

Rare Case of Chronic Diarrhoea in an Immunocompetent Host

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Abstract Chronic diarrhoea is one of the common presenting symptoms of patients attending gastroenterology clinics. Cyclosporacayetanensis is a protozoan parasite causing intestinal infections. Most of these infections are self-limiting in immunocompetent individuals. However prolonged course of infection is often observed in immunocompromised individuals and rarely in normal individuals. In our case report, 50-year-old patient from west Bengal, India presented with chronic small bowel type of diarrhoea with significant weight loss. Serology for HIV was negative. Endoscopic biopsy from duodenum showed villous atrophy and crypt hyperplasia mimicking sprue with presence of oval round structures within parasitophorous vacuoles located in the supra nuclear cytoplasm of enterocytes, consistent with cyclospora infestation. Same biopsy also showed CMV inclusion bodies in the background. He was managed with oral Trimethoprim/sulfamethoxazole for cyclospora and valganciclovir for CMV. Conclusion: Mixed infection of cyclospora and cytomegalovirus presenting as chronic diarrhoea was rarely reported in an immunocompetent individual. Duodenal biopsy may help in differentiating parasitic infections from tropical sprue by demonstrating various forms of pathogens in histology.

Keywords: chronic diarrhoea, malabsorption syndrome, cyclospora, cytomegalovirus

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1. Introduction

Chronic small bowel diarrhoea with malabsorption poses significant impairment to health-related quality of life in India. [1] Tropical sprue and parasitic infections of small intestine are the common causes of chronic diarrhoea India. In general, most of these parasitic infections are self limiting in immunocompetent individual. Chronic diarrhoea resulting from these parasites mainly occurs in immunocompromised patients, such as HIV or on immunosuppressant medication. Mixed parasitic and CMV infection to present as chronic diarrhoea is rarely reported in literature.

2. Patient Information

50-year male, farmer by occupation from west Bengal, India belongs to low socioeconomic status presented with chronic painless small bowel diarrhoea with a stool frequency of 6 times/day for 4 months. He also complained of loss of appetite with significant weight loss of around 10 kg over 4 months. On examination he was moderately built. Oral cavity showed aphthoid ulcers and glossitis. Per abdominal

examination was normal. On evaluation his haemoglobin was 12.4 g/dl and white cell count was 7800 per microliter (Neutrophils-70%, L lymphocytes -18%, Eosinophils -4%, Monocytes -8%) and platelet count was 3.48 lakhs per microliter. ESR level was 10mm/hr (0-22 normal range). Renal function tests and electrolytes were Normal. His stool examination did not revealed any ova, cysts, or pus cells or RBC. Liver function test showed total bilirubin of 0.4 mg/dl and total protein of 5.6 g/dL with albumin of 2.9g/dL. Liver enzymes showed SGPT 53 U/L (Normal range: 7-56 U/L), SGOT49 U/L (Normal range: 5-40 U/L), ALP 168 U/L (Normal range: 44-147 U/L),GGTP 90 U/L (Normal range: 3.3-35U/L). Serology for HIV and HBs Ag antigen and Anti HCV was negative. Ultrasound abdomen did not show any lymph nodes in abdomen. Liver and spleen appeared normal. An upper GI endoscopy was done to evaluate for the cause of small bowel diarrhoea, which showed nodular oedematous duodenal mucosa with scalloping of folds, multiple biopsies were taken from second part of duodenum and sent for histopathological examination.

3. Histopathological Examination

Duodenal mucosa showed villous atrophy and crypt hyperplasia with anincrease in lamina propria by

lymphocytes, plasma cells, histiocytes and eosinophils and some neutrophils with many lymphoid follicles (Figure 2). As shown in Figure 3, Brunner's glands showed nuclear and cytoplasmic inclusions, which was consistent with the morphology of cytomegalovirus

(CMV). Surprisingly on high power field we noticed small oval structures within parasitophorous vacuoles in the supranuclear cytoplasm of enterocytes which was suggestive of the morphology of cyclospora (Figure 4).



Figure 1. Endoscopy showing edematous duodenal mucosa with scalloping of folds

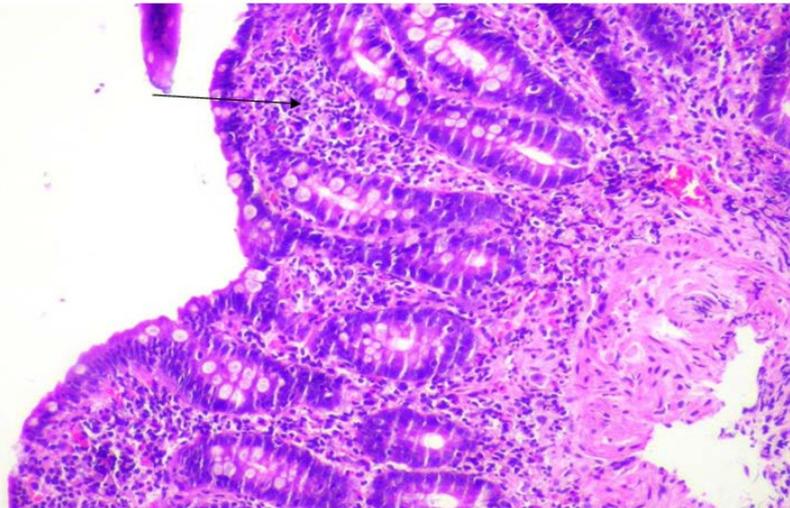


Figure 2. Endoscopic duodenal biopsy specimen showing total villous atrophy and crypt hyperplasia with lymphoplasmocytic infiltration (arrow), eosinophils in lamina propria. (H&E)

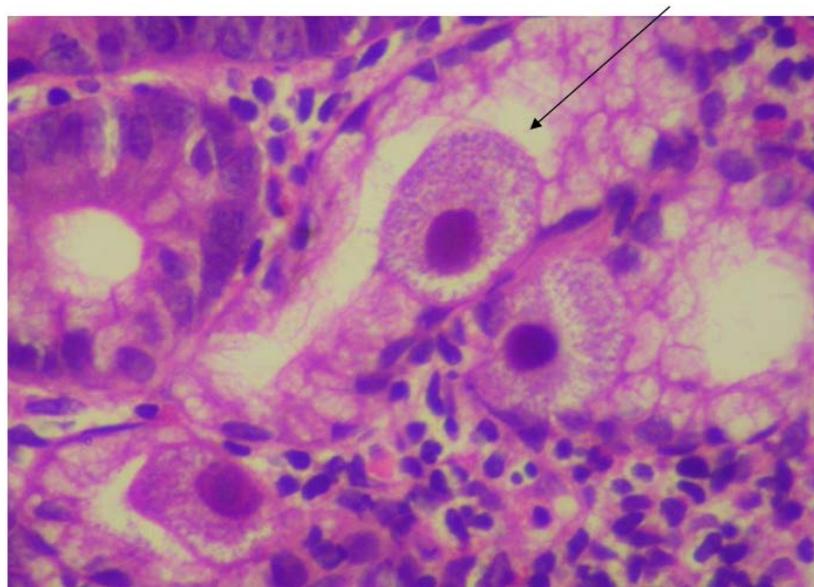


Figure 3. Endoscopic duodenal biopsy on high power field showing Brunner's gland with nuclear and cytoplasmic inclusions (arrow), consistent with the morphology of cytomegalovirus (CMV)

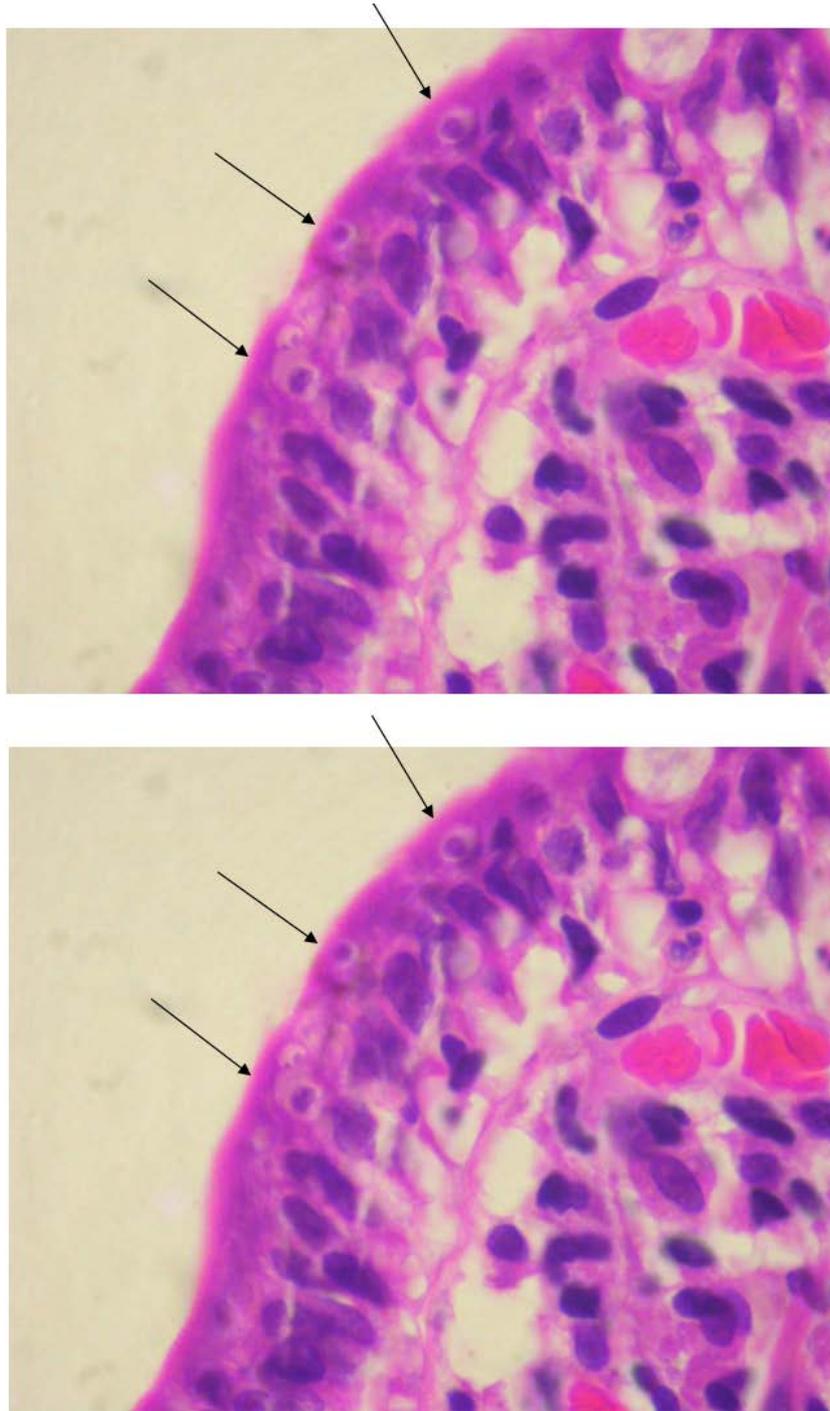


Figure 4. Endoscopic duodenal biopsy specimen on high power field showing small oval round structures within parasitophorous vacuoles located in the supranuclearcytoplasm of enterocytes, consistent with cyclospora infestation

He was managed with TMP /SMX (160/800) twice daily for 10 days as per IDSA guidelines for the treatment of cyclospora. Subsequently he was treated with valganciclovir 900mg twice daily for 21 days for CMV enteritis. On follow up he was symptomatically much better. Stool frequency reduced.

4. Discussion

Cyclospora cayetanensis is an Intestinal coccidian (protozoan) which infects humans on ingestion of contaminated food (raspberries) or water. It is one of the common infection among travellers to endemic area or

patients with HIV/AIDS. Geographically it is most commonly seen in Latin america, Indian sub-continent and south east Asia. Contaminated water or soil, poor sanitation, low socio-economic status are the possible risk factors. Infection with these parasites is often either asymptomatic² or associated with selflimited acute diarrhoea. However, patients with immunocompromised state show prolonged symptoms.

In the present case, our patient had chronic small bowel type of diarrhoea with upper GI symptoms. On evaluation serology for HIV was negative. Liver function tests showed hypoalbuminemia, which suggests protein malabsorption. Endoscopic examination showed oedematous mucosa with scalloping of duodenal folds mimicking

sprue. Biopsies were taken from 2 nd part of duodenum. Histopathological examination showed crypt hyperplasia and villous atrophy with lymphoplasmacytic infiltrate in lamina propria. On high power field we demonstrated the presence of small oval shaped structures surrounded by parasitophilic vacuoles in the supranuclear cytoplasm of enterocytes which suggests 'cyclospora' infestation. Interestingly the same biopsy also showed intranuclear and cytoplasmic "owl-eye" or Cowdry type A inclusion bodies in Brunner glands of duodenum, which was consistent with cytomegalovirus infection. He was managed with trimethoprim and sulfamethoxazole for 10 days. On follow up he was suggested valganciclovir for 21 days. This case was unique in its presentation as it showed mixed infection of CMV and cyclospora infestation in immunocompetent host with features of chronic duodenitis mimicking tropical sprue.

Pipaliyat et al [3] from India, showed that the most common etiology of chronic diarrhoea in India was tropical sprue (n=98, 48.3%) followed by parasitic infections (n=25, 12.3%). In parasitic diseases, many a times, the organism is not picked up in stool examination. So, it is important to differentiate these two diseases on the basis of symptoms, laboratory parameters and endoscopic findings and duodenal biopsy. Santos RB et al [4] reported that parasites in duodenal biopsies corresponded to 1% of biopsies performed.

Severe diarrhoea, florid malabsorption (especially B12 deficiency) and mucosal damage on histology indicate tropical sprue, while presence of more upper GI symptoms indicates parasitic infections.

Similar to the present case, a study by Shlim et al [5] examined the stools of 55 immunocompetent patients who presented to the CIWEC Clinic in Kathmandu, Nepal between June and November 1989. The illness was characterized by prolonged watery diarrhoea, anorexia, fatigue, and weight loss. The mean \pm SD duration of illness was 43 ± 24 days. Later it was diagnosed to be due to Cyclospora infection in travellers to Nepal. However, these patients did not have any associated CMV infection.

Though in literature reported cyclospora was common in HIV/AIDS patients, Gupta s et al [6] study from India reported only one case cyclospora cayetanensis (2.9%) out of 34 HIV patients with chronic diarrhoea. Similarly, Kumar SS et al [7] studied 59 patients of HIV patients with chronic diarrhoea out of which Cyclospora cayetanensis associated diarrhoea were detected in only one chronic case (1.69 %). This suggests that diagnosis of cyclospora was not common even in patients with HIV/AIDS.

Cyclospora can be diagnosed by stool examination for presence of oocysts (diameter 8-10 microns) by using Modified AFB / Safranin stains. Duodenal biopsy will show Duodenal inflammation with increased Intra epithelial lymphocytes, degrees of villous atrophy and crypt hyperplasia with several developmental forms of parasite with in epitheal cells.

Cytomegalovirus (CMV), part of Herpesviridae genus, is a common virus, with positive serology found in more than two-thirds of the population [8]. Initial infection is self-limited in healthy individuals. However, the virus remains latent in immunocompetent

individuals, while reactivation may occur in the setting of immunosuppression.

CMV infections commonly occur in the GI tract, while localized duodenal infection is very rare. Our patient had localised duodenal involvement of CMV which was again one of the rare finding. A study of CMV infection in the upper GI tract, found the stomach to be the most common site of involvement and only one out of thirty cases involved the duodenum [9].

Diagnosis of gastrointestinal CMV infection often requires endoscopy with biopsies. Primary findings include ulcerations, erosions, and mucosal haemorrhage [10]. The diagnostic gold standard for CMV infection is histopathological examination of endoscopic biopsy or surgical specimen.

Haematoxylin-eosin stains typically show intranuclear "owl-eye" or Cowdry type A inclusion bodies in stromal and endothelial cells, which are hypertrophic cells containing eosinophilic intranuclear viral inclusions. Unfortunately, gastrointestinal CMV disease is not always readily diagnosed, especially in an immunocompetent patient as suspicion may be low. First-line treatment for gastrointestinal CMV disease is intravenous ganciclovir 5 mg/kg BID or oral valganciclovir 900 mg BID .There are no conclusive data regarding the use of antiviral treatment for CMV in immunocompetent host in the literature. However, physicians generally tend to prescribe antiviral treatment for the most severe cases of monophasic CMV meningoencephalitis, a severe ocular involvement, and severe lung involvement, GI involvement caused by the CMV infection.Hence our patient was suggested treatment for CMV duodenitis on follow up.

5. Conclusion

Mixed infection of cyclospora and cytomegalovirus presenting as chronic diarrhoea was rare in an immunocompetent host. Any patient presenting with chronic diarrhoea in an endemic area for cyclospora such as India, we should exclude parasitic infections. Duodenal biopsy may help in detecting these parasites on histology, which may also help in differentiating it from tropical sprue. Current line of Treatmentfor cyclospora is trimethoprim/sulfamethoxazole. As there were no consensus regarding treatment of CMV in immunocompetent individuals, choice should be given to treat them with ganciclovir or valacyclovir for 21 days. However, these patients need to be excluded for presence of immunodeficiency syndromes.

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