominis*.

### Discussion:

Recent studies have identified a possible link between *Blastocystis hominis*, a common gut eukaryote, and cognitive function. Specifically, various subtypes of *Blastocystis* have been associated with deficits in executive function and changes in gut bacterial composition, suggesting that *Blastocystis* colonization may contribute to cognitive impairment through mechanisms involving gut microbiota dysbiosis [4].

*Blastocystis* is a genetically diverse unicellular parasite found in humans and a wide range of animals. It is classified as a stramenopile. The parasite's potential to cause gastrointestinal disease in humans is debated, as it has been detected in both symptomatic and asymptomatic individuals [2]. Despite controversies surrounding its pathogenicity, accumulating evidence suggests *Blastocystis* may cause gastrointestinal symptoms such as diarrhea and abdominal pain, as well as extraintestinal manifestations like urticaria [5]. Diagnosis involves identifying *Blastocystis* species, usually in its vacuolar form, in stool samples. Molecular methods are primarily used for research purposes. The parasite's life cycle, including its infectious stage and the significance of its various morphological forms, remains poorly understood despite ongoing studies on its global distribution and host range [2].

The gut microbiota, consisting of bacteria, viruses, fungi, protozoans, and archaea, plays a critical role in maintaining physiological homeostasis, immune system development, and digestion [6]. Dysbiosis, or an imbalance in the gut microbiota, has been linked to numerous diseases, including Parkinson's disease (PD) [7].

Parkinson's disease is the second most prevalent neurodegenerative disorder in the United States, marked by the degeneration of dopaminergic neurons in the substantia nigra and the formation of Lewy Bodies. Motor symptoms include resting tremors, bradykinesia, rigidity, shuffling gait, and postural instability. Non-motor symptoms include cognitive impairment, depression, anxiety, autonomic dysfunction, and sensory/sleep disturbances. The causes are a mix of environmental and genetic factors, with an increased risk from head injuries and exposure to toxins [8].

The gut-brain axis enables bidirectional communication between the gut microbiota and the central nervous system (CNS), influencing each other through neural, immune, and endocrine signals [9]. Dysbiosis in PD patients is characterized by specific changes in gut microbial populations, which contribute to the disease's motor and non-motor symptoms through increased intestinal permeability, systemic inflammation, and disrupted neurotransmitter metabolism [9].

In this case, an elderly male patient with PD developed daily diarrhea that was resistant to loperamide, ciprofloxacin, and metronidazole, along with worsening PD symptoms. Diagnostic tests revealed an infection with *Blastocystis hominis*, which likely further disrupted his gut microbiota. *Blastocystis hominis* is a common gut eukaryote found in humans, capable of asymptomatic long-term colonization [10, 11].

It exhibits a dual nature as both a commensal organism, often residing in the gut without causing symptoms, and a potential pathogen under certain conditions [4]. Research has highlighted its association with increased gut bacterial diversity while also disrupting microbial composition, particularly affecting beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* [12, 13].

These dual characteristics suggest that *Blastocystis hominis* may contribute to gut dysbiosis and related health outcomes, depending on its interactions within the gut microbiota.

The intricate relationship between gut microbiome dysbiosis and Parkinson's disease (PD) is an emerging focus of scientific inquiry [7].

We hypothesize that the pre-existing dysbiosis associated with PD predisposed our patient to infection with *Blastocystis hominis*, which in turn exacerbated the dysbiosis and aggravated the patient's PD symptoms. Pre-existing dysbiosis in PD patients typically manifests as an altered gut microbial composition, increased intestinal permeability, and a compromised immune response [9].

In our patient, these factors likely created a conducive environment for *B. hominis* colonization. Dysbiosis disrupts the normal protective mechanisms of the gut, thereby facilitating the establishment of pathogenic organisms such as *B. hominis*. Once established, this protozoan parasite may have further disrupted the gut microbiota, exacerbating the dysbiotic state.

Colonization by *B. hominis* could have intensified the pre-existing dysbiosis through several mechanisms. It may have further altered the gut microbial community, increased intestinal permeability, and induced both local and systemic inflammation. These changes can disrupt the gut-brain axis, which plays a crucial role in the pathophysiology of PD. The exacerbated dysbiosis likely initiated a vicious cycle, where the infection-induced imbalance of the gut microbiota led to increased systemic inflammation and neuroinflammation. These inflammatory processes are known to contribute to the progression of PD.

Furthermore, the disrupted gut microbiome may have impaired the gut's ability to produce and metabolize neurotransmitters and other bioactive compounds essential for maintaining neurological function. This dysbiosis may have made the patient more susceptible to *B. hominis* infection, creating a vicious cycle where the infection aggravated gut dysbiosis, exacerbating PD symptoms. Addressing *B. hominis* infection and restoring gut microbial balance could potentially alleviate some of the PD symptoms by improving gut health and reducing systemic inflammation.

### Conclusion:

This case underscores the significance of gut microbiota in neurological disorders such as Parkinson's disease. The exacerbation of symptoms observed in our patient following *Blastocystis hominis* infection highlights the potential role of gut dysbiosis in disease progression. Addressing gut microbial balance and understanding its impact on neuroinflammatory processes could offer promising therapeutic strategies for managing Parkinson's disease symptoms. Further research into the mechanisms linking gut microbiota dysbiosis and neurological health is crucial for developing targeted interventions aimed at improving patient outcomes and quality of life.

### Authorship List:

[1] **Mr. Emanuel-Youssef Dib:** Conceptualization, Methodology, Validation, Writing – original draft, Writing – review & editing

[2] **Dr. Karam Karam :** Methodology, Validation, Writing – original draft, Investigation [3] **Dr. Lama Al Akel :** Methodology, Validation, Writing – original draft

- [4] **Dr. Loulewa Al Sayed** : Methodology, Validation, Writing – original draft
- [5] **Dr. Tala Charafeddine** : Methodology, Validation, Writing – original draft
- [6] **Ms. Laila Al Akel** : Methodology, Validation, Writing – original draft
- [7] **Ms. Serena Khoury** : Methodology, Writing – original draft
- [8] **Dr. Walid Abdel Khalek** (*Corresponding Author*): Project administration, Validation, Writing – review & editing

## References:

1. Stenzel DJ, Boreham PF. Blastocystis hominis revisited. *Clin Microbiol Rev.* 1996 Oct;9(4):563-84. doi: 10.1128/CMR.9.4.563. PMID: 8894352; PMCID: PMC172910.
2. CDC - dpdx - blastocystis hominis. Centers for Disease Control and Prevention. October 21, 2019. Accessed June 24, 2024. <https://www.cdc.gov/dpdx/blastocystis/index.html>.
3. Ustün S, Turgay N. Blastocystis hominis ve bağırsak hastalıkları [Blastocystis hominis and bowel diseases]. *Turkiye Parazitoloj Derg.* 2006;30(1):72-6. Turkish. PMID: 17106862.
4. Mayneris-Perxachs, J., Arnoriaga-Rodríguez, M., Garre-Olmo, J., Puig, J., Ramos, R., Trelis, M., Burokas, A., Coll, C., Zapata-Tona, C., Pedraza, S., Pérez-Brocá, V., Ramió, L., Ricart, W., Moya, A., Jové, M., Sol, J., Portero-Otin, M., Pamplona, R., Maldonado, R., & Fernández-Real, J. M. (2022). Presence of Blastocystis in gut microbiota is associated with cognitive traits and decreased executive function. *The ISME journal* , 16 (9), 2181–2197. <https://doi.org/10.1038/s41396-022-01262-3>
5. Tan K. S. (2008). New insights on classification, identification, and clinical relevance of Blastocystis spp. *Clinical microbiology reviews* , 21 (4), 639–665. <https://doi.org/10.1128/CMR.00022-08>
6. Sender, R., Fuchs, S., & Milo, R. (2016). Revised Estimates for the Number of Human and Bacteria Cells in the Body. *PLoS biology* , 14 (8), e1002533. <https://doi.org/10.1371/journal.pbio.1002533>
7. Nishiwaki, H., Ito, M., Ishida, T., Hamaguchi, T., Maeda, T., Kashihara, K., Tsuboi, Y., Ueyama, J., Shimamura, T., Mori, H., Kurokawa, K., Katsuno, M., Hirayama, M., & Ohno, K. (2020). Meta-Analysis of Gut Dysbiosis in Parkinson’s Disease. *Movement disorders : official journal of the Movement Disorder Society* , 35 (9), 1626–1635. <https://doi.org/10.1002/mds.28119>
8. Chaoul, V., Dib, E. Y., Bedran, J., Khoury, C., Shmoury, O., Harb, F., & Soueid, J. (2023). Assessing Drug Administration Techniques in Zebrafish Models of Neurological Disease. *International journal of molecular sciences* , 24 (19), 14898. <https://doi.org/10.3390/ijms241914898>
9. Berthouzoz, E., Lazarevic, V., Zekeridou, A., Castro, M., Debove, I., Aybek, S., Schrenzel, J., Burkhard, P. R., & Fleury, V. (2023). Oral and intestinal dysbiosis in Parkinson’s disease. *Revue neurologique* , 179 (9), 937–946. <https://doi.org/10.1016/j.neurol.2022.12.010>
10. Scanlan, P. D., Stensvold, C. R., Rajilić-Stojanović, M., Heilig, H. G., De Vos, W. M., O’Toole, P. W., & Cotter, P. D. (2014). The microbial eukaryote Blastocystis is a prevalent and diverse member of the healthy human gut microbiota. *FEMS microbiology ecology* , 90 (1), 326–330. <https://doi.org/10.1111/1574-6941.12396>
11. Beghini, F., Pasolli, E., Truong, T. D., Putignani, L., Cacciò, S. M., & Segata, N. (2017). Large-scale comparative metagenomics of Blastocystis, a common member of the human gut microbiome. *The ISME journal* , 11 (12), 2848–2863. <https://doi.org/10.1038/ismej.2017.139>
12. Nourrisson, C., Scanzi, J., Pereira, B., NkoudMong, C., Wawrzyniak, I., Cian, A., Viscogliosi, E., Livrelli, V., Delbac, F., Dapoigny, M., & Poirier, P. (2014). Blastocystis is associated with decrease of fecal microbiota protective bacteria: comparative analysis between patients with irritable bowel syndrome and control subjects. *PloS one* , 9 (11), e111868. <https://doi.org/10.1371/journal.pone.0111868>
13. Yason, J. A., Liang, Y. R., Png, C. W., Zhang, Y., & Tan, K. S. W. (2019). Interactions between a pathogenic Blastocystis subtype and gut microbiota: in vitro and in vivo studies. *Microbiome* , 7 (1), 30. <https://doi.org/10.1186/s40168-019-0644-3>