Coexistent human immunodeficiency virus infection and systemic lupus erythrematosus: case report

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Abstract Human immunodeficiency virus infection (HIV) manifests a variety of clinical features resembling systemic lupus erythrematosus (SLE), and must be distinguished from one another. HIV infection in SLE is rare and it has been suggested that the coexistence of HIV infection may ameliorate SLE activity. We report a case of SLE complicated by HIV infection. During 15 weeks of pregnancy, her SLE activity exacerbated and was found to be co-infected with HIV. The pregnancy was terminated. Over 5 years of follow up, her SLE coexisting with HIV infection has been quiescent without any immunosuppressive drugs and she has not had any opportunistic infections from HIV infection.

บทคัดย่อ **การติดเชื้อไวรัสภูมิคุ้มกันบกพร่องในผู้ป่วยเอสแอลอี**

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อาการแสดงทางคลินิกในผู้ป่วยติดเชื้อไวรัสภูมิคุ้มกันบกพร่อง (HIV) สามารถให้อาการได้คล้ายคลึงกับโรคเอสแอลอี (SLE) จำเป็นต้องให้การวินิจฉัยแยกโรคจากกัน อุบัติการณ์การเกิดการติดเชื้อไวรัสภูมิคุ้มกันบกพร่องในผู้ป่วยเอสแอลอีพบได้ไม่บ่อยแต่เมื่อเกิดขึ้นพบว่าไวรัสภูมิคุ้มกันบกพร่องทำให้ความรุนแรงของโรคเอสแอลอีลดลง ได้รายงานผู้ป่วยหญิง 1 ราย หลังการวินิจฉัยว่าเป็นโรคเอสแอลอี 3 ปี ขณะตั้งครรภ์ 15 สัปดาห์ มีอาการของโรคเอสแอลอีรุนแรงขึ้นร่วมกับตรวจพบมีการติดเชื้อไวรัสภูมิคุ้มกันบกพร่อง หลังยุติการตั้งครรภ์ อาการของโรคเอสแอลอีที่มีการติดเชื้อไวรัสภูมิคุ้มกันบกพร่องสงบลงโดยไม่ต้องควบคุมโดยยากดภูมิต้านทาน หลังการติดตาม 5 ปีไม่พบอาการของโรคเอสแอลอีและการติดเชื้อฉวยโอกาสจากการติดเชื้อไวรัสภูมิคุ้มกันบกพร่อง

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Introduction

Human immunodeficiency virus infection shares a variety of clinical features of many organs and systems. Rheumatic, dermatologic, gastrointestinal, neurologic, hematologic and renal disorders have been reported[1]. HIV infection may also present manifestations of autoimmune diseases including systemic lupus erythrematosus. HIV infection in SLE is rare. There have been reports suggested that HIV infection might attenuate SLE activity. The imbalance of immunological states in both diseases may be a factor. Here we report a case of HIV infection in SLE with pregnancy. As far as we know this is the first reported case in Thailand.

A case report.

A 23-year-old Thai female presented in June 1992 with fever, malar rash, polyarthritis, alopecia and oral ulcers. Initial laboratory studies revealed hematocrit of 29 %, white blood count of 5400/mm^3 with 27% lymphocyte. Urinalysis showed protein free, and no urine sediment. LE test was positive, ANA positive, anti DNA positive of titer 1:2560, anti Sm positive, C_3 level of 0.16 mg/dl. She was diagnosed as having systemic lupus erythrematosus and was treated with prednisolone 45 mg/day. Her symptoms improved and prednisolone dose was gradually reduced to 20 mg/day.

In March 1993, she developed fever and generalized seizure. This was attributed to SLE. The prednisolone was increased to 60 mg/day. She responded well and no episode of seizure occurred. She was followed up with low dose prednisolne.

In November 1994 after losing to follow up for 2 months, she was admitted with high fever and generalized edema. Physical examination showed

Table 1 Laboratory manifestations of reported patient

Date	06/92	03/93	11/94	02/95	06/95	10/95	01/96	07/96
B.P.	120/80	160/110	160/110	100/80	100/60	100/60	100/60	100/60
Hct %	29	21	19	32	32	35	32	nd
Albuminuria	Neg	Neg	3+	2+	2+	2+	2+	Neg
BUN(mg/dl)	10	10	29	8	12	12	14	10
Cr (mg/dl)	0.8	0.9	1.4	0.5	0.4	0.6	0.4	0.5
Uric acid	6.1	6.2	9.9	9.1	5.7	4.5	4.2	5.1
Albumin	3.6	4.0	1.6	2.7	3.5	3.9	3.4	4.9
Globulin	2.9	3.3	2.4	2.4	3.3	4.2	4.5	3.7
anti ds DNA	+	nd	Neg	nd	nd	Nd	Neg	nd
ANA	+	+	nd	nd	nd	+	+	nd
C3	0.16	0.21	0.21	nd	nd	Nd	nd	nd
total T lymph	nd	nd	900	nd	2750	5130	3440	nd
CD4	nd	nd	170	nd	610	750	585	nd
CD8	nd	nd	700	nd	2230	4490	2641	nd
CD4/CD8	nd	nd	0.25	nd	0.27	0.17	0.22	nd
CD8 %	nd	nd	0.77	nd	0.81	0.87	0.76	nd

nd: not done

BP 180/110 mmHg, pitting edema 4+, tenderness of left cervical lymphnodes and enlargement of uterus. Hematocrit was 21%, white blood cells count 14,700/mm^3, 94 % neutrophiles, 5% lymphocyte, platelet 320,000, and Coombs' test negative. The urine was positive 4+ for protein. The sediment contained 20 to 30 red cells and 8 to10 white cells. Ultrasound of uterus showed 15 weeks fetus. The test for HIV by ELISA was positive. Confirmatory test by Western blot was also positive. CD4 count was 170. CD4/CD8 ratio was 0.25. Her husband without history of intravenous drug use was also positive for HIV test. Active lupus nephritis with pregnancy was diagnosed. She was treated with prednisolone 60 mg/day. After family counseling in the presence of active lupus nephritis and HIV infection, the therapeutic abortion was performed. The prednisolone was tapered to 5 mg/day in 2 months, and discontinued. Over 5 years of follow up, she has been well and her SLE activity has been in remission (table 1). She has not had any opportunistic infections from HIV.

Discussion

Acquired immunodeficiency syndromes caused by human immunodeficiency virus (HIV) infection was originally described in 1981[2]. It is recognized that it is an end result of an immune dysfunction characterized by a loss of CD4 T helper cells[3] and high frequency of opportunistic infections. Ziegler and Stites in 1986 made a hypothesis that HIV infection is an autoimmune disease directed at the immune system[4]. HIV infection has clinical manifestations in many organs and has many clinical features that are similar to autoimmune diseases such as rheumatoid arthritis, Reiter's syndrome, vasculitis, and systemic lupus erythrematosus[5] HIV infection and SLE share many clinical, serologic features, and renal pathologies[6], so they must be distinguished from one another. Both HIV infection and SLE are characterized by immune dysregulation and autoantibody production. The common immunological features of HIV infection and SLE are summarized in table 2. In HIV infection, antinuclear antibodies (ANA) may be positive in titer of 1:20 to 1:160, but anti DNA antibodies and anti Sm are not found[7].The presence of antinuclear antibodies may contribute to polyclonal B cell activation, and diffuse hypergammaglobulinemia in HIV infection patient[8].

Table 2 Immunological features in AIDS and SLE

Common features in AIDS and SLE

1. B cell activation
2. Increased immune complexes
3. Increased levels of β 2-microglobulin
4. Acid labile α interferon production
5. Decreased autologous MLR
6. Decreased lymphokine production (IL1, IL2)
7. Decreased NK activity
8. Viral etiology
9. Lymphopenia
10. Lymphocytotoxic antibodies
11. Decreased response to mitogens
12. Skin test anergy
13. Natural autoantibody production
14. Multiple organ involvement

Differences between AIDS and SLE

1. CD8 T lymphocyte
   - Relative increase in AIDS (decreased CD4/CD8 ratio)
   - Decreased number and function in SLE
2. CD4 T lymphocyte
   - Depleted in AIDS
   - Normal or depleted in SLE

Table 3 Cases of human immunodeficiency virus infection in systemic lupus erythrematosus

Author	Number of patient	Age (year)	Sex	First diagnosis	Risk factor	Renal pathology
Adult cases						
Kopelman RG[7]	1	23	f	SLE	Renal transplantation	LN type V
Furie RA[11]	3	37	m	SLE	IVDU	ND
		40	f	SLE	Heterosexual	ND
		30	m	SLE	IVDU	ND
Yeh CK[12]	1	24	f	SLE	Blood transfusion	ND
Bambery P[13]	1	23	m	SLE	Blood transfusion	ND
Molina JF[14]	2	26	m	SLE	Homosexual	ND
		43	f	SLE	Heterosexual	ND
Maradona JA[15]	1	28	f	HIV	IVDU	ND
Lu I[16]	1	22	f	SLE	Heterosexual	ND
Byrd VM[17]	1	23	m	SLE	Unknown	ND
Contreras G[18]	2	44	f	HIV	Heterosexual	LN type IV
		37	m		Heterosexual	Collaspsing focal sclerosis (HIV)
Kudva YC[19]	1	39	m	HIV	Homosexual	LN type V
Cimmino MA[20]	1	22	m	SLE	IVDU	ND
Fernandez-Miranda C[21]	1	35	f	SLE	Heterosexual	ND
Fox RA[22]	1	30	f	SLE	Heterosexual	ND
Chang BG[23]	2	32	f	SLE	Unknown	LN type IV, HIVAN
		27	m	HIV	Homosexual	LN type IV
Reported case	1	23	f	SLE	Heterosexual	ND
Pediatric cases						
Strauss J[24]	2	2 1/2	m	HIV	Congenital HIV	?LN type IIb
		3 1/12	m	HIV	Congenital HIV	LN type III
D'Agati V[25]	1	2 1/2	m	HIV	Congenital HIV	LN type V
Chang BG[23]	2	10	m	HIV	Congenital HIV	LN type III, V
		5	f	HIV	Congenital HIV	LN type V, HIVAN

m: male, f: female, IVDU: intravenous drug use, ND: not done, LN: lupus nephritis, HIVAN: HIV associated nephropaty

SLE also has false positive results in HIV test by ELISA technique and indeterminate result by Western blot test[9]. They may result from cross reactivity of retroviral particle which make possibility of a retrovirus as a causative agent in pathogenesis of SLE[10], by impurities in the antigenic preparation used in ELISA or Western blot test, and by production of antibodies due to polyclonal antibodies stimulation such as in HIV infection.

Concurrent HIV infection and SLE is rare only 19 cases in adults[7,11-23] and 5 cases in children[23-25] have been reported in the literature (table 3). The rare co-incidence of HIV infection and SLE may be epidemiologic as SLE occurs predominantly in female whereas HIV infection occurs in male. The immunologic disturbances from HIV infection that may attenuate the clinical manifestation of SLE or SLE may be protection of HIV infection[26] make less co-incidence of both diseases. There were 12 males and 13 females including this reported case. Ages of patients were between 2.5 to 44 years. Thirteen patients were diagnosis as having SLE before being infected with HIV. Furie[11] and Molina[14] described the improvement of SLE when infected with HIV. The clinical and serologic features were improved when CD4 T lymphocyte decreased, and SLE was flare when CD4 increased by azathymidine treatment. They suggested that improvement of SLE might be due to CD4 depletion and supported the role of CD4 in the pathogenesis of SLE[27].

Our patient fulfilled the ARA criteria for diagnosis of SLE[28]. She had periodic flare of SLE despite being treated with prednisolone before complicated by HIV infection. Her pregnancy was considered to be the cause of SLE flare. Pregnancy may increase SLE exacerbation in 20-50%[29] and prone to develop preeclampsia[30]. Low C3 level and anti DNA antibody help to differentiate SLE exacerbation and preeclampsia[30]. C3 level increases in normal pregnancy. Failure of C3 level to rise or decreased C3 level has been associated with SLE exacerbation[31] and increases risk of abortion[32]. CD4 decreases during normal pregnancy[33], and turns to be normal level after delivery. Pregnancy can also accelerate HIV induced CD4 depletion, increases risk of opportunistic infection and increases mortality[34]. After therapeutic abortion and discontinuing all immunosuppressive drugs, her symptoms of SLE ameliorated. Her SLE and HIV infection has been quiescent for 5 years of follow up. CD4 lymphocyte was rising and higher than that when her SLE exacerbated. CD8 and CD8 percentage increased. It was different from reports from Furie and Molina. The mechanism that attenuated SLE progression may be from CD4T lymphocyte dysfunction before CD4 depletion or from increased CD8 and increased CD8 percentage caused by HIV infection which may support the role of decreased CD8 number and function in the pathogenesis of SLE[35].

Though T cell abnormalities are important in the pathogenesis of SLE, however the immune mechanisms that occur in SLE are multiple, complex and unclear. Other immunological mechanisms, including inappropriate induction of cytokines system[36], may play role. Transforming growth factor-β(TGF-β) has immunoregulatory properties to enhance monocyte function[37] and to suppress both T and B cell proliferation and function[38]. Mice that lacked TGF-β produce SLE-like autoantibodies[39] and die of an autoimmune like illness[40]. So TGF-β may play role in suppressing activity of SLE. Ohtsuka found that lymphocytes from SLE patients produced less TGF-β and interleukin 2(IL-2) than normal control and spontaneous IgG production was suppressed by adding TGF-β and IL-2[41,42]. Monthly intramuscular injection of cDNA encoding TGF-β gene decreased IgG production and increased survival in murine SLE[43]. Plasma TGF-β increased in HIV infection patients[44] and may suppress autoantibodies in SLE but may lead to extracellular matrix deposition and fibrosis[45]. Future investigations are needed to elucidate the pathogenesis of this phenomenon and provide insight into pathogenesis and treatment of SLE.

Conclusion

We report a case of coexisting HIV infection in SLE with pregnancy. Clinical improvement of SLE was observed when complicated by HIV infection, with low CD4, high CD8, and high CD8 percentage. Immunological regulatory defects other than CD4 depletion may play role to ameliorate SLE activity.

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