

Significance of CD4+ T-cell count in the management of appendicitis in patients with HIV

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SUMMARY

Identification of complicated appendicitis (CA) is critical to the management of appendicitis. However, previous studies have not investigated indicators of CA among patients with HIV or whether it is safe to use conservative treatment for appendicitis in these patients. Among 322 patients with appendicitis, we identified 14 who had HIV. Six of them were operated and 8 were treated with antibiotics; CA was diagnosed in 4. Patients with HIV and CA had a significantly lower CD4+ T-cell count than those with uncomplicated appendicitis. A white blood cell count lower than $7.4 \times 10^9/L$ was observed exclusively in patients with CA. No patient with HIV whose appendicitis was treated conservatively died or experienced a recurrence. We discuss our findings, which suggest the possibility of conservative treatment of appendicitis in patients with HIV and identification of CA by low CD4+ T-cell count.

Appendicitis has been described in connection with HIV infection, and initially researchers emphasized higher incidence and etiological uniqueness in patients with HIV. In particular, opportunistic infection has been considered to be connected to the pathogenesis of acute appendicitis or an appendicitis-like condition among patients with HIV. In addition, earlier studies of patients with appendicitis who had HIV revealed increased risk of perforation and high perioperative mortality. Some authors suspect that a depressed level of cell-mediated immune response and delay in surgical interventions increase complication in patients with HIV. Other authors reported that lack of elevated white blood cell (WBC) count and delay in presentation to the emergency department were responsible for the higher morbidity and mortality. The general consensus among researchers is that accurate diagnosis is a key to successful management.

Gangrenous appendicitis, appendicitis with perforation and appendicitis with abscess formation are often collectively called complicated appendicitis (CA) because of the higher morbidity and mortality. Some laboratory markers, such as elevation of WBC and C-reactive protein (CRP) levels, have been found to be useful for the diagnosis of CA. Moreover, studies have proven the importance of various computed tomography (CT) findings in the context of diagnosis of appendicitis, including discontinuity of the appendiceal wall, appendiceal diameter, appendicolithiasis and retroperitoneal involvement. Various clinical parameters have been investigated to identify CA. However, to our knowledge, no previous study has been conducted to identify CA in patients with HIV.

We studied 322 patients in whom appendicitis was diagnosed at a single urban university hospital (tertiary referral centre for patients with HIV) between Jan. 1, 2007, and Dec. 31, 2012 (119 female, 203 male). The mean age was 31 (range 4–94) years. Patients were assigned to the CA group if perforation of the appendix, abscess formation, or purulent peritoneal fluid was described in surgical reports; if histology reports indicated

perforation of the appendix, abscess formation, peritonitis, or gangrenous appendicitis; or if abscess was found in proximity to the appendix on CT and appendiceal rupture was the only possible explanation after all diagnostic examinations had been conducted. The remaining patients were included in the uncomplicated appendicitis (UA) group. In all, 121 patients had CA (37.5%). All multidetector noncontrast or contrast CT images were reviewed for signs of appendicitis, abscess, perforation and appendicolithiasis and for maximal appendiceal diameter. Data on baseline characteristics, WBC, CRP, CD4 level and serum RNA detection were retrieved from medical records.

Patients were divided into 2 groups depending on their HIV seropositivity. Fourteen patients (13 men, 1 woman, mean age 37 yr) had HIV (4.3%; Table 1). As to radiographical signs, appendicolith was observed in only 4 patients with HIV despite it being commonly associated with appendicitis and CA in the general population. The mean diameter of the appendix was similar in both groups.

Ten patients with HIV were admitted and treated with antibiotics (71.4%), and 4 were treated as outpatients with antibiotics (28.6%). Surgery was performed in 6 patients, including all 4 patients with appendicolithiasis.

In total, CA was diagnosed in 121 patients, 4 of whom had HIV. Immunosuppression was associated with CA in both groups: CA was found in 3 of 4 (75%) patients in whom HIV had progressed to AIDS, in both patients with chronic kidney disease, in the only patient who had undergone bone marrow transplant, in 1 of 2 patients with liver cirrhosis and in 2 of 3 patients with diabetes.

There were some distinguishing clinical features among patients with CA who also had HIV. Notably, CD4+ T-cell count was significantly lower in those with CA than in those UA (222.5 v. 571.0 cells/mm³, $p =$

0.023). Three of the 4 patients with HIV and CA had HIV RNA detection. The mean WBC count in these 4 patients was considerably lower than in patients with HIV and UA (6.8 v. $14.9 \times 10^9/L$). A WBC count lower than $7.4 \times 10^9/L$ was observed exclusively in patients with both HIV and CA. Lower CRP level was also more frequent in these patients (41.0 v. 96.2 nmol/L). Immunosuppression was related to the presence of CA in patients with HIV. Finally, larger appendiceal diameter, which is associated with severe appendicitis in the general population, was also associated with CA in patients with HIV.

There were no hospital deaths in either group. There was no readmission associated with nonoperative management in the HIV-positive group. Thirteen of the patients with HIV continued regular follow-up at the HIV clinic for more than 20 months. None of these patients experienced a recurrence of appendicitis or died from illness during the follow-up period.

Our study showed higher risk of CA among immunosuppressed patients and in patients with HIV who had lower CD4+ T-cell counts. This finding is in agreement with previous reports that CD4+ T-cell count reduction was associated with increased all-cause morbidity and mortality. Low WBC count is another indicator of CA in patients with HIV. Importantly, a CT finding of large appendiceal diameter served as an indicator of CA regardless of the status of HIV infection. These findings highlight the importance of identification of CA and suggest the possibility of conservative treatment among selected patients with HIV. More studies are needed to investigate the effectiveness of conservative management in patients with HIV.

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Table 1. Comparison of clinical variables in patients with HIV

Category	Group; mean (95% CI)*		OR (95% CI)
	CA, n = 4	UA, n = 10	
Appendix diameter, mm	14.4 (10.7–18.1)	9.7 (6.6–12.8)	—
Appendicolith, no.	2	2	4 (0.3–48.7)
CD4+ T-cell count, cells/mm ³ †	222.5 (19.6–425.5)	571.0 (402.2–739.9)	—
RNA detection†	3	4	3.8 (0.3–51.4)
WBC count, $\times 10^9/L$ ‡	6.8 (6.2–7.4)	14.9 (9.6–20.2)	—
CRP level, nmol/L	41.0 (0–83.9)	96.2 (39.1–153.3)	—
Age, yr	33.8 (27.8–39.8)	37.7 (33.9–41.5)	—
Sex, male:female	4:0	9:1	—

CA = complicated appendicitis; CI = confidence interval; CRP = C-reactive protein; OR = odds ratio; UA = uncomplicated appendicitis; WBC = white blood cell.
*Unless otherwise indicated.
†In 1 patient with UA, CD4 count and RNA detection were not obtained.
‡Shapiro-Wilk normality test = 0.8717, $p = 0.044$; Fisher exact test = 12.6, $p = 0.07$.