RESEARCH COMMUNICATION

A unique seroepidemiological pattern of HBV, HCV and HTLV-I in Nenets and Komi in Northwestern Russia

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Abstract

An epidemiological study of hepatitis viruses type B (HBV) and type C (HCV) and human T-cell leukemia virus type I (HTLV-I) was carried out among 105 residents (male:female=19:86) regarded as Nenets partly mixed with Komi, in the region of Krasnoe, the Nenets Autonomous District of the Arkhangelsk Region, in northwestern Russia in 2004. Blood was drawn from apparently healthy volunteers at ages of 41.6±16.5 (range 14-85) years. HBsAg, HBsAb, HBcAb, HBeAb and HCV Ab were measured by microparticle enzyme-immunoassay, and HTLV-I Ab was measured by particle agglutination. Prevalences of HBsAg(+), HBsAb(+), HBcAb(+) and HBeAb(+) were 0.0%, 29.5.%, 20.0% and 7.6%, respectively. The overall HBV infection rate (positive HBsAb or HBcAb) was 34.3%, while no positive HCV or HTLV-I Abs could be detected. A serological subgroup with positive HBsAb and negative HBcAb, consisting of 15(14.3%) females, contrasted sharply to other serological subgroups in sex, age, parent's ethnicity, positive HBeAb rate, and HBcAb inhibition%. We conclude that HBV is prevalent with unique serological patterns among the Nenets, while HCV and HTLV-I infections are negligible.

Key Words: HBV - HCV - HTLV-I – Nenets – Komi - Russia

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Introduction

Viral hepatitis caused by hepatitis B virus (HBV) and hepatitis C virus (HCV) is a major global public health problem. The epidemiological information of HBV and HCV is essential for strategic prevention of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. The prevalence of HBV and HCV infections is quite different among geographical regions, and each region shows a unique serological and genetic feature of hepatitis viruses, which is partly related to anthropological human migration and also modern medications such as vaccination. However, as to Mongoloid populations living in peripheral and undeveloped regions, currently available information of viral infections is limited.

In 2000, we conducted an epidemiological study of HBV at four isolated villages in eastern and western remotes of Tibet (China), and reported that HBV was highly prevalent among native Tibetans in these regions; 19.1% for positive HBsAg and 29.0% for positive HBsAb or HBcAb (Zhao, et al., 2001). In particular, one of the villages in eastern Tibet showed extremely high prevalence (37.5% for positive HBsAg and 45.0% for positive HBsAb or HBcAb). In 2004, we carried out a similar study in Sherpas, a people indigenous to the Himalayan region of Nepal, and reported the prevalence of positive HBsAg, and positive HBsAb or HBcAb were 1.9% and 28.2%, respectively (Chiba, et al., 2004). HBV genotype was found to be distinct between the Tibetans and the Sherpas, and HCV infection was negligible in both populations.

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Here we report a seroepidemiological study of HBV and HCV in the Nenets, an indigenous people of northwestern Russia. The Nenets is representative of the Uralic race with strong Mongoloid characteristics. They have been mixed with the Komi, another indigenous people of this area with weaker Mongoloid features. We also report the prevalence of human T-cell leukemia virus (HTLV-I) among these indigenous people. Regarding this latter retrovirus, foci are known to exist in Japanese southwestern and northern regions and in the Andes of South America (Tajima and Takezaki, 2003). A 1500-year-old Andean mummy and contemporary Japanese and Chileans are reported to share similar HTLV-I provirus sequences, indicating that the Andean HTLV-I was transmitted from Asia by people with genetic link to the contemporary Japanese carrying HTLV-I (Li et al., 1999). Thus, investigating the prevalence of HTLV-I among the Nenets and the Komi might possibly add our knowledge concerning ancient migration of Mongoloids.

Materials

EDTA Blood and information were collected from apparently healthy volunteers (n=105; male:female=19:86; age 41.6±16.5 year old, mean±SD), living in the settlement of Krasnoe, the Nenets Autonomous District of the Arkhangelsk Region, Russia (Figure 1). The sampling was done in December 2004, and the blood samples were immediately separated by centrifugation and then stored below -20˚C until use. The distributions of ethnicity, age and sex of the studied subjects are summarized in Tables 1 and 2.

Ethics

To perform this study, we obtained the permissions from the Russian Academy of Sciences, and also from the local government of the Nenets Autonomous District of the Arkhangelsk Region. Informed consent was obtained from each volunteer after giving the information concerning this research.

Figure 1. Location of the Studied Region. Sampling was done at Krasnoe

Table 1. Ethnicity of the Studied Subjects

Father	Mother	n	%
Nenets	Nenets	67	63.8%
Nenets	Komi	11	10.5%
Komi	Nenets	4	3.8%
Nenets	Russian	2	1.9%
Russian	Nenets	13	12.4%
Belorussian	Nenets	1	1.0%
Komi	Komi	5	4.8%
Komi	Russian	1	1.0%
Russian	Komi	1	1.0%
Total		105	100.0%

Methods

HBsAg, HBsAb, HBcAb, HBeAb and HCV Ab were measured by microparticle enzyme-immunoassays (Abbott). HTLV-I infection was serologically screened using a commercial test kit (SERODIA HTLV-I, FUJIREBIO Inc., Tokyo) based on passive particle-agglutination (Fujiyama et al., 1995). The result was regarded as positive when HBsAg, HBsAb, HBcAb, HBeAb, HCV Ab, and HTLV-I Ab were >2.0 (S/N ratio), >5.0 mIU/ml, >50 inhibition%, >60 inhibition%, >1.00 (sample/control ratio), and 8-fold or more, respectively.

Results

Positive HBsAg, HCV Ab, and HTLV-I Ab were not detected in this study (Table 2). According to the results of HBsAb and HBcAb testings, the studied subjects were divided into four serological groups as Groups I with positive HBsAb and HBcAb, Group II with positive HBsAb and negative HBcAb, Group III with negative HBsAb and positive HBcAb, and Group IV with negative HBsAb and HBcAb (Table 3). The overall prevalence of HBV infection, represented by Group I+II+III, was 34.3% (36/105). The overall positive rates were 29.5%(31/105) for HBsAb, 20.0%(21/105) for HBcAb, and 7.6%(8/105) for HBeAb.

Of the three groups positive for HBV infection, Group II was distinct in several aspects. All members of Group II were female, and more young subjects were included in this group than in others (the difference in age distribution was not statistically significant). As to parent's ethnicity, Group II was the highest in the frequency of a Russian or Belorussian parent. Further, Group II lacked positive HBeAb and had the HBc inhibition% as low as Group IV. Additionally, Groups II was as high as Group I in the appearance rate of a higher HBsAb level (>300 mIU/ml).

Discussion

The vast portion of Nenets (or Yurak-Samoyedes) live in the polar regions of northeastern Europe and northwestern Siberia from the Kanin Peninsula to the Yenisey delta, and also in the Arctic Ocean islands and the Kola Peninsula

Table 2. Age, Sex, and Serological Profile of The Studied Subjects

		Male	Female	Total
Age (year)	14-19	1 (5.3%)	11 (12.8%)	12 (11.4%)
	20-29	2 (10.5%)	13 (15.1%)	15 (14.3%)
	30-39	2 (10.5%)	19 (22.1%)	21 (20.0%)
	40-49	5 (26.3%)	20 (23.3%)	25 (23.8%)
	50-59	6 (31.6%)	14 (16.3%)	20 (19.0%)
	60-85	3 (15.8%)	9 (10.5%)	12 (11.4%)
	total	19 (100%)	86 (100%)	105 (100%)
Serological tests	HBsAg(+)	0	0	0
(total n=105)	HBsAb(+)	6 (5.7%)	25 (23.8%)	31 (29.5%)
	HBcAb(+)	9 (8.6%)	12 (11.4%)	21 (20.0%)
	HBsAb(+) or HBcAb(+)	9 (8.6%)	27 (25.7%)	36 (34.3%)
	HBeAb(+)	4 (3.8%)	4 (3.8%)	8 (7.6%)
	HCV Ab(+)	0	0	0
	HTLV-I Ab(+)	0	0	0

(Figure 1). Administratively, their habitat in this area is divided into the Nenets Autonomous District of the Arkhangelsk Region and the Yamal-Nenets Autonomous District of the Tyumen Region, which is on the east of the former. The Nenets have been living as Nomads (reindeer keepers) and fishermen as seasonally determined, which is similar with the Sami, an indigenous people of Scandinavian polar regions.

As to the prevalence of HBV infection in the Nenets, only a single Russian article is available, in which the Nenets (n=108) in the Tyumen region was studied and found to be positive for HBsAg in 1.85%, HBcAb in 10.2%, and HCV Ab for 0.93% (Netesova IG, et al., 1995). Their report and our present results suggest that HCV infection is negligible but HBV infection is prevalent in the Nenets. HBV infection is known to have a perinatal/neonatal transmission and also a sexual transmission. Hence, it is important to clarify how the HBV prevalence rate varies with age and sex. The unique characteristics in sex, age, and parent's origin in Group II is worth regarding for this reason.

The combination of positive HBsAb and negative HBcAb, as seen in Group II, is infrequent in Japan. The most remarkable serological feature of the present population is the relatively frequent (14.3%) occurrence of this combination. This combination usually indicates three possibilities. One is vaccination for HBV, which is unlikely for Group II, considering the living of the Nenets as reindeer keepers in the Tundra region. At least, no information suggesting the past history of HBV vaccination has been obtained so far. The second possibility is a decreased production of HBcAb due to a long duration of HBV infection, which is unlikely for Group II because of the involvement of younger subjects (5 subjects were 14-17 years old) and the lack of any sign of elevation in HBcAb inhibition%.

The third and most likely explanation is a precore/core mutation in the HBV gene, which can suppress core protein synthesis (Uchida et al., 1993). We suppose that at least the younger subjects in Group II might be infected with such a mutant virus and exhibited the HBsAB(+)/HBcAb(-) pattern after seroconversion. Both the distinct parental ethnicity and the involvement of younger subjects of this group might suggest a perinatal/neonatal transmission of the virus. A possible complication of a common-type HBV infection on the mutant virus infection would change the serological pattern from the HBsAB(+)/HBcAb(-) to the HBsAb(+)/HBcAb(+) which corresponds to Group I. Since no HBsAg-positive sample was detected in this study, and therefore, no nucleotide sequence of the virus was obtained, we cannot test this possibility. The lack of positive HBeAb in Group II

Table 3. Characteristics of Four Serological Groups of The Studied Subjects

Group	HBsAb/ HBcAb	n(%)	sex	age(year)			Russian or Belorussian parent	positive HBeAb	HBcAb inhibition%	HBsAb level >300 mIU/ml
			m/f	14-29	30-49	50-85	n(%)	n(%)	%	n(%)
I	+/+	16 (15.2%)	6/10	2	7	7	1 (6%)	4 (25.0%)	85.6+14.7[d]	8 (50%)
II	+/-	15 (14.3%)	0/15[a]	7	4	4	7 (47%)[b]	0	10.9+13.9	6 (40%)
III	-/+	5 (4.8%)	3/2	0	3	2	0	4 (80%)[c]	88.2+16.3[d]	-
IV	-/-	69 (65.7%)	10/59	18	32	19	10 (14%)	0	10.7+10.7	-
Total		105 (100%)	19/86	27	46	32	18 (17%)	8 (7.6%)	25.9+38.4	14 (13.3%)

[a]$p<0.05$ vs. Group I and $p<0.001$ vs. Group III (Fisher's exact probability test).
[b]$p<0.05$ vs. Groups I and IV (Fisher's exact probability test).
[c]$p<0.05$ vs. Group I , $p<0.01$ vs. Group II, and $p<0.0001$ vs. Group IV (Fisher's exact probability test).
[d]$p<0.001$ vs. Group IV (Mann-Whitney U test).

does not always contradict with any of the above explanations, since HBeAb production is not expected after vaccination, and is vigorous only at early periods of infection, and could be affected by a mutation in the precore/core region. After all, the unique serological pattern of Group II. remains to be addressed.

On the other hand, the association of negative HBsAb, positive HBcAb, and positive HBeAb in Group III is typical as an acute phase pattern, indicating a recent infection within 2 months. Taken this together with the fact that Group III contained only adult men and women, the most likely cause of their HBV infection is the sexual contact.

We conclude that HCV and HTLV-I are negligible among the Nenets, and that HBV is prevalent but inactive. As to HTLV-I, we have reported the same negative result for the Sami (Chiba et al., 2004), suggesting that these indigenous people of northern Europe might not be anthropologically approximate to the ancestors of contemporary HTLV-I-carrying Japanese and Chileans.

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