Digestive Diseases and Sciences, Vol. 30, No. 5 (May 1985), pp. 497–504

CASE REPORT

Intestinal Infection with *Mycobacterium avium* in Acquired Immune Deficiency Syndrome (AIDS)

Histological and Clinical Comparison with Whipple's Disease

ROBERT I. ROTH, MD, ROBERT L. OWEN, MD, DAVID F. KEREN, MD, and PAUL A. VOLBERDING, MD

In a patient with AIDS (acquired immune deficiency syndrome) we initially diagnosed Whipple's disease because of a morphologic picture which was subsequently found to reflect systemic *Mycobacterium avium* infection. Our experience may be helpful in distinguishing these two conditions and raises questions about the pathophysiology of each. Whipple's disease is an uncommon intestinal disorder, characterized by diarrhea, abdominal pain, anorexia, weight loss, migratory arthritis, and steatorrhea. While the clinical setting may suggest the diagnosis, radiologic findings are often inconclusive, and confirmation of Whipple's disease requires small bowel biopsy. Characteristic pathologic findings include villus widening, foamy macrophages in the lamina propria filled with periodic acid-Schiff (PAS) staining material, and dilated lymphatics. Electron microscopy reveals large numbers of ingested bacteria within macrophages. While no specific organism has been cultured, treatment with tetracycline or other broad spectrum antibiotics is usually curative.

M. avium-intracellulare (M. avium) is an ubiquitous microorganism in the environment, found in the soil and carried by birds and domestic farm animals. Human infection with *M. avium* is uncommon, but purely cutaneous involvement has been reported, both as granulomatous disease (1) and as lepromatous lesions (2). Unlike *Mycobacterium tuberculosis, M. avium* is only rarely found as disseminated disease in humans. Systemic infection may develop in patients with immune depression presenting as pneumonitis, lymphadenitis, or osteomyelitis (3, 4).

Manuscript received December 20, 1983; revised manuscript received April 23, 1984; accepted June 25, 1984.

From the Departments of Medicine and Pathology, University of California, San Francisco; and Department of Pathology, University of Michigan, Ann Arbor.

Address for reprint requests: Dr. Robert L. Owen (151E), V.A. Medical Center, San Francisco, California 94121.

CASE REPORT

Methods. Endoscopic biopsies from the second portion of the duodenum were immersed in 2.5% glutaraldehyde in 0.1 M phosphate buffer, pH 7.6, for 3 hr, rinsed in the same buffer twice, left overnight at 4°C, and then post-fixed with 2% osmium tetroxide for 1 hr. The fixed tissue was embedded in LX112. Thick sections were stained with toluidine blue. Thin sections on uncoated grids could not be adequately examined because of holes due to poor infiltration around intracellular bacilli. Subsequent sections were mounted on parlodion and carbon-coated grids, stained with lead citrate and uranyl acetate, and examined at 20 kV using a Phillips 201 transmission electron microscope.

Additional endoscopic biopsies taken in nearby locations were embedded in paraffin and processed for light microscopy.

Formalin-fixed lymph nodes from our patient were sectioned, deparaffinized, treated with trypsin, then incubated for 30 min at room temperature with undiluted rabbit antibacterial grouping sera (5) and with specific antiserum to *M. avium*. Slides were washed in three

changes of 0.01 M phosphate-buffered saline (PBS), pH 7.2. A 1:20 dilution of fluorescein-conjugated goat anti-rabbit IgG (Meloy) was applied for 30 min at room temperature. The slides were again washed with PBS three times, and cover slips were applied over a 9:1 glycerol–PBS solution. Slides were examined and intensity of fluorescence of bacilli within macrophage granules was evaluated with each antiserum on a scale of 0 (no staining) to 4 (intense fluorescence) by a single observer (D.F.K.) without knowledge of the antibacterial serum used. The profile of cross-reactivity with antibacterial typing sera from this case was compared with profiles previously observed with three Whipple's cases (5), with results from paraffin-embedded small intestinal and colon tissue from a macaque monkey with chronic diarrhea and *M. avium* serotype 1 infection, and with intestine from a recent case of Whipple's disease.

Patient. A 30-year-old white homosexual male was admitted in March 1982 to San Francisco General Hospital with fever of unknown origin. His past medical history included a rectal fissure with subsequent fistula, perianal and sacral ulcerations, hepatitis A and B, gonorrhea, syphilis, and intestinal amebiasis. He had multiple sexual partners and gave a history of nonintravenous drug use. Two years earlier he was evaluated at another hospital for recurrent fevers to 40°C, at which time massive splenomegaly was noted. Liver biopsy demonstrated chronic active hepatitis and HB_sAg, anti-HB_c, and anti-HA were present. Nonspecific granulomas were noted on bone marrow biopsy. A mumps skin test was positive. The patient also complained of diarrhea. No fever source was determined, and the fevers continued after discharge. Approximately one year prior to admission he noted erythematous, pruritic lesions on his upper thorax and arms.

He had already lost 11 pounds five months prior to admission when his diarrhea increased to more than 10 watery, yellow stools per day. Nasogastric hyperalimentation was attempted, but quickly discontinued when it precipitated even more massive diarrhea. Three months prior to admission, he noted violaceous leg lesions and nonhealing mouth ulcerations. On admission to San Francisco General Hospital, physical examination revealed cachexia, multiple violaceous skin lesions, hepatosplenomegaly, and diffuse lymphadenopathy. The hemoglobin was 9.3 g/dl, the white blood count was 4200/ml with an absolute lymphocyte count of 336. T-cell function was greatly depressed as measured by mixed lymphocyte culture (2431 cpm of tritiated thymidine incorporated after six days compared to a normal range of 5800–9999 cpm) and phytohemagglutinin stimulation (500 cpm incorporated after three days compared to normal incorporation of more than 11,150 cpm). Helper–suppressor cell ratios were not available locally during this patient's hospitalization and were not done. The sedimentation rate was 136. He was anergic to mumps skin testing. Kaposi's sarcoma was diagnosed on skin biopsy. Herpes simplex virus was isolated from sacral ulcers, cytomegalovirus from urine, and *Candida* from throat cultures. Multiple routine blood cultures were negative. Abdominal CT scan demonstrated splenomegaly and periaortic and mesenteric lymphadenopathy. Quantification of the patient's diarrhea demonstrated a 24-hour volume of 2475 ml. Because of nausea and anorexia, the patient was unable to consume a 100-g fat diet for quantitative stool

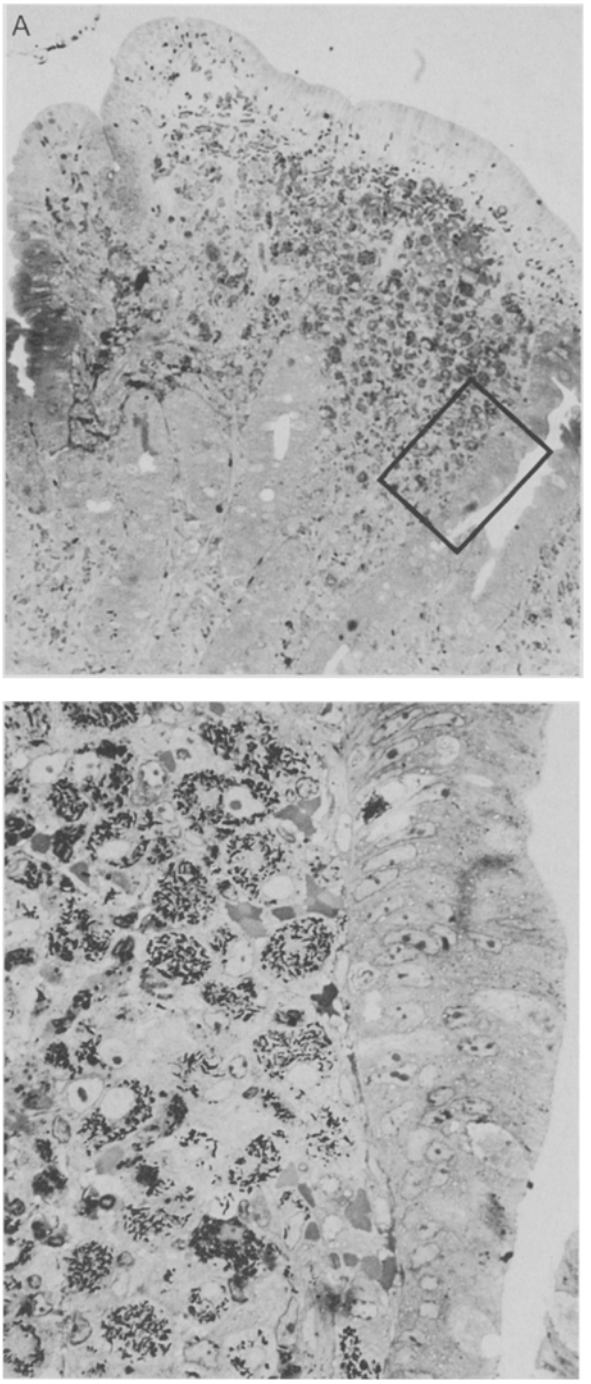

Fig 1. (A) Endoscopic duodenal biopsy of broad, fused villi with "foamy" macrophages filling the lamina propria (×134). (B) Rodlike bacilli in macrophages from area in rectangle in Figure 1A. LX112 plastic-embedded sections stained with toluidine blue (×640).

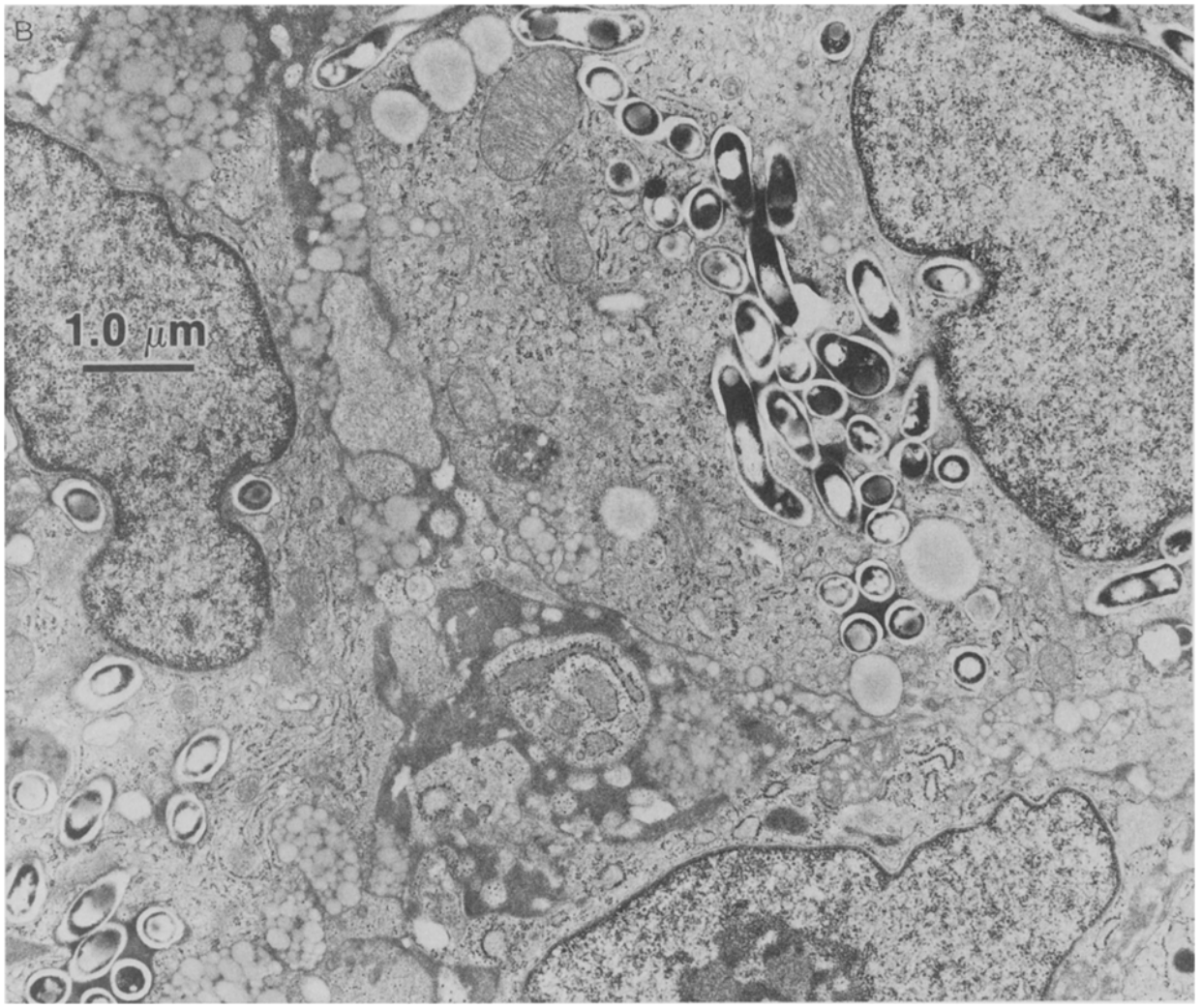

Fig 2. Electron micrograph showing mycobacteria with rodlike longitudinal profiles and round cross-sectional profiles within cytoplasm of villus macrophages. Mycobacteria have an unstained cell wall, dense peripheries, and lucent central areas (×13,600).

fat determination. D-Xylose absorption was abnormally low with only 2.1 g urinated in 5 hr after a 25-g dose. Stool cultures for pathogenic bacteria were negative as were multiple examinations for ova and parasites including *Cryptosporidia*.

Endoscopy revealed erythematous macular mucosal lesions in the duodenum. In duodenal biopsies, large foamy macrophages were present in the lamina propria (Figure 1A and B). These macrophages contained PAS-positive rodlike material which, by electron microscopy, was shown to consist of bacillary bodies (Figure 2). Initially, this histologic picture was interpreted as a variant of Whipple's disease, and the patient was treated with tetracycline but did not improve. Subsequently, *M. avium* was cultured from blood and sputum, and the foamy macrophages were shown to contain acid-fast bacilli.

The Kaposi's sarcoma was treated with three courses of vinblastine, adriamycin, and bleomycin, resulting in significant tumor regression but chemotherapy was then discontinued due to severe neutropenia. Treatment for disseminated *M. avium* included isoniazid, rifampin, ethambutol, amikacin, and cycloserine, but blood cultures remained positive. Numerous symptomatic medications were ineffective in controlling diarrhea. Three months after his initial admission, stool revealed *Isopora belli* for which therapy with furazolidone was ineffective. Diarrhea increased to more than 12 yellow or orange malodorous stools per day accompanied by a 40-pound weight loss over seven months. There was no hematochezia or melena. Pancytopenia persisted, and the patient died at home.

Postmortem examination revealed several violaceous skin lesions showing dermal hemorrhage no longer diag-

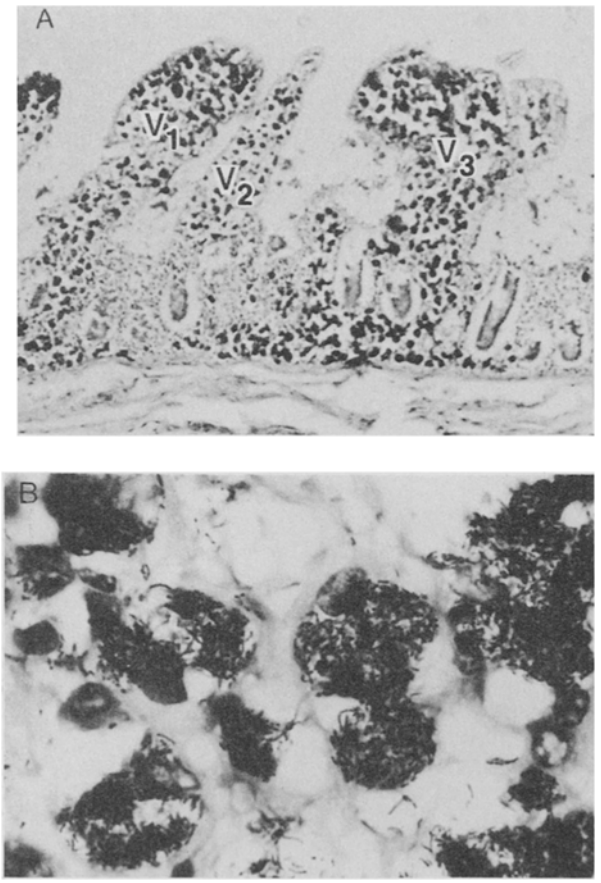

Fig 3. (A) Postmortem section of autolyzed small intestine showing patchy distribution of *Mycobacterium*-filled macrophages distending and distorting villi V_1 and V_3 but largely absent from intervening villus V_2 (Fite acid-fast stain, ×127). (B) Macrophages in villi contain large numbers of rod-shaped mycobacteria completely filling and distending the cytoplasm of each cell (Fite acid-fast stain, ×995).

nostic of Kaposi's sarcoma. Visceral Kaposi's sarcoma was not noted. Involvement with *M. avium* was manifested by aggregates of foamy macrophages containing acid-fast bacteria in the small bowel (Figures 3A and B), in liver portal triads, in splenic white pulp, in thoracic and retroperitoneal lymph nodes (Figure 4), in mesenteric lymph nodes adjacent to the small bowel, and in bone marrow. The lymph nodes were totally replaced by foamy macrophages. Although *M. avium* was massively involving pulmonary lymph nodes, no organisms were found in the lung parenchyma itself. The spleen was large (400 g), firm, had prominent follicles and, in addition to infiltration by *M. avium* which extensively replaced the white pulp, there was histologic evidence of hemosiderosis and multiple small abscesses without demonstrable organisms. Mycobacterial isolates from this patient were identified as *M. avium*, serotype 1, by the National Jewish Hospital, Denver, Colorado. Colonic erosions and rectal ulcerations were seen grossly. Microscopic sections revealed cytomegalovirus, which was also detected in lung, liver, thyroid, and adrenal gland. The liver was large (1950 g) and grossly demonstrated several purple nodules, shown histologically to be multifocal cavernous hemangiomas, and several light grey nodules, shown histologically to be multicentric large cell lymphoma. In addition to histologic evidence of infiltration by *M. avium* and CMV, the liver demonstrated hemosiderosis. Presence of *Isospora belli* could not be evaluated in sections of the gastrointestinal tract because of postmortem autolysis of the epithelium.

Indirect immunofluorescence patterns with bacterial grouping sera on lymph node specimens from the present patient and on colon and small bowel from a macaque monkey infected with *M. avium* were compared to the immunofluorescence on tissue from a patient with typical Whipple's disease. As shown in Table 1, tissue from the Whipple's disease patient had strong reactivity with antisera to *Streptococcus* groups B and G but not to *Salmonella* or *M. avium*. On the contrary, tissues from the present patient and from the monkey with *M. avium* infection had strong reactivity with antisera to *Streptococcus* group D, *Salmonella*, and *M. avium* but no reactivity with antisera to *Streptococcus* groups B and G. These studies demonstrate that the contents of foamy macrophages in Whipple's disease are immunologically distinct from those in the present case of *M. avium* despite the similar histologic appearance. Ziehl-Neelsen stain for mycobacteria was strongly positive in tissue in the present case and in the macaque but was negative in tissue from the patient with Whipple's disease.

DISCUSSION

Acquired Immune Deficiency Syndrome. The patient described in this report had multiple infections during the six months following the diagnosis of Kaposi's sarcoma. In the United States, as of December 1983, 3000 patients had been identified with AIDS (6), in which susceptibility to opportunistic infections resulted in major morbidity and mortality. These patients demonstrate a variety of abnormalities in cell-mediated immunity (7–9). The mechanism for the immunosuppression in these groups of patients is not understood, but because of this immunosuppression previously uncommon infections have attained life-threatening importance. Cytomegalovirus (10), *Pneumocystis carinii*, *Candida* (7), and herpes simplex virus (11) have been described in AIDS patients and contribute to an ever increasing mortality rate, reaching 100% in patients diagnosed for three years or longer.

***Mycobacterium avium* Infection.** Until very recently, disseminated disease with *M. avium* was rarely reported. The most extensive involvement included

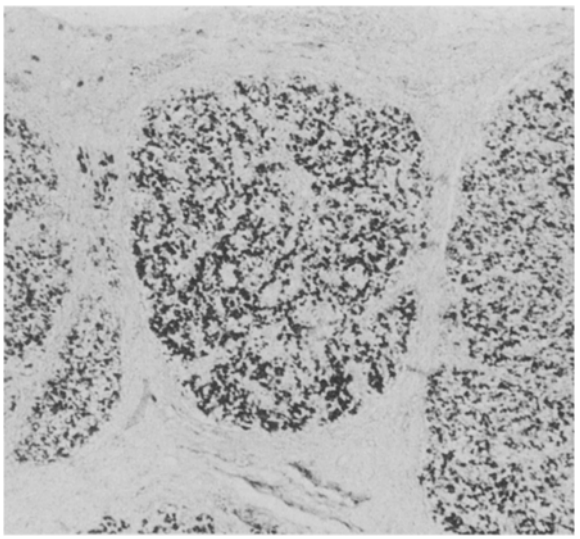

Fig 4. Mesenteric lymph nodes, surrounded by fibrous tissue, are markedly depleted of lymphocytes and almost totally replaced by *Mycobacterium*-filled macrophages. There is little residual nodal cortex, and there are no discernible geminal centers (Fite acid-fast stain, ×50).

lungs, liver, spleen, lymph nodes, and bone marrow (12) but did not include infiltration of the gastrointestinal tract. Reports, however, have described widespread granulomatous disease due to *M. avium* in homosexual men (3, 13, 14), and disseminated nongranulomatous disease in four homosexual men and in one male heterosexual drug abuser who were also found to have multiple other infections including *Pneumocystis carinii,* cytomegalovirus pneumonia, anal herpes simplex type II, and cytomegalovirus colitis (15). In another study of opportunistic infections in five formerly healthy women, *M. avium* was found in two of the patients, both of whom were heterosexual intravenous drug abusers (16). *M. avium* has also been reported with acquired immune deficiency in a hemophiliac patient (17) and in an infant after receiving transfusions from multiple blood donors including a subsequent AIDS victim (18). An AIDS patient with malabsorption and intestinal lesions similar to our patient was confirmed to have *M. avium* only after completion of his postmortem examination (19).

Sexually Transmitted Enteric Diseases. Chronic and recurrent gastrointestinal disease in homosexual men is a well-described entity. Viral, bacterial, and protozoan infections have been detected with high frequency. Sexually transmitted enteric pathogens include *Shigella,* amebas, and *Giardia* (20–23). In stool samples from 89 homosexual men (24), amebas were present in 20%, *Giardia* in 12%, ameba and *Giardia* combined in 7%, *Entamoeba coli* in 13%, and *Endolimax nana* in 11%. The patient in this current report gave a history of previous infection with amebas and, during his hospitalization, was found to have *Isospora belli.*

Whipple's Disease. In Whipple's disease, jejunal villi are widened by macrophages distended by vesicles containing periodic acid-Schiff (PAS) staining bacilli and have dilated lacteals (lymphatics) (25). The bacilli do not stain with acid-fast stains but they do cross-react with antibacterial typing sera. Indirect immunofluorescent staining with these antisera produces a pattern of cross-reactivity which is characteristic for Whipple's disease (5, 26, 27). The constancy of this pattern from case to case suggests that a specific, although unidentified, bacillus is responsible in the majority of Whipple's infections. The markedly different pattern obtained with the same antisera in tissue from our case confirms that *M. avium* is not the organism responsible for classical Whipple's disease (Table 1).

Villus distension by macrophages filled with PAS-positive bacilli in *M. avium* infection indicates that this histologic picture is no longer pathognomonic of Whipple's disease. Dilated lymphatics within villi in Whipple's have been attributed to obstructed lymphatic drainage secondary to engorgement of lymph nodes by bacteria-filled macrophages. The absence of lymphatic distension in our patient, despite extensive mesenteric lymph node involvement, indicates that dilated lacteals observed in Whipple's disease may represent more than simply increased lymphatic back-pressure. In Whipple's disease, thickened enlarged villi produce a yellow–white granular appearance of the small

TABLE 1. CROSS-REACTIVE STAINING OF MACROPHAGES BY INDIRECT IMMUNOFLUORESCENCE

	Tissue source and diagnosis		
	Human Whipple's	*Human M. avium*	*Monkey M. avium*
Antisera			
Streptococcus B	3+	–	±
Streptococcus D	1+	3+	2+
Streptococcus G	4+	–	–
Salmonella	–	2+	2+
M. avium	–	2+	4+

intestinal surface during endoscopy (28). In our case, erythematous macular lesions were seen, possibly related to increased capillary fragility.

The finding of symptomatic gastrointestinal involvement with *M. avium-intracellulare* was noted in one of five homosexual AIDS patients reported with disseminated mycobacterial disease (3). In the current report our patient with disseminated *M. avium* had extensive disease which distorted the small intestine and probably contributed to the malabsorption and severe diarrhea. In immunosuppressed patients with a propensity toward opportunistic infections, the possibility of unusual gastrointestinal organisms can present a difficult diagnostic problem. It is important to make an accurate diagnosis since treatment varies. As demonstrated in this report, disseminated *M. avium* should be included in the differential diagnosis of diarrhea in AIDS patients. Small bowel biopsy may be useful in this setting. Diarrhea, malabsorption, and progressive inanition can persist in AIDS patients even after elimination of identifiable pathogens due to an enteropathy which may reflect viral or immunologic damage to the mucosa (29). Cytomegalovirus inclusion bodies, such as in our patient, have been found in association with a variety of gastrointestinal lesions in immunosuppressed patients, but the causal role of CMV is unconfirmed except in primary infection (30).

Even though the specific bacterial cause of Whipple's disease remains unknown, clinicians have been remarkably successful in controlling the condition through the empiric use of broad-spectrum antibiotics. Following our initial interpretation of this patient's endoscopic biopsy as Whipple's disease, tetracycline was given with no effect on symptoms. After *M. avium* was isolated, triple therapy with antituberculosis drugs was instituted; however, this mycobacterial strain was subsequently found to be resistent to INH, streptomycin, rifampin, capreomycin, and ethambutol but was sensitive to cycloserine. *Mycobacterium avium* and *Mycobacterium intracellulare* are generally much more drug resistant than tuberculosis strains and have been placed in a common group (III) because of their similarities. A variety of serotypes have been identified which can be discriminated by agglutination reactions and by thin-layer chromatography. Serotypes 1–3 are *M. avium* strains, 4–7 are intermediate, and 8–28 are *M. intracellulare* strains. Because we were unable to eliminate *M. avium* in this patient we could not confirm the extent to which this organism was responsible for his diarrhea. We presume *M. avium* was at least contributory to his symptoms because of the widespread intestinal infiltration.

Infection with *M. avium* has been reported in monkeys with a syndrome of acquired immune deficiency and intestinal histologic findings remarkably similar to those in our patient (31–33). In these veterinary reports, the similarity to Whipple's disease in humans was not noted. The histologic picture of bacillus-filled macrophages, distorting and enlarging villi in Whipple's patients with no known organism, in our case and in monkeys infected with *M. avium* suggests that Whipple's and *M. avium* infections are examples of a syndrome of malabsorption with immune dysfunction affecting macrophages. In these situations, the underlying cause of the immune dysfunction may be of greater etiologic significance than the specific infecting microorganisms propagating within macrophages.

Because of the difference in therapeutic approach, it is important to differentiate Whipple's disease from *M. avium* infection when the histologic picture of PAS-positive inclusions within intestinal macrophages is observed. Our case would suggest that the clinical presentation may be helpful in diagnosis. Malabsorption, fever, and cachexia, present in classical Whipple's were seen in our patient, but migratory arthritis which is prominent in Whipple's was absent. Whipple's patients typically have few detectable immunologic deficits and do not have multiple opportunistic infections. After treatment with broad-spectrum antibiotics, Whipple's patients typically feel quite well. In our patient with AIDS, a variety of opportunistic infections were present which may have contributed to malabsorption and weight loss. Anorexia and nausea were increased in our patient during tetracycline treatment, and institution of potentially helpful antimycobacterial drugs was delayed.

Because of the large number of *M. avium* infections observed thus far in patients with AIDS, *M. avium* should be suspected when the histologic picture previously associated with Whipple's is seen in this group of patients. A report of Whipple's disease in a Haitian woman with AIDS and cardiac Kaposi's sarcoma may well have represented systemic *M. avium* infection, although no cultures were reported (34). Even without culture data, acid-fast stain of tissue can be used to differentiate between the two conditions. Microorganisms in Whipple's do not stain with acid-fast tissue stains.

Both the Fite stain for *Mycobacterium leprae* and the Ziehl-Neelsen stains reacted with the bacterial inclusions in macrophages in our case, although the staining intensity was greater with the Fite stain. When PAS-positive macrophages are seen within intestinal biopsies, a diagnosis of Whipple's disease should no longer be made until acid-fast stains have been carried out.

SUMMARY

At endoscopy, a 30-year-old man with acquired immune deficiency syndrome (AIDS), Kaposi's sarcoma, diarrhea, and unexplained malabsorption showed erythematous macular duodenal lesions consistent with Whipple's disease by histology and electron microscopy. Symptoms did not respond to tetracycline. Subsequent cultures revealed systemic *Mycobacterium avium (M. avium)* infection. Tissue from this patient, from patients with Whipple's disease and from a macaque with *M. avium* were compared. All contained PAS-positive macrophages but *M. avium* could be distinguished by positive acid-fast stains and a difference in pattern of indirect immunofluorescence staining with bacterial typing antisera. PAS-positive macrophages in the intestinal lamina propria are no longer pathognomonic of Whipple's disease. Ultrastructural and histological similarities between Whipple's disease and *M. avium* infection suggest that both are manifestations of immune deficits limiting macrophage destruction of particular bacteria after phagocytosis. *M. avium* must be considered in the differential diagnosis of diarrhea in patients with AIDS and other immunosuppressed conditions.

ACKNOWLEDGMENTS

We wish to acknowledge the kindness of Dr. S. Prahalada, pathologist at the California Primate Research Center in Davis, California, who provided paraffin-embedded tissue from the macaque with *M. avium* for use in the investigation. We also wish to acknowledge the help and advice of Dr. William Margaretten, pathologist at San Francisco General Hospital, in interpreting the postmortem findings in this case, and the assistance of Donald Halteman in preparing this manuscript.

REFERENCES

1. Schmidt JD, Yeager H, Smith EB, Raleigh JW: Cutaneous infection due to a Runyon group III atypical mycobacterium. Am Rev Respir Dis 106:469–471, 1972
2. Cole GW, Gebhard J: *M. avium* infection of the skin resembling lepromatous leprosy. Br J Dermatol 101:71–74, 1979
3. Zakowski P, Fligiel S, Berlin GW, Johnson BL: Disseminated *Mycobacterium avium-intracellulare* infection in homosexual men dying of acquired immunodeficiency. JAMA 248:2980–2982, 1982
4. Elliott JL, Hoppes WL, Platt MS, Thomas JG, Patel IP, Gansar A: The acquired immunodeficiency syndrome and *Mycobacterium avium-intracellulare* bacteremia in a patient with hemophilia. Ann Intern Med 98:290–293, 1983
5. Keren DF, Weisburger WR, Yardley JH, Salyer WR, Arthur RR, Charache P: Whipple's disease: Demonstration by immunofluorescence of similar bacterial antigens in macrophages from three cases. Johns Hopkins Med J 139:51–59, 1976
6. Centers for Disease Control: Update: Acquired immunodeficiency syndrome (AIDS)—United States. Morbidity and Mortality Weekly Report 32(52):688–691, 1984
7. Gottlieb MS, Schroff R, Schanker HM, Weisman JD, Fan PT, Wolf RA, Saxon A: *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men: Evidence of a new acquired cellular immunodeficiency. N Engl J Med 305:1425–1431, 1981
8. Kornfeld H, Vande Stouwe RA, Lange M, Reddy MM, Grieco MH: T-Lymphocyte subpopulations in homosexual men. N Engl J Med 307:729–731, 1982
9. DeStefano E, Friedman RM, Friedman-Kien AE, Goedert JJ, Henriksen D, Preble OT, Sonnabend JA, Vilček J: Acid-labile human leukocyte interferon in homosexual men with Kaposi's sarcoma and lymphadenopathy. J Infect Dis 146:451–455, 1982
10. Drew WL, Mintz L, Miner RC, Sands M, Ketterer B: Prevalence of cytomegalovirus infection in homosexual men. J Infect Dis 143:188–192, 1981
11. Siegal FP, Lopez C, Hammer GS, Brown AE, Kornfeld SJ, Gold J, Hassett J, Hirschman SZ, Cunningham-Rundles C, Adelsberg BR, Parham DM, Siegal M, Cunningham-Rundles S, Armstrong D: Severe acquired immunodeficiency in male homosexuals, manifested by chronic perianal ulcerative herpes simplex lesions. N Engl J Med 305:1439–1444, 1981
12. Volini F, Colton R, Lester W: Disseminated infection caused by Battey type mycobacteria. Am J Clin Pathol 43:39–46, 1965
13. Fainstein V, Bolivar R, Mavligit G, Rios A, Luna M: Disseminated infection due to *Mycobacterium avium-intracellulare* in a homosexual man with Kaposi's sarcoma. J Infect Dis 145:586, 1982
14. Sohn CC, Schroff RW, Kliewer KE, Lebel DM, Fligiel S: Disseminated *Mycobacterium avium-intracellulare* infection in homosexual men with acquired cell-mediated immunodeficiency: A histologic and immunologic study of two cases. Am J Clin Pathol 79:247–252, 1983
15. Greene JB, Sidhu GS, Lewin S, Levine JF, Masur H, Simberkoff MS, Nicholas P, Good RC, Zolla-Pazner SB, Pollock AA, Tapper ML, Holzman RS: *Mycobacterium avium-intracellulare:* A cause of disseminated life-threatening infection in homosexuals and drug abusers. Ann Intern Med 97:539–546, 1982
16. Masur H, Michelis MA, Wormser GP, Lewin S, Gold J, Tapper ML, Giron J, Lerner, CW, Armstrong D, Setia U, Sender JA, Siebken RS, Nicholas P, Arlen Z, Maayan S, Ernst JA, Siegal FP, Cunningham-Rundles S: Opportunistic infection in previously healthy women. Initial manifestations of a community acquired cellular immunodeficiency. Ann Intern Med 97:533–539, 1982

17. Poon M-C, Landay A, Prasthofer EF, Stagno S: Acquired Immunodeficiency syndrome with *Pneumocystis carinii* pneumonia and *Mycobacterium avium-intracellulare* infection in a previously healthy patient with classic hemophilia. Ann Intern Med 98:287–290, 1983
18. Ammann AJ, Cowan MJ, Wara DW, Weintrub P, Dritz S, Goldman H, Perkins HA: Acquired immunodeficiency in an infant: Possible transmission by means of blood products. Lancet 1:956–958, 1983
19. Gillin JS, Urmacher C, West R, Shike M: Disseminated *Mycobacterium avium-intracellulare* infection in acquired immunodeficiency syndrome mimicking Whipple's disease. Gastroenterology 85:1187–1191, 1983
20. Owen WF: Sexually transmitted diseases and traumatic problems in homosexual men. Ann Intern Med 92:805–808, 1980
21. Dritz SK, Ainsworth TE, Back A, Boucher LA, Garrard WF, Palmer RD, River E: Patterns of sexually transmitted enteric diseases in a city. Lancet 2:3–4, 1977
22. Kean BH: Venereal amebiasis. NY State J Med 76:930–931, 1976
23. Schmerin MJ, Jones TC, Klein H: Giardiasis: association with homosexuality. Ann Intern Med 88:801–803, 1978
24. William DC, Shookhoff HB, Felman YM, DeRamos SW: High rates of enteric protozoal infections in selected homosexual men attending a venereal disease clinic. Sex Transm Dis 5:155–157, 1978
25. Keren DF: Whipple's disease: A review emphasizing immunology and microbiology. CRC Crit Rev Clin Lab Sci 14:75–108, 1981
26. Bhagavan BS, Hofkin GA, Cochran BA: Whipple's disease: Morphologic and immunofluorescence characterization of bacterial antigens. Hum Pathol 12:930–936, 1981
27. DuBoulay CEH: An immunohistochemical study of Whipple's disease using the immunoperoxidase technique. Hum Pathol 13:925–929, 1982
28. Volpicelli NA, Salyer WR, Milligan FD, Bayless TM, Yardley JH: The endoscopic appearance of the duodenum in Whipple's disease. Johns Hopkins Med J 138:19–23, 1976
29. Kotler DP, Gaetz HP, Lange M, Holt PR: The enteropathy of AIDS. Ann Intern Med 101:421–428, 1984
30. Myerowitz RL: Cytomegalovirus infection. *In* The Pathology of Opportunistic Infections. New York, Raven Press, 1983, pp 161–176
31. Sesline DH, Schwartz LW, Osburn BI, Thoen CO, Terrell T, Holmberg C, Anderson JH, Henrickson RV: *Mycobacterium avium* infection in three rhesus monkeys. J Am Vet Med Assoc 167:639–645, 1975
32. Costallat LF, deCastro AFP, Simon F, Diniz L de SM, Giorgi W: Mycobacteriosis in monkeys: A report of two cases. Vet Med 73:651–655, 1978
33. Smith EK, Hunt RD, Garcia FG, Fraser CEO, Merkal RS, Karlson AG: Avian tuberculosis in monkeys: A unique mycobacterial infection. Am Rev Respir Dis 107:469–471, 1973
34. Autran BR, Gorin I, Leibowitch M, Laroche L, Escande JP, Hewitt J, Marche CL: AIDS in a Haitian woman with cardiac Kaposi's sarcoma and Whipple's disease. Lancet 1:767–768, 1983