Bacillary Angiomatosis and Bacillary Peliosis in Patients Infected with Human Immunodeficiency Virus: Clinical Characteristics in a Case-Control Study

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Clinical characteristics associated with bacillary angiomatosis and bacillary peliosis (BAP) in patients with human immunodeficiency virus (HIV) infection were evaluated in a case-control study; 42 case-patients and 84 controls were matched by clinical care institution. Case-patients presented with fever (temperature, >37.8°C; 93%), a median CD4 lymphocyte count of 21/mm^3, cutaneous or subcutaneous vascular lesions (55%), lymphadenopathy (21%), and/or abdominal symptoms (24%). Many case-patients experienced long delays between medical evaluation and diagnosis of BAP (median, 4 weeks; range, 1 day to 24 months). Case-patients were more likely than controls to have fever, lymphadenopathy, hepatomegaly, splenomegaly, a low CD4 lymphocyte count, anemia, or an elevated serum level of alkaline phosphatase (AP) ($P < .001$). In multivariate analysis, a CD4 lymphocyte count of <200/mm^3 (matched odds ratio [OR], 9.9; $P < .09$), anemia reflected by a hematocrit value of <0.36 (OR, 19.7; $P < .04$), and an elevated AP level of ≥2.6 μkat/L (OR, 23.9; $P < .05$) remained associated with disease after therapy with zidovudine was controlled for. BAP should be considered an AIDS-defining opportunistic infection and should be included in the differential diagnosis for febrile, HIV-infected patients with cutaneous or osteolytic lesions, lymphadenopathy, abdominal symptoms, anemia, or an elevated serum level of AP.

Bacillary angiomatosis is a newly described disease occurring primarily in patients infected with HIV [1]. The lesions of bacillary angiomatosis are vascular-proliferative and contain protuberant endothelial cells surrounded by bacilli that are visualized by electron microscopy, Warthin-Starry staining, or both [2, 3]. The classic and most frequently reported manifestations of bacillary angiomatosis are cutaneous [1, 3–6], but the characteristic histopathologic features have also been found in the lymph nodes, brain, bronchi, and bone [1]. Parenchymal bacillary peliosis is a vascular-proliferative disease affecting the liver (peliosis hepatis) and spleen; these lesions are typified by numerous thin-walled, blood-filled spaces surrounded by bacilli in the adjacent parenchyma [7–9]. Because bacillary angiomatosis and bacillary peliosis are different manifestations of the same infection, the term bacillary angiomatosis–bacillary peliosis (BAP) will be used herein to refer to this disease process.

For editorial response, see pages 801–2.

In 1990 Relman et al. used molecular biological techniques for identifying uncultured pathogens to establish that the causative organism of BAP was closely related to *Bartonella* (formerly *Rochalimaea*) *quintana* [10], the causative agent of trench fever [11]. Just a few years earlier, a new species [12], later named *Bartonella henselae* [13, 14], was isolated from the blood of several HIV-infected patients with fever and bacteremia [12–14]. The 16S ribosomal DNA sequence of this organism was found to be identical to that of the bacterial DNA extracted from BAP lesions by Relman et al. [10]. Soon thereafter, Koehler et al. isolated a bacterium from cutaneous and osseous lesions of bacillary angiomatosis; surprisingly, it was found that either *B. henselae* or *B. quintana* caused these lesions [15]. The genera *Bartonella* and *Rochalimaea* were subsequently unified within the family Bartonellaceae on the basis of their genetic relatedness and of historical precedence [16].

In addition to BAP, the recognized spectrum of illness caused by the *Bartonella* species has continued to expand and includes cat-scratch disease (due to *B. henselae*), endocarditis,

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This study was approved by the Committee for Human Research, University of California, San Francisco, and all participants or their surrogates provided informed consent before enrollment in the study.

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and relapsing fever [17–21]. Traumatic exposures to cats (cat scratches, cat bites, or both) were recognized as risk factors for both BAP and cat-scratch disease [2, 18]. Subsequently, the domestic cat was identified as a major vertebrate reservoir for *B. henselae;* as many as 41% of cats have been documented to be bacteremic with this organism [22]. Most recently, Spach et al. reported on a cluster of 10 inner-city patients with *B. quintana* bacteremia [23], suggesting that *B. quintana* has the capacity to cause urban outbreaks, in addition to the rural epidemics that ravaged soldiers fighting in the trenches during World War I [11].

While the histopathologic [3, 7] and microbiological [10, 12–16, 22] features of BAP have been intensively investigated, the clinical features of this disease have been described only in reports of cases and small series [1, 3–10, 15, 22] and have never been studied systematically in HIV-infected patients. Because HIV infection causes many clinical and laboratory abnormalities, defining the clinical characteristics specific for BAP requires comparison with the characteristics of HIV-infected controls. The two components of our study included (1) identification of the clinical features of 42 HIV-infected patients with histologically confirmed BAP and (2) a case-control study conducted to identify symptoms, signs, and laboratory values significantly associated with BAP.

Methods

A case was defined as an illness in a patient ≥18 years of age with HIV infection and histologically confirmed BAP. Persons with biopsy-confirmed BAP were culled from the hospitals and clinics of the University of California, San Francisco, from San Francisco Bay area community clinicians, and from clinicians and pathologists outside the San Francisco Bay area who were informed of the study [2]. Before participants were enrolled, the lesions of all potential case-patients were examined by a pathologist (P. E. L.) experienced in the diagnosis of BAP [1, 2, 4–7]. The criteria for histologic confirmation were described previously [2].

Eligible case-patients and controls were asked by their health care provider to participate. Two adult HIV-infected controls were selected for each case-patient; case-patients and controls were matched by the clinical institution or primary care physician. Matched controls were selected from the same inpatient ward service or primary-care-physician outpatient clinic at which the BAP of case-patients was diagnosed. A copy of the inpatient or outpatient schedule registry used to identify matched controls was maintained to verify that each control was selected in a systematic manner, as well as to confirm that controls were interviewed as close as possible to the same day on which the BAP case-patient (or surrogate) was interviewed [2]. On average, study investigators called 3 eligible controls per case. When contacted by phone, only 5 eligible controls declined to participate, and 84 controls were enrolled. The 42 case-patients and 84 controls in this study were enrolled between 1987 and 1991; subjects were systematically queried about environmental risk factors for BAP, and the findings were described previously [2].

Using a standardized questionnaire, three investigators interviewed case-patients (in person or by telephone), surrogates (relatives or close associates of case-patients who had dementia or had died), and controls about demographic characteristics and symptoms in the 6 months before diagnosis of BAP (for case-patients) or enrollment in the study (for controls). This 6-month period will be referred to as the reference period. Clinic and hospital records of case-patients and controls were reviewed to collect information about medical history, physical findings, laboratory values, and antimicrobial therapy during the reference period. The study was approved by the Committee for Human Research of the University of California, San Francisco, and all participants or their surrogates provided informed consent before enrollment in the study.

Statistical Analysis

For dichotomous variables, univariate matched odds ratios (ORs) with 95% confidence intervals (CIs) were calculated by the Mantel-Haenzel method with use of Epi-Info (Centers for Disease Control and Prevention [CDC], Atlanta), a statistical software package [24]. The Mann-Whitney *U* test was used to compare distributions of continuous variables between cases and controls. For the continuous laboratory variables of CD4 cell count, hematocrit value, alkaline phosphatase (AP) level, and aspartate aminotransferase (AST) level, we also evaluated the distribution of values among (1) case-patients with peliosis of the liver or spleen (parenchymal BAP), (2) case-patients without parenchymal BAP, and (3) controls.

Step-wise conditional logistic regression was performed to determine which laboratory variables were independently associated with disease with use of the SAS procedure (SAS Institute, Cary, NC) based on the Cox proportional hazards model [25]. Laboratory variables were included in the multivariate analysis if they were univariately associated with disease or were potential confounders (e.g., history of treatment with zidovudine in the preceding 6 months). For the multivariate analysis, the continuous laboratory values of hematocrit, AP, and AST were dichotomized with methods described by Hosmer and Lemeshow [26]. The variables were dichotomized as follows: <0.36 vs. ≥0.36 for hematocrit; ≥2.6 vs. <2.6 μkat/L (≥153 U/L vs. <153 U/L) for AP; and ≥1.3 vs <1.3 μkat/L (≥78 U/L vs. <78 U/L) for AST.

Between 1987 and 1992, the CDC surveillance case definition of AIDS was based on the development of an HIV-associated opportunistic infection or malignancy [27]. The 1993 revised and expanded surveillance case definition of AIDS identifies HIV-infected patients with a CD4 lymphocyte count of <200/mm^3 as having an AIDS-defining condition, with or without an accompanying HIV-associated opportunistic infection, malignancy, or condition [28]. Therefore, the CD4 lymphocyte counts were dichotomized as <200/mm^3 vs. ≥200/mm^3. To test the robustness of this model, we repeated the

multivariate analyses with the substitution of CD4 lymphocyte counts dichotomized by methods described by Hosmer and Lemeshow [26] ($<100/mm^3$ vs. $\geq 100/mm^3$), the same methods used to dichotomize the other laboratory values (hematocrit, AP, and AST).

Finally, although we were unable to normalize laboratory values from different laboratories, all analyses that used cutoff points maintained the matched nature of the data. Therefore, reported normal laboratory value ranges were identical for matched case-control sets (i.e., laboratory work was performed by the same clinical institution). If a cutoff point introduced a misclassification bias, both case-patients and controls would be misclassified (nondifferential misclassification) and the measure of effect would be biased toward the null [29].

Results

Forty-two case-patients and 84 controls were enrolled in the study; surrogate interviews were necessary for 14 case-patients (13 deceased and 1 with HIV-associated dementia). The case-patient and control groups did not significantly differ with regard to sex (95% vs. 96% males), age (median, 37 vs. 36 years), race (93% vs. 93% white), ethnicity (79% vs. 77% non-Hispanic), or HIV risk factors (e.g., 21% vs. 15% injection-drug users; $P = .41$). Seventy-one percent of case-patients and controls received their medical care in the San Francisco Bay area of California. Nine (21%) of the 42 case-patients were interviewed about a reference period ≥ 1 year before that of their matched controls.

Clinical Characteristics of Case-Patients

The presenting complaints of the 42 case-patients were as follows: cutaneous vascular lesions in 13 (31%) (7 of these also had weight loss, 1 had abdominal pain, and 4 had asymmetric lymphadenopathy); subcutaneous nodules or masses in 10 (24%) (2 also had weight loss and 1 had abdominal pain); asymmetric lymphadenopathy but no cutaneous or subcutaneous lesions in 9 (21%); and abdominal symptoms (anorexia, nausea, vomiting, or abdominal pain) and fever, without cutaneous or subcutaneous lesions or asymmetric lymphadenopathy, in 10 (24%). Case-patients were more likely than controls to have had fever (temperature of >37.8°C) and a decreased appetite; on physical examination case-patients were more likely than controls to have lymphadenopathy, hepatomegaly, and splenomegaly (table 1).

The median time from development of symptoms to evaluation by a physician was 4 weeks for case-patients with cutaneous lesions or lymph node lesions and 5 weeks for those with subcutaneous lesions (table 2). However, case-patients with liver or spleen lesions were evaluated within a median of 1 week after symptoms developed. The time between medical evaluation and pathologic diagnosis of BAP was a median of 4 days (0.5 week) for patients with cutaneous vascular lesions, 8 weeks for patients with subcutaneous nodules or masses, 5 weeks for patients with lymph node lesions, and 4 weeks for patients with liver or splenic lesions (table 2). Notably, BAP in three case-patients with liver or spleen lesions was not diagnosed until after death (attributed to BAP). There was a trend toward earlier diagnosis among case-patients whose symptoms began after 1989; for 75% of patients whose symptoms began in 1990 or later, BAP was diagnosed within 2 months of their presentation to their physician, while only 55% of case-patients whose symptoms began before 1990 had their BAP diagnosed within 2 months of presentation (OR, 2.5; CI, 0.6–11.8; $P = .2$).

Table 1. Symptoms and signs of 42 HIV-infected patients with bacillary angiomatosis-peliosis, compared with those of 84 matched controls.

Symptom or sign	No. (%) Patients	Controls	Matched OR	95% CI
Fever*	38 (93)	45 (54)	17.0	2.7–108
Poor appetite	29 (69)	33 (39)	3.5	1.5–8.1
Lymphadenopathy	32 (76)	31 (37)	4.7	2.0–11.0
Hepatomegaly	21 (50)	9 (11)	12.0	3.4–42
Splenomegaly	14 (33)	2 (2)	Undef.†	5.9–Undef.†

* Temperature of >37.8°C.

† Conditional maximum-likelihood estimates were used to determine one-sided confidence intervals for undefined (undef.) odds ratios.

BAP was confirmed by biopsy of cutaneous tissue in 11 case-patients (26%); subcutaneous tissue in 4 (10%); subcutaneous tissue and bone or bone marrow in 3 (7%); subcutaneous tissue and liver or spleen in 2 (5%); lymph nodes in 11 (26%); and liver or spleen in 11 (26%). BAP in 52% of case-patients was diagnosed solely on the basis of the histopathologic appearance of lymph node, liver, or spleen lesions (i.e., biopsy specimens were obtained from only one site).

Antimicrobial Therapy

There was no protective effect identified between antimicrobial therapy with several classes of antibiotics during the reference period and the development of BAP. Antibiotics evaluated included sulfonamides (trimethoprim-sulfamethoxazole and dapsone [43% of case-patients and 48% of controls; OR, 0.8; CI, 0.4–1.8; $P = 0.7$]), ciprofloxacin (12% of cases and 20% of controls; OR, 0.4; CI, 0.4–2.7; $P = 0.3$), penicillins (penicillin, ampicillin, and dicloxacillin), a variety of cephalosporins, macrolides (erythromycin and clarithromycin), aminoglycosides (gentamicin and amikacin), and rifampin. However, among case-patients with a CD4 lymphocyte count of <200 cells/mm^3, there was an increasing trend toward a protective effect from treatment with sulfonamides (43% of cases vs. 59% of controls; OR, 0.6; CI, 0.2–1.4; $P = 0.3$), and ciprofloxacin (10% of cases vs. 28% of controls; OR, 0.1; CI, 0.04–1.03; $P = 0.06$).

Table 2. Length of time from onset of symptoms to medical evaluation and from medical evaluation to diagnosis for HIV-infected patients with bacillary angiomatosis-peliosis.

Interval	Lesion	Median time period (range)
Onset of symptoms to medical evaluation	All lesions	4 w (1 d to 5 mo)
	Skin	4 w (1 d to 5 mo)
	Subcutaneous mass	5 w (3 d to 2 mo)
	Lymph node	4 w (4 d to 2 mo)
	Liver or spleen	1 w (1 d to 3 mo)
Medical evaluation to diagnosis	All lesions	4 w (1 d to 24 mo)
	Skin	0.5 w (1 d to 3 mo)
	Subcutaneous mass	8 w (2 d to 13 mo)
	Lymph node	5 w (7 d to 24 mo)
	Liver or spleen	4 w (3 d to 2 mo)

Laboratory Characteristics

Evaluation of laboratory values for case-patients and controls revealed some significant differences (table 3). The median CD4 lymphocyte count among case-patients was 21/mm^3, compared with 186/mm^3 for controls ($P < .001$). The median hematocrit value was lower among case-patients than among controls ($P < .001$). The median AP and AST levels were higher among case-patients than among controls ($P < .001$ for both variables). There was no difference between case-patients and controls with regard to the following laboratory values: WBCs, creatinine, bilirubin, and alanine aminotransferase. Case-patients with peliosis of the liver or spleen (parenchymal BAP) had lower hematocrit levels (median, 0.27 vs. 0.33; $P < .007$) and higher AP levels (median, 409 U/L vs. 126.5 U/L; $P < .06$) than case-patients without parenchymal BAP. Case-patients with parenchymal BAP also had CD4 lymphocyte counts lower than those of case-patients without parenchymal disease (median, 17.5/mm^3 vs. 30.0/mm^3, respectively), but this difference was not statistically significant ($P < .37$).

Severity of HIV Disease

Univariate odds ratios for major medical diseases and recent laboratory values are listed in table 4. Using the 1987 surveillance case-definition for AIDS [27], we noted no difference in the frequency of AIDS between case-patients and controls (45% vs. 52%; OR, 0.8; 95% CI, 0.3–1.7; $P > .5$). Among these patients with AIDS, no AIDS-defining opportunistic infection or malignancy [27, 28] was associated with BAP disease. For example, 6 (32%) of 19 case-patients and 24 (55%) of 44 controls with AIDS had *Pneumocystis carinii* pneumonia (OR, 0.4; 95% CI, 0.1–1.4; $P > .15$); 3 (16%) of 19 case-patients and 12 (27%) of 44 controls had Kaposi's sarcoma (OR, 0.5, 95% CI, 0.1–2.3; $P > .5$). When the 1993 revised and expanded surveillance case definition for AIDS was used [28], case-patients were more likely than controls to be classified as having AIDS (94% vs. 54%; OR, 10.7; 95% CI, 2.5–45.3; $P < .001$).

Multivariate Models

Continuous variables were dichotomized as described in the methods section. Two-way interaction terms were examined and found not to be significant, so they were not included in

Table 3. Median and range of selected laboratory values for HIV-infected patients with bacillary angiomatosis-peliosis and for controls.

	Median (range)		
Laboratory value	Patients (n = 42)*	Controls (n = 84)*	P value†
CD4$^+$ lymphocyte count (cells/mm^3)	21 (1–228)	186 (0–910)	<.001
Hematocrit	0.30 (0.15–0.42)	0.38 (0.14–0.51)	<.001
Alkaline phosphatase			
μkat/L	3.2 (1.0–19.5)	1.5 (2.2–12.3)	<.001
U/L	192 (60–1,171)	91 (13–738)	
Aspartate aminotransferase			
μkat/L	1.26 (0.25–26.47)	0.57 (0.15–4.98)	<.001
U/L	76 (15–1,588)	34 (9–299)	
Alanine aminotransferase			
μkat/L	0.70 (0.03–17.23)	0.54 (0.17–5.55)	>.4
U/L	42 (2–1,034)	33 (10–333)	
Bilirubin			
μmol/L	9 (3–116)	9 (3.4–137)	>.4
mg/dL	0.6 (0.2–6.8)	0.5 (0.2–8.0)	

* The number of cases and controls used in the analysis of each laboratory value varied because data were not available for all variables for all subjects.

† Mann-Whitney U test.

Table 4. Clinical variables among HIV-infected patients with bacillary angiomatosis-peliosis and among controls.

Clinical variable	No. (%) with variable		Univariate matched OR	95% CI
	Patients*	Controls*		
AIDS (1987 case definition†)	19 (45)	44 (52)	0.7	0.32–1.6
CD4 lymphocyte count ($<200/mm^3$)	33 (94)	37 (53)	10.7	2.5–45.3
Hematocrit (<0.36)	33 (80)	23 (29)	22.5	5.0–102.5
Alkaline phosphatase (≥2.6 μkat/L [≥153 U/L])	22 (56)	8 (10)	19.5	4.3–83.6
Aspartate aminotransferase (≥1.30 μkat/L [≥78 U/L])	19 (49)	11 (14)	5.5	2.1–14.8

* The number of cases and controls used for each laboratory value varied because for some subjects data were not available for all variables.

† Of the CDC [21].

multivariate models. A matched, stepwise multivariate model containing treatment with zidovudine (in the reference period), CD4 lymphocyte count ($<200/mm^3$ vs. $\geq 200/mm^3$), and levels of hematocrit, AP, and AST resulted in the deletion of AST levels from further analyses. A model that included zidovudine therapy, hematocrit, and CD4 lymphocyte count revealed that BAP was associated with both anemia (hematocrit of <0.36) (adjusted OR, 14.2; CI, 1.8–114.5; $P < .02$) and a CD4 lymphocyte count of $<200/mm^3$ (adjusted OR, 10.6; CI, 1.3–82.9; $P < .03$). Similar results were obtained in the matched, stepwise model when the CD4 lymphocyte count was dichotomized by the method of Hosmer and Lemeshow [26]; BAP was associated with both anemia (hematocrit of <0.36) (adjusted OR, 8.6; CI, 1.5–51.6; $P < .003$) and a CD4 lymphocyte count of $<100/mm^3$ (adjusted OR, 19.1; CI, 2.9–127.3; $P < .0001$).

Addition of AP to the three-variable model resulted in significant improvement of the model (log-likelihood ratio test); elevated AP (OR, 23.9; CI, 1.1–497.6; $P < .05$), anemia (adjusted OR, 19.7; CI, 1.3–307.7; $P < .04$), and a CD4 lymphocyte count of $<200/mm^3$ (adjusted OR, 9.9; CI, 0.7–132.2; $P < .09$) were associated with disease (table 5). In this model, only 30 matched sets could be used, resulting in a loss of statistical power. Although the statistical significance of CD4 lymphocyte count was marginal in the 4-variable model, the point estimate for the association between low CD4 lymphocyte count and BAP remained elevated (adjusted OR, 9.9) and stable, consistent with an association between BAP and low CD4 lymphocyte count. With substitution of a CD4 lymphocyte count dichotomized by the method of Hosmer and Lemeshow ($<100/mm^3$ vs. $\geq 100/mm^3$) [26], the matched, 4-variable model demonstrated an association between elevated AP (adjusted OR, 19.4; CI, 1.6–227.8; $P < .02$) and anemia (adjusted OR, 20.9; CI, 1.9–230.7; $P < .02$). A model with additional variables (zidovudine therapy and CD4 lymphocyte count) could not be estimated.

Discussion

There are numerous reports of single cases and small case series describing patients with BAP [1, 3–10, 15, 22]. We systematically examined a large series of BAP patients and controls to define more clearly the clinical manifestations and characteristics associated with BAP in HIV-infected patients. A broad clinical spectrum of presenting symptoms and signs was noted among BAP patients. Cutaneous and subcutaneous lesions, considered the most common manifestation of bartonella infection in the immunocompromised host, were found in only 55% of our case-patients; 21% of patients presented with lymphadenopathy alone, while 24% had only fever and abdominal symptoms. BAP should therefore be included in the differential diagnosis for HIV-infected patients who present with lymphadenopathy or with fever and abdominal symptoms, in addition to those presenting with cutaneous and subcutaneous lesions.

Patients with BAP disease were more severely immunocompromised (median CD4 lymphocyte count, $21/mm^3$) than controls ($186/mm^3$). Only two (6%) of 35 case-patients had CD4 lymphocyte counts of $\geq 200/mm^3$. These findings suggest that BAP is a disease that occurs late in the course of HIV infection and should be considered an AIDS-defining opportunistic infection.

On the basis of the relatively long interval between presentation of patients to a physician and a histologic diagnosis of BAP disease (table 2), it is evident that many physicians did not consider bartonella infection in their initial differential diagnosis. While the median time to diagnosis was only 4 days for cutaneous lesions, for other presentations the median was much longer, possibly because cutaneous lesions are readily accessible for biopsy and because most published descriptions of BAP are of cutaneous lesions [1, 3–10, 15, 22]. Although not statistically significant, the trend toward earlier diagnosis among patients whose symptoms began after 1989 suggests that there is a greater awareness of BAP. However, both before and after 1990, a high percentage of cases of BAP were diagnosed ≥2 months after the patients presented to a physician.

Patients with parenchymal BAP presented to their physicians earlier than patients with cutaneous or lymphatic bacillary angiomatosis (table 2). Patients with hepatic and splenic lesions

Table 5. Matched, stepwise multivariate models of laboratory variables associated with bacillary angiomatosis-peliosis.

Model	No. of patients in model	No. of controls in model	Variables in model	Matched OR	95% CI
1	34	59	CD4 lymphocyte count*	10.7	2.5–45.3
2	30	51	CD4 lymphocyte count*	10.6	1.3–82.9
			Hematocrit†	14.2	1.8–114.5
			Zidovudine therapy‡	0.2	0.1–1.02
3	30	51	CD4 lymphocyte count*	9.9	0.7–132.2
			Hematocrit†	19.7	1.3–307.0
			Zidovudine therapy‡	0.2	0.04–1.2
			Alkaline phosphatase level§	23.9	1.1–497.6

* $<200/mm^3$ vs. $\geq 200/mm^3$.
† <0.36 vs. $\geq .36$.
‡ Yes vs. no.
§ ≥ 2.6 μkat/L vs. <2.6 μkat/L.

had more severe symptoms and signs of infection. Because not all patients in our study were systematically evaluated for parenchymal lesions, it is possible that some patients with cutaneous and lymphatic bacillary angiomatosis had undetected liver or spleen lesions, which may have led to underestimation of hepatic or splenic involvement in these patients. Despite this possibility, patients with documented parenchymal BAP had lower hematocrit levels than did those with bacillary angiomatosis in the absence of hepatic and splenic lesions, a finding consistent with a more severe infection.

In the case-control study, after CD4 lymphocyte count and zidovudine therapy were controlled for in the multivariate analysis, anemia remained significantly associated with BAP, a finding suggesting that these infections (presumed due to either *B. henselae* or *B. quintana* bacilli [15]) cause anemia independent of HIV infection and chemotherapy with zidovudine. Anemia may result from bone marrow infiltration by *Bartonella* bacilli; such bone marrow infiltration has been reported previously in several patients with BAP [9, 30]. Anemia could also result from a prolonged infection (anemia of chronic disease), or from increased red cell destruction due to splenomegaly. After adjusting for anemia and CD4 lymphocyte counts, we found that an elevated AP level remained associated with BAP. LeBoit et al. described eight patients with bacillary peliosis hepatis who had elevated AP levels, which were attributed to infiltration of hepatic parenchyma with bacilli [7]. Unidentified bone infiltration or destruction may have contributed to an elevated AP level.

Although this study found a trend to suggest that prophylaxis with either sulfonamides or ciprofloxacin is protective against BAP among HIV-infected patients with CD4 lymphocyte counts of $<200/mm^3$, the protective effect was not statistically significant. However, because of the small number of matched sets available for this analysis, we may not have had enough power to confirm a protective effect if one exists. Chemoprophylaxis with both the sulfonamides and ciprofloxacin should be further evaluated.

In summary, BAP is a recently recognized, potentially fatal disease associated with a broad spectrum of presentations in severely immunocompromised HIV-infected patients. The clinical and laboratory characteristics found to be associated with BAP in this study will be useful to clinicians in recognizing this emerging treatable disease. BAP may not be considered at initial presentation, and delays in diagnosis can result in increased morbidity and mortality. More work is needed to determine the prevalence of bartonella infections and BAP and to develop prevention strategies for the immunocompromised population. However, at present, timely recognition of BAP by the clinician remains the most important intervention for this disease.

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