INTRODUCTION

In 1986, Soave et al. reported the presence of coccidian-like bodies in the diarrhoeal stools of four American tourists who had spent some time in Haiti and in Mexico, and suggested that they might be a new enteropathogen. More recently, five AIDS patients and three international travellers with a similar diarrhoeal picture and organism were described (Hart et al., 1990; Long et al., 1990). Although the authors noted that the organism resembled oocysts of coccidian protozoa, they concluded that they were photosynthetic, thylakoid algae-like structures (so-called “blue-green algae” or “cyanobacteria-like bodies”), ultrastructurally related to Chlorella spp. (Long et al., 1990). Subsequent epidemiological studies showed that this pathogen is more widespread than previously thought, and it is prevalent in Asia, Latin America, and the Caribbean, particularly in Nepal, Peru and Mexico (Shlim et al., 1991; Hoge et al., 1993; Gascon et al., 1993; Ortega et al., 1993). To date, only few cases have been reported in immunocompromised patients, specifically those with HIV infection (Hart et al., 1990; Long et al., 1990; Bendall et al., 1993; Brandonisio et al., 1993; Wurtz et al., 1993).

We describe the first case of co-infection with Cyclospora sp. and Cryptosporidium parvum in an AIDS patient with diarrhoea.

CASE REPORT

The patient was a 33-yr old Italian male, shipyard worker with a long history of intravenous heroin abuse, dating back to before 1987. Between 1987 and 1989 the patient lived in Nepal. When he returned to Italy in July, 1989, he was admitted to the Infectious Diseases Unit of the Ravenna Hospital (Emilia Romagna region, central Italy) because of weight loss, profound weakness, persistent cough and malaise. He was found to be
Fig. 1 - *Cyclospora* oocyst (arrow) and some others of *C. parvum* (arrowheads) are seen in stool sediment (Ziehl-Neeelsen mod., × 1000).

Fig. 2 - Several immature *Cyclospora* oocysts in feces. Note the typical internal granulations and the thick wall (Nomarski interference contrast, × 1000).
HIV-positive and to have bilateral cavitary pulmonary tuberculosis (TB), pityriasis of the hair, scabies and seborrhoeic dermatitis of the face. The patient appeared chronically ill and had lost 15 Kg; he was anemic (hemoglobin: 11 g/100 ml; RBC: 4,000,000/mm$^3$) and had a CD4 count of 149/mm$^3$, with a CD4/CD8 ratio of 0.16. Six months anti-TB therapy (rifampicin, isoniazide and ethambutol), and AZT (500 mg twice daily) resulted in resolution of the radiographic findings and an overall clinical improvement for the patient (CD4 > 400/mm$^3$). The patient felt quite well until May, 1992, when he was re-admitted to the same hospital because of P. carinii pneumonia (PCP) and diarrhoea (5-6 bowel movements/day) of one month's duration. Stool specimens examined by two of us (M.S. and S.G.) with an acid-fast stain showed a mixed intestinal infection with both Cyclospora sp. and C. parvum oocysts (fig. 1). The CD4 count was 9/mm$^3$.

Treatment with co-trimoxazole (120 mg/Kg/day for three weeks) for PCP and with spiramycin (9,000,000 IU/qd for one month) for cryptosporidiosis was started. The patient had a good clinical response both of pulmonary and intestinal symptoms. He had a reduction in diarrhoea frequency (1-2 bowel movements/day), despite persistence of the two pathogens in the stool and he was discharged. In September, 1992, after a brief admission to the Piacenza Hospital (Northern Italy), he was re-admitted to the Infectious Diseases Unit of the Ravenna Hospital because of CMV retinitis, persistent diarrhoea and mass lesions on a brain CT scan, probably due to Toxoplasma gondii infection. Empiric therapy with pyrimethamine (75 mg/day) and clindamycin (600 mg qd) was started, with progressive regression of symptoms and of the CNS lesions seen on CT scan.

A repeat stool examination was positive for Cyclospora sp. oocysts (fig. 2) but negative for C. parvum. An intestinal biopsy was not performed.

The patient died suddenly of a cardiac arrest on November 18, 1992. Autopsy was not permitted.

**DISCUSSION**

Chronic diarrhoea is a common problem in symptomatic HIV-infected subjects (Bartlett et al., 1992). The spectrum of microorganisms potentially responsible for diarrhoea is widening; however, particularly in tropical areas, several cases are due to coccidian protozoa such as Cryptosporidium parvum and Isospora belli (Soave and Johnson, 1988).

Recently, in some cases of diarrhoeal enteritis in HIV positive patients (Hart et al., 1990; Long et al., 1990; Bendall et al., 1993; Brandonisio et al., 1993; Wurtz et al., 1993), the etiological agent has been identified as a new human coccidian of Cyclospora genus according to Ortega et al. (1993), and previously named “cyanobacterium-like” or “alga-like” by other authors (Long et al., 1990 and 1991). To our knowledge, this is the first reported case of co-infection with Cyclospora sp. and C. parvum in an AIDS patient.

To date, the vast majority of human infection due to Cyclospora sp. has been reported in immunocompetent travellers and in foreigners residing in some tropical areas such as Asia (Nepal), the Caribbean and Latin America (Peru, Mexico) (Shlim et al., 1991; Hoge et al., 1993; Gascon et al., 1993; Ortega et al., 1993). An autochthonous epidemic outbreak in the USA among the medical and nursing staff working at an hospital of Chicago (WHO, 1991) and other sporadic cases elsewhere were also reported (Bendall et al., 1993; Brandonisio et al., 1993).

From the epidemiologic point of view, it is significant that our patient lived in Nepal for about two years. He complained abdominal symptoms only after several months from the return in Italy, when he was severely immunocompromised. This could mean for Cyclospora, as for other opportunistic AIDS-defining infections (Smith et al., 1992), the re-activation of a latent infection due to a cell-mediated immunodeficiency.

Both in the immunocompetent and in the immunocompromised host, Cyclospora infection is usually associated with watery “intermittent” diarrhoea that tends to be self-limited, lasting weeks or months, even in AIDS patients.

In our patient it was impossible to evaluate temporary clinical remissions during Cyclospora infection, because of the presence of C. parvum. On the other hand, Cyclospora oocysts have been still recognized in patient stools five months after the first positive fecal identification.

It is likely that the treatment schedule with spiramycin and co-trimoxazole temporarily improved the diarrhoea due to these coccidia, in relation with the partial efficacy of spiramycin on C. parvum (Georgiev, 1993) and the preliminary data of the effectiveness of co-trimoxazole on Cyclospora both in immunocompetent (Madico et al., 1993) and immunocompromised patients with AIDS (Wurtz et al., 1993).

We also believe that the negative stool examination for C. parvum few days before the patient's death would be critically evaluated, in the light of the well-known irregular oocyst shedding and of the low sensitivity of the temporary and permanent staining methods (Weber et al., 1991). Moreover, an intestinal
biopsy to confirm a complete parasitological cure was not performed.

In conclusion, clinicians and laboratory operators should be alerted that *Cyclospora* sp. is a new etiological agent of diarrhoeal enteritis both in immunocompetent and in immunodeficient humans. As in our patient, the possibility of a mixed infection with other intestinal pathogens, namely *C. parvum*, should also be considered: in these cases the careful microscopic evaluation of oocyst morphology in fresh and acid fast stained specimens (Long et al., 1991) is an useful diagnostic method for differentiating these coccidia.

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REFERENCES


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