

Chronic Plasma Cell Endometritis in Hysterectomy Specimens of HIV-Infected Women: A Retrospective Analysis

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ABSTRACT

Objective: Abnormal uterine bleeding is a common and troublesome problem in human immunodeficiency virus (HIV)-infected women. We sought to evaluate endometrial pathology among HIV-infected women requiring hysterectomy to explore if endometritis may be common among these patients.

Methods: We performed a retrospective analysis of uterine pathology specimens obtained from HIV-infected and control patients requiring hysterectomy in two urban hospitals between 1988 and 1997 matched for age, surgical indication, and history of gonadotropin-releasing hormone (GnRH) use. Cases were evaluated for the presence of plasma cells and assigned a grade between 0 and 3.

Results: Indications included cervical dysplasia (4), carcinoma in situ (2), abnormal uterine bleeding (3), and adnexal mass (3). Some degree of abnormal uterine bleeding occurred in all cases. Plasma cell endometritis was twice as common in HIV-infected women compared to HIV-negative specimens (11/11 versus 11/22) ($P < 0.05$). Plasma cell endometritis was also of a higher grade in specimens from HIV-infected women than in controls ($P = 0.001$).

Conclusion: Chronic endometritis was common and of a higher grade among HIV-infected women requiring hysterectomy in our series. Diagnosis and treatment of endometritis should be considered in HIV-infected women with uterine bleeding and/or tenderness. We speculate that antiretroviral and/or antimicrobial treatment for endometritis may effectively treat endometritis and eliminate the need for surgery in some HIV-infected women. We suggest that consideration and treatment of endometritis in HIV-1 infected women being evaluated for possible hysterectomy has the potential to reduce costs and morbidity for patients and providers who may be exposed during surgical procedures. *Infect. Dis. Obstet. Gynecol.* 6:186-190, 1998. © 1998 Wiley-Liss, Inc.

KEY WORDS

human immunodeficiency virus; endometritis; bleeding; hysterectomy

Menstrual irregularities are common among human immunodeficiency virus (HIV)-infected women.^{1,2} Studies report bleeding abnormalities in approximately one third of HIV-infected women.² As treatment and survival rates improve for HIV-infected patients, care of the reproductive tract will

become increasingly important. It therefore becomes important to understand the underlying mechanisms for abnormal menstrual bleeding in HIV-infected patients. We hypothesize that HIV-infected women suffer endometritis more frequently than uninfected women and that endome-

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TABLE 1. Age, indication for hysterectomy, and history of GnRH use for HIV-infected patients and matched controls

HIV-Infected patients				Controls			
Patient	Age (y)	Indication	GnRH use	Patient	Age (y)	Indication	GnRH use
1	32	Cervical dysplasia	No	1A	30	Cervical dysplasia	No
				1B	34	Cervical dysplasia	No
2	25	Cervical dysplasia	No	2A	25	Cervical dysplasia	No
				2B	25	Cervical dysplasia	No
3	41	Menorrhagia	Yes	3A	41	Menorrhagia	Yes
				3B	41	Menorrhagia	Yes
4	22	Cervical dysplasia	No	4A	29	Cervical dysplasia	No
				4B	31	Cervical dysplasia	No
5	25	Abnormal uterine bleeding, dysmenorrhea	Yes	5A	29	Abnormal uterine bleeding, dysmenorrhea	Yes
				5B	26	Abnormal uterine bleeding, dysmenorrhea	Yes
6	35	Symptomatic fibroids	Yes	6A	35	Symptomatic fibroids	Yes
				6B	37	Symptomatic fibroids	Yes
7	36	Pelvic mass	No	7A	33	Pelvic mass	No
				7B	43	Pelvic mass	No
8	33	Pelvic mass	No	8A	40	Pelvic mass	No
				8B	41	Pelvic mass	No
9	33	Cervical dysplasia	No	9A	38	Cervical dysplasia	No
				9B	38	Cervical dysplasia	No
10	29	Cervical dysplasia	No	10A	26	Cervical dysplasia	No
				10B	28	Cervical dysplasia	No
11	30	Cervical dysplasia	No	11A	32	Cervical dysplasia	No
				11B	33	Cervical dysplasia	No

TABLE 2. Histopathology results for HIV-infected patients and controls^a

HIV-Infected patients				Controls			
Patient	Plasma cells	Grade (0-3)	Other pathology	Patient	Plasma cells	Grade (0-3)	Other pathology
1	Yes	3	LSIL/adenomyosis	1A	Yes	1	LSIL
				1B	Yes	2	LSIL
2	Yes	2	HSIL	2A	Yes	1	HSIL, HPV
				2B	Yes	1	LSIL
3	Yes	1	Chronic cervicitis/fibroids	3A	Yes	1	Chronic cervicitis/fibroids
				3B	Yes	1	Chronic cervicitis/fibroids
4	Yes	2	HSIL/condyloma acuminatum	4A	No	0	None
				4B	No	0	HPV
5	Yes	1	Chronic cervicitis	5A	Yes	1	None
				5B	No	0	Chronic cervicitis
6	Yes	2	Fibroids	6A	Yes	1	Fibroids
				6B	No	0	Adenomyosis/fibroids
7	Yes	3	TOA/fibroids	7A	No	0	Chronic cervicitis, adenomyosis, endometriosis
				7B	No	0	TOA/fibroids
8	Yes	1	Mucinous cystadenoma	8A	Yes	2	Mucinous cystadenoma
				8B	No	0	Mucinous cystadenoma
9	Yes	1	HPV	9A	No	0	Adenomyosis
				9B	No	0	HPV
10	Yes	3	Adenomyosis	10A	Yes	0	None
				10B	Yes	1	None
11	Yes	2	HPV	11A	No	1	HPV
				11B	No	0	None

^aAbbreviations: LSIL, low-grade squamous-intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; HPV, human papillomavirus; TOA, tuboovarian abscess.

TABLE 3. Frequency of endometriosis based on surgical indication among HIV-infected patients and controls*

Indication	HIV-Infected patients	Controls
	No. with chronic endometritis	No. with chronic endometritis
Cervical dysplasia	4/4	6/12
Abnormal uterine bleeding	5/5	4/6
Adnexal mass	2/2	1/4
Total	11/11 (100%)	11/22 (50%)

*P < 0.05.

TABLE 4. Breakdown by grade of plasma cell endometritis specimens

Grade	HIV-Infected patients	Controls
	No.	No.
0	0/11 (0%)	11/22 (50%)
1	4/11 (36%)	9/22 (41%)
2	4/11 (36%)	2/22 (9%)
3	3/11 (27%)	0/22 (0%)

tritis may be a treatable cause of abnormal uterine bleeding in HIV-infected women.

SUBJECTS AND METHODS

To evaluate this hypothesis, we retrospectively compared the clinical history and hysterectomy specimens of HIV-positive patients with HIV-negative control women to determine 1) the frequency of endometritis, 2) the severity of endometritis, and 3) the specific symptoms associated with histologic endometritis. We used databases in two urban hospitals in Denver, Colorado, to identify 11 HIV-infected patients who underwent hysterectomy between 1992 and 1997. Indications included severe cervical dysplasia (4 cases), carcinoma in situ (2 cases), abnormal uterine bleeding (3 cases), and adnexal mass (2 cases). Each case was matched with two controls for age (± 1 year), past use of gonadotropin-releasing hormone (GnRH)-agonist therapy, and indication for surgery. Controls either had a negative HIV test or were presumed to be HIV-negative. A staff pathologist reviewed slides from each case. All slides had identifying informa-



Fig. 1. Histologic examination of grade-3 HIV-infected patient #7, demonstrating plasma cell infiltrate diagnostic of chronic endometritis. Routine hematoxylin and eosin stain magnified at 40x.

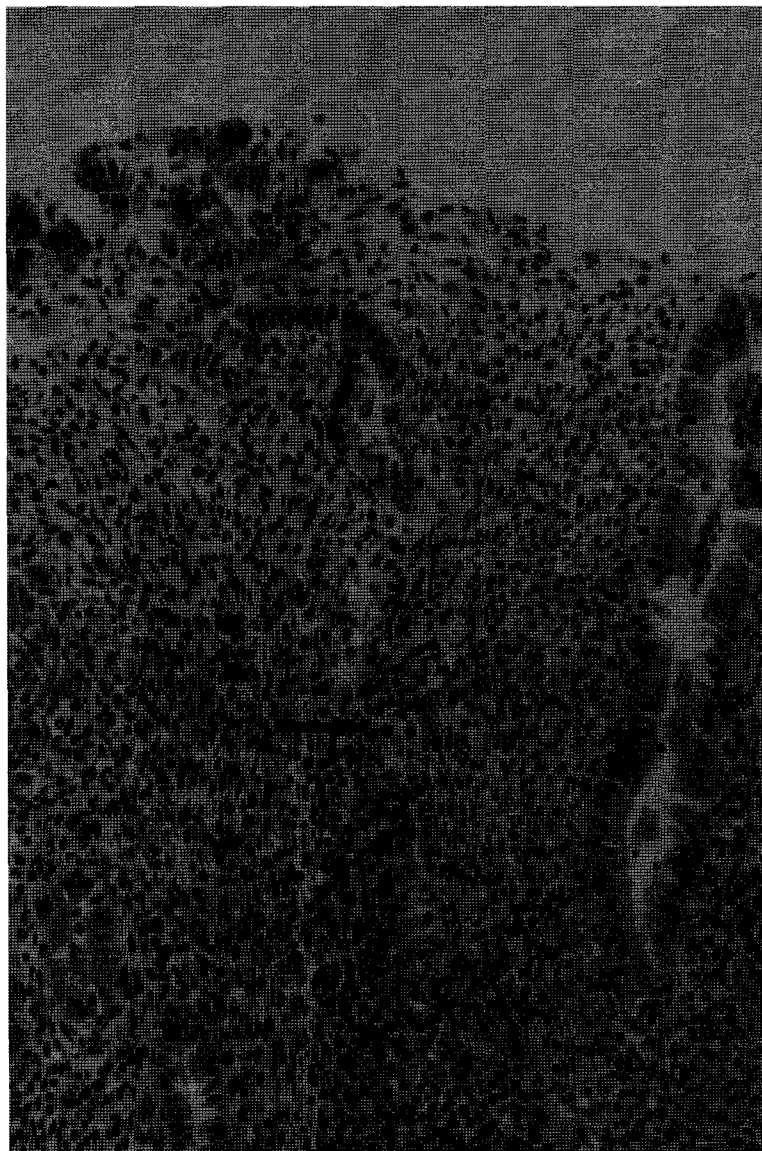


Fig. 2. Histologic examination of grade-3 HIV-infected patient #10, demonstrating plasma cell infiltrate diagnostic of chronic endometritis. Routine hematoxylin and eosin stain magnified at 400 \times .

tion removed. A diagnosis of chronic endometritis was based on presence of plasma cells within the endometrium.³ Specimens were assigned a semi-quantitative score based upon the total number of plasma cells as follows: grade 0 for obscured plasma cells, grade 1 for 1-3, grade 2 for 4-9, and grade 3 for 10 per high power (400 \times) field.⁴ At least 10 fields were examined for each specimen. After blinded scoring, we compared plasma cell endometritis among HIV-positive and HIV-negative women using chi-square tests for proportions and trend; alpha was set at 0.05.

RESULTS

Tables 1 and 2 show the presence of plasma cells, grade of endometritis, and other pathologic diagnoses. The HIV-infected patients demonstrated significantly greater incidence of plasma cell endometritis when compared with controls (11/11 versus 11/22; $P < 0.05$). The HIV-infected women were significantly more likely to have grade I endometritis ($P = 0.001$, odds ratio = 6), grade II endometritis (odds ratio = 20), and grade III endometritis (odds ratio = 48) when compared with controls

(Tables 3 and 4). Figures 1 and 2 show plasma cells in the endometrium.

DISCUSSION

In this convenience sample of reproductive-aged women who were treated with hysterectomy, we found 1) more frequent chronic endometritis among HIV-infected women and 2) more severe chronic endometritis than in control women. A link between endometritis and HIV infection has been noted previously by Peuchmaur and colleagues.⁵ These investigators used *in situ* hybridization in endometrial samples obtained from an HIV-infected woman and suggested that HIV is a direct cause of endometritis in HIV-infected women.⁵ There may be other causes of endometritis among HIV-infected women. HIV-induced impairment of mucosal and systemic immune functions could reduce reproductive tract host defenses and increase susceptibility to spread of lower reproductive tract microorganisms into the endometrium. Additionally, women with HIV may be at increased risk for acquiring sexually transmitted infections or other conditions, including bacterial vaginosis, that are associated with endometritis.^{5,6}

This study is limited by its retrospective design and the small number of cases. However, our findings of an increased frequency and severity of endometritis among HIV-infected women requiring hysterectomy suggest that an active approach to diagnosis and medical treatment of endometritis should be considered prior to surgical management of abnormal uterine bleeding in HIV-infected

women. Treatment with antiretroviral and indicated antimicrobial agents aimed at eliminating endometritis may obviate the necessity for surgical treatment and reduce the risks and costs for both patients and care providers. We presently provide HIV-infected women with triple antiretroviral treatment, including a protease inhibitor, prior to elective gynecologic surgery.

Further studies are needed to determine 1) the pathogenic mechanisms, 2) the microorganisms associated with endometritis in HIV-infected women, and 3) optimal ways to treat endometritis in these women.

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