Detection of HTLV-1 in the Labial Salivary Glands of Patients with Sjögren's Syndrome: A Distinct Clinical Subgroup?

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ABSTRACT. ***Objective.*** To examine whether patients with Sjögren's syndrome (SS) can be distinguished based on the expression of human T cell lymphotrophic virus type I (HTLV-1) and, if so, whether the subgroups differ in their clinical features and serological measures.

Methods. Polymerase chain reaction (PCR) and nested PCR were used to amplify viral DNA from peripheral blood mononuclear cells (PBMC) in 53 patients with SS, using primers from the HTLV-1 pX, p19, pol, and tax regions. Minor salivary gland biopsy specimens from 33 patients with SS were examined for the presence of HTLV-1 p19 or tax proteins immunohistochemically. The sociodemographic, glandular, and extraglandular manifestations, and laboratory findings including autoantibodies, complement, and immunoglobulin levels, were analyzed.

Results. The HTLV-1 *tax* gene was detected in PBMC samples from 2 of 53 patients (3.8%), whereas the HTLV-1 *pX*, *p19*, and *pol* genes were not expressed. As well, 100% of PBMC samples from 4 family members of patients in whom the *tax* gene was detected also expressed the *tax* gene. Immunohistochemical staining for HTLV-1 p19 and tax was seen in 10 out of 33 (30.3%) patients with SS each. Overall, 14 (42.4%) patients expressed HTLV-1 p19 or tax proteins, and they had lower rheumatoid factor and C3 levels ($p = 0.015$ and $p = 0.005$, respectively) and higher lymphocyte counts ($p = 0.016$). The prevalence of glandular and extraglandular manifestations did not differ between the HTLV-1-positive and negative patients.

Conclusion. Our findings suggest that HTLV-1 in the salivary glands is involved in the pathogenesis of a subpopulation of SS, and HTLV-1-associated SS might have different immunological patterns than idiopathic SS. (First Release March 1 2012; J Rheumatol 2012;39:809–15; doi:10.3899/jrheum.111075)

Key Indexing Terms:
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The human T cell lymphotrophic virus type I (HTLV-1) is a human retrovirus associated etiologically with adult T cell leukemia[1]. Individuals infected with HTLV-1 may develop other diseases, including HTLV-1-associated myelopathy/tropical spastic paraparesis[2,3], HTLV-1-associated arthropathy[4], polymyositis[5], and uveitis[6]. HTLV-1 is transmitted vertically from mother to infant and the virus is maintained within ethnic groups[7]. HTLV-1 infection is clustered in Africa, Central and South America, and Japan[8]. Although the prevalence of HTLV-1 in southwest Japan is very high, HTLV-1 is uncommon in neighboring Korea. Recently, one study reported that the HTLV-1 seroprevalence rate was 0.007% in a Korean blood donor population[9].

Sjögren's syndrome (SS) is an autoimmune connective tissue disease characterized by the destruction of salivary and lacrimal glands, resulting in xerostomia and keratoconjunctivitis sicca, and the systemic production of autoantibodies[10]. The pathogenesis of SS remains unclear, but in genetically predisposed individuals, hormonal and environmental factors (i.e., virus) are thought to be capable of triggering this autoimmune exocrinopathy[11]. Among such factors, viral infections including Epstein-Barr virus, Coxsackie virus, human immunodeficiency virus (HIV), hepatitis C virus, and HTLV-1 could prompt epithelial cells to activate the immune system[12].

Retroviruses such as HTLV-1 and HIV infect immune system cells, resulting in the destruction or overstimulation of T cells, and act as potential triggers of autoimmune disease[13,14].

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Several studies have suggested an association between HTLV-1 and SS. For example, transgenic mice possessing the HTLV-1 *tax* gene developed an exocrinopathy resembling SS[15]. Some HTLV-1-infected patients with tropical spastic paresis develop features of SS[16]. A high seroprevalence rate of HTLV-1 and high prevalence of IgA class antibodies to HTLV-1 in the saliva of patients with SS in an area endemic for HTLV-1 has been reported[17,18]. Moreover, the accumulation and expression of HTLV-1 in the salivary glands of patients with SS has been described[19,20,21]. These observations suggest that HTLV-1 plays a role in the pathogenesis of SS.

However, the association of SS with HTLV-1 in regions where HTLV-1 is not endemic remains unclear. In addition, the clinical and serological differences in SS patients with and without this infection are not well characterized. We examined whether SS patients could be distinguished based on the expression of HTLV-1 in salivary glands. We describe the clinical features and serological characteristics of patients with HTLV-1-associated SS.

MATERIALS AND METHODS

Patients. The study group included 53 patients with primary SS. All patients met the diagnostic criteria proposed by the American-European Consensus Group criteria for primary SS[22]. Patients with serious systemic diseases, such as malignancy, viral hepatitis or liver cirrhosis, infection, and endstage renal disease, were excluded. Salivary gland tissues were obtained from minor lip biopsies in 33 patients.

The study was approved by the institutional review board of the Chonnam National University Hospital. All patients provided their written informed consent.

HTLV-1 molecular study. Cellular DNA was isolated from peripheral blood mononuclear cells (PBMC) of all 53 patients. Different regions of the HTLV-1 genome were amplified using polymerase chain reaction (PCR) or nested PCR with specific primer sets (Table 1)[23,24,25]. HTLV-1 proviral DNA *pX* and *p19* genes were detected using PCR, and the *pol* and *tax* genes were detected using nested PCR, as reported[26]. PCR products corresponding to the HTLV-1 tax fragment were purified and sequenced directly using an ABI Prism 3100 genetic analyzer with the BigDye Terminator v3.1 ready reaction kit (Applied Biosystems, Foster City, CA, USA).

Immunohistochemical staining for HTLV-1. Minor salivary gland biopsy specimens were fixed in formaldehyde and embedded in paraffin according to standard protocols. Hematoxylin and eosin staining was performed for histological evaluation. Sections (4 μm thick) were cut for immunohistochemistry. After washing 3 times in phosphate-buffered saline, the sections were incubated with the mouse anti-HTLV-1 p19 monoclonal antibody TP-7 (Abcam, Cambridge, MA, USA) and mouse monoclonal antibody to Tax, Lt-4 at dilutions of 1:100 and 1:250, respectively[27]. Positive immunoreactivity appeared as a brown color.

Clinical manifestations and laboratory tests. For clinical data, we assessed dryness of the eyes, enlargement of the parotid glands, photosensitivity, swollen hand or sclerotic skin, Raynaud's phenomenon (RP), joint pain, lymphadenopathy, renal disease, psychosis, interstitial lung disease, peripheral neuropathy, and autoimmune thyroid disease. Laboratory tests included the antinuclear antibody (ANA) titer, anti-Ro/SSA, anti-La/SSB, rheumatoid factor (RF) titer, C3, C4, IgG, IgA, IgM, peripheral white blood cell, lymphocyte and platelet counts, and hemoglobin level.

Statistical analysis. The Mann-Whitney U test or chi-square test was applied to determine the significance of associations between the presence of p19 or tax antibody in the minor salivary glands and the clinical manifestations of SS. For statistical evaluations of the results, $p < 0.05$ was considered statistically significant. All statistical analyses were conducted using SPSS for Windows v. 17.0 (SPSS, Chicago, IL, USA).

RESULTS

Patient characteristics and clinical manifestations. Fifty-three patients with SS were studied. The median age of the patients was 48 years (range 23–70), and 52 patients (98.1%) were women. Fifty-two patients (98.1%) had ocular symptoms, and dry mouth symptoms were observed in 52 patients (98.1%). A total of 45 of 52 (86.5%) patients had a positive result on Schirmer's I test, and 50 of 52 patients (96.2%) had a positive result on a salivary scan. Parotid gland swelling was observed in 15 (28.3%) patients. The most frequent extraglandular manifestation was arthralgia or arthritis (52.8%), followed by RP (30.2%), peripheral neuropathy (18.9%), lymphadenopathy (17%), and photosensitivity (15.1%; Table 2).

Detection of HTLV-1 DNA in PBMC. We examined the presence of HTLV-1 in DNA samples isolated from PBMC of 53 patients. Four independent regions of the HTLV-1 genome (pX, p19, pol, and tax) were amplified using PCR or 2-step

Table 1. Primer sequences used to identify HTLV-1 DNA.

Amplified Region	Primers	Sequence (5' – 3')	Reaction	Product Size, base-pair
pX	pX1	CCT CCG TCA GCT ACG ACA C	Single PCR	317
	pX2	GGA GCG CCG TGA GCG CAA G		
p19	p19a	CAC CCC TTT CCC TTT CAT TCA CGA	Single PCR	411
	p19b	CCG GCC GGG GTA TCC TTT T		
pol	HL110	CAA GCC TAG CTA CAT AAA C	Nested PCR	188
	HL111	GCG GCT ATT AAG ACC AGG AAG	(outer primer)	
	SK110-2	TCC CCT ACA ATC CAA CCA GCT C	Nested PCR	
	SK111	ATG GGT TTG TTT ATT GCT GAG GG	(inner primer)	
tax	HL43	ATG CTT ATT ATC AGC CCA CTT	Nested PCR	159
	HL44	AGG GTC TTA GAG GTT CTC TGG GT	(outer primer)	
	SK43	CCA GTC TAC GTG TTT GGA GA	Nested PCR	
	SK44	AGC CGA TAA CGC GTC CAT CGA	(inner primer)	

HTLV-1: human T cell lymphotrophic virus type I; PCR: polymerase chain reaction.

Table 2. Baseline characteristics of 53 patients with Sjögren's syndrome.

Median age, yrs (range)	48 (23–70)
Number men:women	1:52
Median followup, yrs (range)	2 (1–11)
Glandular manifestations (%)	
Ocular symptoms	52/53 (98.1)
Oral symptoms	52/53 (98.1)
Positive salivary scan	50/52 (96.2)
Positive findings in minor salivary glands	31/33 (93.9)
Positive Schirmer I test	45/52 (86.5)
Partoid gland swelling	15/53 (28.3)
Extraglandular manifestations (%)	
Arthralgia/arthritis	28/53 (52.8)
Raynaud's phenomenon	16/53 (30.2)
Peripheral neuropathy	10/53 (18.9)
Lymphadenopathy	9/53 (17.0)
Photosensitivity	8/53 (15.1)
Interstitial lung disease	4/53 (7.5)
Autoimmune thyroid disease	3/53 (5.7)
Renal tubular acidosis	3/53 (5.7)
Psychosis	1/53 (1.9)

nested PCR. The only region detected was the HTLV-1 tax region, which was amplified from the PBMC of 2 patients. The PCR product of the *tax* gene was sequenced directly in both the forward and reverse directions and the sequencing result confirmed the HTLV-1 *tax* gene. Therefore, the rate of detection of HTLV-1 tax in the PBMC of patients with SS was 2/53 (3.8%). Subsequently, we tested for HTLV-1 DNA in PBMC from family members of 2 patients who expressed HTLV-1 *tax* gene. Patient 1 was married with 2 sons, and her husband and younger son were studied; both were positive for the HTLV-1 *tax* gene by PCR, but not for the *pX*, *p19*, and *pol* genes. Patient 2 was married with 1 daughter and 1 son, and her husband and daughter were examined; both samples were positive for tax, but negative for the other 3 regions.

Detection of HTLV-1 p19 and tax antigens in the salivary glands. Minor salivary gland biopsies were performed in 33 patients. On salivary gland staining, 10 (30.3%) of 33 patients with SS were positive for HTLV-1 p19 antigen, and 10 (30.3%) patients were positive for tax antigen. Six of the patients (18.2%) expressed both p19 and tax. In total, 14 patients (42.4%) were positive for HTLV-1 p19 or tax antigens. In the positive cases, the p19 and tax antibodies stained the acinar and ductal epithelial cells. A representative case is shown in Figure 1. Of the 2 patients with HTLV-1 PCR-positive PBMC, Patient 1 expressed both p19 and tax antigens in the salivary gland, whereas Patient 2 expressed neither.

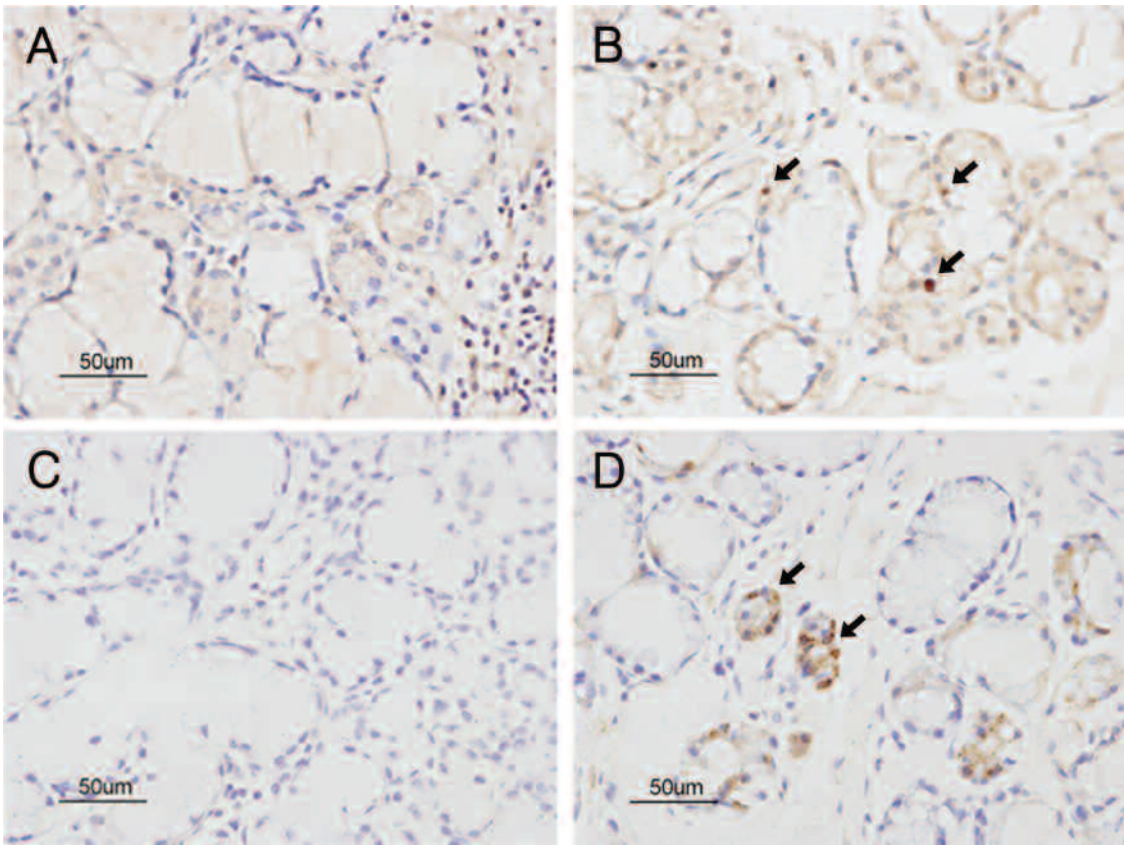

Figure 1. Representative immunohistochemistry for human T cell lymphotrophic virus type I (HTLV-1) antibody in minor salivary gland sections from different patients: (A) negative staining for p19; (B) positive staining for p19; (C) negative staining for tax; and (D) positive staining for tax. HTLV-1 p19 and tax were detected in acinar and ductal epithelial cells (original magnification ×400 for all panels). Arrows indicate antibody expression.

Characterization of HTLV-1-associated SS. Clinical and laboratory features of patients were compared according to the immunohistochemical results (Table 3). The p19-positive patients had lower anti-Ro/SSA titers, RF, and C3 levels ($p = 0.049$, $p = 0.019$, and $p = 0.018$, respectively). The lymphocyte count was significantly higher among the HTLV-1 p19-positive group than the negative group ($p < 0.001$). However, only RF was significantly different ($p = 0.016$) between the patients with and those without tax antibody. When analyzed according to the expression of p19 or tax, the patients who expressed p19 or tax antibodies to HTLV-1 had lower RF and C3 levels ($p = 0.015$ and $p = 0.005$, respectively) and higher lymphocyte counts ($p = 0.016$). The prevalence of glandular and extraglandular manifestations did not differ between the HTLV-1-positive and negative patients (Table 4). The 2 patients who were positive for the *tax* gene in PBMC had a short disease duration (< 1 year), and anti-Ro/SSA, anti-La/SSB, and RF were not detected in the patient who exhibited activity against HTLV-1 p19 and tax in the salivary gland.

DISCUSSION

We studied the presence of HTLV-1 in PBMC and minor salivary glands in patients with SS by PCR and immunohistochemical assays. In PBMC, the HTLV-1 sequence was detected in 2 of 53 (3.8%) patients by PCR analysis. All the samples were positive for tax, but negative for pX, p19, and pol. Using anti-HTLV-1 p19 or tax antibody staining, we found that HTLV-1 proteins were expressed in the minor salivary glands of 42.4% (14/33) of patients with SS. A total of 6 (18.2%) of 33 patients expressed both p19 and tax proteins. Viral expression was detected in acinar and ductal epithelial cells by immunohistochemical staining for HTLV-1 p19 and tax protein.

Table 3. Laboratory findings in patients with Sjögren's syndrome, with and without p19 or tax antibody in the salivary glands.

Characteristic	p19		tax		p19 or tax	
	Positive, n = 10	Negative, n = 23	Positive, n = 10	Negative, n = 23	Positive, n = 14	Negative, n = 19
Antinuclear antibody titer	164.0 ± 125.7	243.5 ± 121.8	220.0 ± 135.0	219.1 ± 125.8	191.4 ± 127.6	240.0 ± 125.1
High anti-Ro titer, > 200 U/ml (%)	4/10 (40)*	18/23 (78.3)	6/10 (60)	16/23 (69.6)	8/14 (57.1)	14/19 (73.7)
Anti-La titer, U/ml	33.1 ± 61.6	44.9 ± 63.6	56.7 ± 77.7	34.0 ± 55.1	41.7 ± 69.3	40.2 ± 58.8
Rheumatoid factor titer, IU/ml	14.8 ± 10.9*	54.6 ± 86.0	19.1 ± 20.1*	51.3 ± 84.5	18.1 ± 17.4*	58.7 ± 91.5
C3, mg/dl	87.6 ± 23.3*	108.7 ± 22.3	94.5 ± 15.3	105.7 ± 27.0	89.1 ± 21.6**	112.0 ± 21.9
C4, mg/dl	18.6 ± 6.2	21.6 ± 7.3	19.8 ± 6.1	21.1 ± 7.5	18.6 ± 6.2	22.3 ± 7.3
IgG, mg/dl	1409.9 ± 902.1	1952.8 ± 1304.8	1549.0 ± 1000.0	1892.3 ± 1297.0	1472.2 ± 965.2	2021.2 ± 1339.4
IgA, mg/dl	336.6 ± 191.9	303.2 ± 117.0	369.1 ± 181.5	289.0 ± 116.4	328.9 ± 168.8	302.2 ± 121.6
IgM, mg/dl	112.3 ± 43.2	167.9 ± 79.9	146.3 ± 70.5	152.8 ± 78.0	138.9 ± 64.1	159.5 ± 82.3
White blood cells, /mm^3	5510.0 ± 1969.5	5356.5 ± 2179.8	5130.0 ± 1566.3	5522.0 ± 2300.0	5421.4 ± 1763.8	5389.5 ± 2347.1
Hemoglobin, g/dl	12.6 ± 1.9	12.7 ± 0.8	12.4 ± 1.3	12.8 ± 1.2	12.7 ± 1.6	12.7 ± 0.9
Platelets, × 10^3/μl	228.3 ± 81.1	344.6 ± 528.0	477.4 ± 799.2	236.3 ± 77.8	404.7 ± 676.2	239.1 ± 82.2
Lymphocytes, /μl	2364.0 ± 948.0***	1228.2 ± 523.0	2014.0 ± 1165.3	1380.4 ± 605.9	2002.9 ± 1027.8*	1255.3 ± 519.5

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 4. Clinical manifestations in patients with primary Sjögren's syndrome, with and without p19 or tax antibody in the salivary glands.

Manifestations	p19		tax		p19 or tax	
	Positive, n = 10	Negative, n = 23	Positive, n = 10	Negative, n = 23	Positive, n = 14	Negative, n = 19
Glandular (%)						
Dryness of eyes	9/10 (90)	23/23 (100)	9/10 (90)	23/23 (100)	13/14 (92.9)	19/19 (100)
Dryness of mouth	9/10 (90)	23/23 (100)	9/10 (90)	23/23 (100)	13/14 (92.9)	19/19 (100)
Parotid gland enlargement	2/10 (20)	4/23 (17.4)	1/10 (10)	5/23 (21.7)	2/14 (14.3)	4/19 (21.1)
Extraglandular (%)						
Joint pain	6/10 (60)	16/23 (69.6)	6/10 (60)	16/23 (69.6)	9/14 (64.3)	13/19 (68.4)
Raynaud's phenomenon	4/10 (40)	10/23 (43.5)	4/10 (40)	10/23 (43.5)	7/14 (50)	7/19 (36.8)
Photosensitivity	2/10 (20)	4/23 (17.4)	1/10 (10)	5/23 (21.7)	2/14 (14.3)	4/19 (21.1)
Peripheral neuropathy	3/10 (30)	3/23 (13)	3/10 (30)	3/23 (13)	4/14 (28.6)	2/19 (10.5)
Lymphadenopathy	0/10 (0)	6/23 (26.1)	0/10 (0)	6/23 (26.1)	0/14 (0)	6/19 (31.6)
Interstitial lung disease	1/10 (10)	3/23 (13)	0/10 (0)	4/23 (17.4)	1/14 (7.1)	3/19 (15.8)
Renal tubular acidosis	1/10 (10)	2/23 (8.7)	1/10 (10)	2/23 (8.7)	1/14 (7.1)	2/19 (10.5)
Autoimmune thyroid disease	2/10 (20)	1/23 (4.3)	1/10 (10)	2/23 (8.7)	2/14 (14.3)	1/19 (5.3)
Psychosis	1/10 (10)	0/23 (0)	1/10 (10)	0/23 (0)	1/14 (7.1)	0/19 (0)

Previous studies reported a high prevalence of anti-HTLV-1 antibodies in the peripheral blood of patients with SS (23%–36.7% compared to 3%–8.4% of normal controls) in endemic areas[17,18,28]. However, only a few studies have evaluated the salivary glands of patients with SS in an endemic area. In Ohyama, *et al*[20], HTLV-1 DNA from the salivary glands was amplified by PCR in 100% of HTLV-1-seropositive patients with SS in an area endemic for HTLV-1. In addition, Yamano, *et al*[29] reported that the salivary glands of 47% of patients with SS expressed retroviral antibody p24, and all affected patients were positive for p24 antibody in serum. Regarding the seroprevalence of patients with SS from a region not endemic for HTLV-1, Shattles, *et al*[30] and Mariette, *et al*[19] reported that HTLV-1 antibodies were not detected in the peripheral blood of patients with SS. In contrast, HTLV-1 was detected in the salivary glands in about one-third of these seronegative SS patients[19,30]. In our study, the seroprevalence of HTLV-1 in patients with SS was 3.8% (2/53) in the PCR analysis. The prevalence of HTLV-1 in our SS patients was lower than the prevalence observed in an endemic area such as Japan, but was significantly higher than the rate of 0.007% reported from healthy Korean blood donors[9]. Further, when the seropositivity of the family members of 2 seropositive patients was evaluated, all 4 family members studied were positive for HTLV-1 tax by PCR. Interestingly, in minor salivary gland biopsies, HTLV-1 proteins p19 or tax were detected in 42.4% (14/33) of the patients with SS, including 1 seropositive patient.

Several studies have examined the salivary glands of HTLV-1 seronegative SS patients, with conflicting results. Shattles, *et al*[30] showed that 31% of 39 HTLV-1 seronegative patients with SS expressed p19 antigen in salivary gland biopsies. Sumida, *et al*[31] reported the presence of HTLV-1 tax/rex messenger RNA in labial minor salivary gland samples from 4 (29%) of 14 HTLV-1 seronegative SS patients. Mariette, *et al*[32] detected the *tax* gene, but not the *env* or *pol* genes, in minor salivary gland samples by PCR from 9 (23%) of 40 HTLV-1 seronegative French patients. In contrast, Rigby, *et al*[33] found that none of 49 British patients with SS were positive for the *tax* gene in the salivary glands by PCR. However, our result is consistent with those of several studies that detected HTLV-1 p19 or tax in the salivary glands of seronegative SS patients in nonendemic areas[19,30,31]. The discrepancy between the HTLV-1 seroprevalence and positivity of salivary glands in seronegative patients with SS could be explained in the following ways. First, it has been postulated that HTLV-1 transcription is repressed by a factor in serum or by a product of HTLV-1 itself[34,35], leading to transient HTLV-1 expression by individual cells. Second, a "hit-and-run" mechanism is possible, in which acute infection with a specific virus elicits a chronic pathological response that persists after the original infection has been cleared. Third, the proteins detected in these patients could belong to another yet-unknown exogenous or endogenous retrovirus.

In our study, comparison of the laboratory data of HTLV-1 p19 or tax-positive and negative patients from minor salivary glands showed that autoantibodies including anti-Ro/SSA and RF were lower in HTLV-1-positive patients. Talal, *et al*[36] reported that a subset of patients with SS had serum antibodies to the retroviral proteins (p24 gag), and had lower anti-Ro/SSA and anti-La/SSB autoantibody levels. In addition, Eguchi, *et al*[17] showed that patients with antibodies to HTLV-1 had lower levels of ANA, anti-Ro/SSA, and anti-La/SSB, although the difference was not significant. In contrast, Hida, *et al*[28] found no differences comparing the prevalence of autoantibodies between seropositive and seronegative patients. Although our results differ from some studies[19,20,28], the presence of sicca symptoms in HTLV-1 patients does not seem to depend on the production of autoantibodies. Further, the lymphocyte count in the HTLV-1-positive patients with SS was significantly higher than that in the HTLV-1-negative patients. HTLV-1 infection rapidly induces the activation and proliferation of peripheral blood lymphocytes in patients with HTLV-1-associated myelopathy[37,38], as well as in healthy carriers[39], and this is consistent with the hypothesis that such cells cause the inflammatory lesions that result in tissue damage in the associated diseases. Clinically, there was no significant difference between the HTLV-1-positive and negative patients. Our result concurs with that of Mariette, *et al*[32] and contrasts with data from 2 groups in Japan[17,40], which reported that the frequency of extraglandular manifestations tended to be higher in the HTLV-1-seropositive group than in the HTLV-1-negative group.

Several possible mechanisms have been proposed for the pathogenesis of HTLV-1-associated SS. As we found, HTLV-1 may infect glandular epithelial cells and impair the function of the salivary glands directly. The salivary gland could represent a reservoir in which the virus replicates, and the infection could in turn lead to a cytotoxic immune reaction and cytokine secretion against HTLV-1-infected cells in the salivary glands. In addition, the infiltration of salivary glands by HTLV-1-infected or activated T lymphocytes might contribute to the development of exocrinopathy[20]. In this regard, Sasaki, *et al* reported the accumulation of common T cell clonotypes with an identical TCR *Vß* gene in the salivary glands and PBMC of HTLV-1-associated patients with SS[41].

Our study has some limitations. First, because it is impossible to biopsy normal subjects for ethical reasons, we could not compare the salivary glands of patients with SS to normal control samples. Second, we cannot exclude the possibility that detection of HTLV-1 in the salivary glands of patients with SS represents an incidental presence because of the cross-sectional study design. Third, as several endogenous retroviruses may encode p19 or tax[42], we cannot rule out the possibility that the discovery of HTLV-1 antibodies in the salivary glands involves a cross-reaction of the antibodies with other human endogenous retroviruses.

Our study confirms previous findings and provides addi-

tional evidence that suggests a relationship between HTLV-1 infection and SS. We identified a subset of patients with SS characterized by the presence of HTLV-1 proteins in the labial salivary glands and a relative absence of autoantibodies including anti-Ro/SSA and RF. Larger prospective studies that provide a precise characterization of infected cells are warranted to evaluate the implications of these observations on the pathogenesis of SS.

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