Leprosy and Hepatitis B Virus Markers: Incidence of HB_sAg and HB_eAg in Somalian Patients[1]

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Since the beginning of his studies on the Australia antigen, Blumberg, *et al.* [1] have reported that surface B antigen carriers have been observed most frequently in association with leprosy, especially in the lepromatous forms [2, 3]. These data have been confirmed, and this phenomenon was initially attributed to a genetic predisposition [1].

Another view is that this predisposition may represent a greater opportunity for infection by virus B of hepatitis because of the patients' confinement to institutions. The lepromatous patients, in fact, are more frequently hospitalized in closed communities where virus B is more widespread whereas this is rarely the case with patients presenting with the less severe tuberculoid or indeterminate forms [8, 9].

The HB_sAg carrier rate in leprosy patients can also be probably attributable to the fact that today the majority of leprosy patients live in tropical countries where hepatitis is highly prevalent and can reflect the incidence of antigen in the surrounding population. This hypothesis would therefore attribute more responsibility to the climate and environmental conditions in influencing the HB_sAg diffusion among leprosy patients than to the disease itself [10, 15].

An acquired immunological deficiency has also been taken into consideration in Hansen's disease to explain the persistence of HB_sAg in carriers [4, 17]. The presence of cell-mediated impairment in leprosy seems to be sufficiently, though not completely, ascertained on the basis of many reports; however, the causes of the above alteration remain unknown, and it has not yet been resolved whether the deficiency represents a predisposing condition or a consequence of the disease [11].

During the last three years in Somalia we have collected blood samples from patients with leprosy and have had the opportunity of studying the HB_sAg and HB_eAg tests in these patients [7, 13]. In this paper we will give the results of our most recent study concerning the distribution of some hepatitis B virus markers in long-term institutionalized patients.

PATIENTS AND METHODS

Two-hundred and twenty-two Somalian patients from the Leprosy Hospital of Alexandra Island in Jilib, south of Mogadishu, were studied. All the patients were classified by the clinical and histological criteria of the Ridley-Jopling classification [14]. Only the polar TT tuberculoid forms (87 cases) and polar LL lepromatous forms (135 cases) were included in this survey. Controls (146 persons) were healthy adult Somalians living in the same area.

The age of the patients ranged from 16 to 66 years. One-hundred-fifty-eight were males and 64 were females.

Serum samples were collected during 1975–77 and stored at −20°C until tested. Screening for HB_sAg and anti-HB_s was done by radioimmunoassay (RIA); e-antigen and anti-e antibody were determined by an immunodiffusion technique. For further details, see our preceding reports [7, 12, 13].

RESULTS

Surface B antigen. HB_sAg was present in 33 (24.4%) of the 135 patients with lepromatous leprosy and in 10 (11.5%) of the 87 patients with tuberculoid leprosy while

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TABLE 1. *Percentages of HB_sAg and anti-HB_s in leprosy patients and controls.*

Patients	HB_sAg			anti-HB_s		
	No. cases tested	No. cases positive	%	No. cases tested	No. cases positive	%
Lepromatous	135	33	24.4	135	63	46.6
Tuberculoid	87	10	11.5	87	51	58.6
Controls	146	26	17.8	146	65	44.5

it was found in 26 healthy controls for a frequency of 17.8%.

The antibody, anti-HB_s, was present in 63 patients with the LL form (46.6%) and in 51 patients with the TT form (58.6%), against a frequency of 44.5 percent (65 positive cases) found in the controls (Table 1).

The frequency of HB_sAg in the lepromatous group is higher than in the tuberculoid group and the difference was significant ($p < 0.05$). No significant statistical differences, however, were found between the lepromatous patients and controls ($p > 0.2$) or between the tuberculoid patients and controls ($p > 0.2$). Similarly, there are no significant differences in the prevalence of anti-HB_s between the two groups of leprosy patients and between these patients and controls.

e-antigen. The "e" antigen was found in none of our leprosy patients, tuberculoid or lepromatous, nor in controls.

The anti-e antibody was present in 7 (8.1%) of the 86 lepromatous patients tested and in 2 (3.5%) of the 56 patients with the tuberculoid form while its frequency rate was 10.6% (5 positive cases) among 47 healthy controls (Table 2). There were no statistically significant differences between the two leprosy groups or between the leprosy patients and the controls.

Regarding sex, the frequency of HB_sAg in the lepromatous group was higher in females (36.8%) than in males (19.5%), but the difference was not statistically significant ($p > 0.1$); in the tuberculoid group the males showed a higher rate (13.1%) than the females (7.7%), with no significant statistical difference (Table 3).

The rate of HB_sAg increases with age but the differences among the three groups were not significant (Table 4).

DISCUSSION

Many researchers have studied the problem of the association of HB_sAg with leprosy, but until now the results obtained have differed from author to author and from area to area, and the problem remains debatable.

Analysis of the results obtained in the present study in Somalia has shown the presence of a difference in the distribution of HB_sAg among leprosy patients with an increased antigenemia in the lepromatous form which was statistically significant ($p < 0.05$); no differences have been found, however, between leprosy patients and healthy controls.

Regarding institutional status, all our patients can be considered to be institutionalized patients because they live in a hospital village on an island in the Juba river. Therefore, in addition to their medical isolation, these patients are isolated because of their environmental conditions, which cause a complete separation from the surrounding population. For this reason, we

TABLE 2. *Percentage of HB_eAg and anti-e in leprosy patients and controls.*

Patients	HB_eAg			anti-e		
	No. cases tested	No. cases positive	%	No. cases tested	No. cases positive	%
Lepromatous	86	0	0	86	7	8.1
Tuberculoid	56	0	0	56	2	3.5
Controls	47	0	0	47	5	10.6

TABLE 3. *Prevalence (%) of HB_sAg and anti-HB_s in relation to sex.*

	HB_sAg	anti-HB_s	HBV-positive
	LL form		
Males (97 cases)	19.5	48.4	68.0
Females (38 cases)	36.8	42.1	78.9
	TT form		
Males (61 cases)	13.1	54.0	67.2
Females (26 cases)	7.7	59.2	76.9

can call this a closed community, where the virus B of hepatitis is widespread, as is demonstrated by the high number of chronic HB_sAg carriers and by the even higher number of subjects having anti-HB_s antibodies. The rate of HBV seropositivity (HB_sAg plus anti-HB_s) was the same in the LL patients (71.1%) as in the TT patients (70.1%) and could reflect the conditions of life in that closed community.

Very few reports on the prevalence of anti-HB_s antibodies exist in medical literature; until a few years ago only 11 cases of leprosy having anti-HB_s in the blood had been reported ([12]). These workers pointed out that patients who are immunodepressed from various causes, including genetic ones, usually acquire the antigen and rarely the antibody, and this could explain the low frequency of anti-HB_s in leprosy patients.

On the other hand, it should be pointed out that only cell-mediated immunity is implicated as being depressed in leprosy. The high frequency of various types of antibodies and the presence of autoantibodies in a large number of these patients would imply that humoral immunity is not subject to alteration or depression ([11]). It would be strange if in leprosy the depression of humoral immunity were limited to anti-HB_s antibodies, the only ones involved in the disease. Even if that selective alteration could explain the absence of anti-HB_s antibodies in leprosy patients, it seems to us to be rather questionable. Furthermore, our studies ([12, 13]) and other recent ones ([6, 16, 17, 18]) using more sensitive techniques (RIA methods) have shown a frequency of anti-HB_s antibodies ranging from 23% to 58% in both polar forms of leprosy.

It has been suggested that in leprosy patients the probability of producing an effective immune response is expressed by the following relationship:

$$\frac{HB_sAg}{HB_sAg + \text{anti-}HB_s};$$

the more the ratio decreases, the higher the probability of an effective antibody response ([15]). When we applied this formula to our cases of leprosy, we found a value of 0.343 for the lepromatous form and of 0.164 for the tuberculoid form while in healthy contacts the ratio was 0.285. Our results correspond to those found by others only in regard to the polar forms of leprosy, with a higher index in lepromatous than in tuberculoid leprosy.

Regarding the "e" antigen/antibody system in leprosy, we have confirmed our earlier data ([12, 13]) in not having found the e-antigen in any of our cases of leprosy and a rate of anti-e antibodies of 8% in the LL forms and of 3.5% in TT. The absence of e-antigen and the simultaneous finding of anti-e antibodies suggest that these subjects are HB_sAg carriers with low or no infectivity risk.

Recently, two other papers on this subject were presented at the XI International Leprosy Congress in Mexico City ([5, 19]). Although the results obtained by these authors differ partially from ours (Table 5) because of the presence in some leprosy

TABLE 4. *Prevalence (%) of HB_sAg and anti-HB_s in leprosy patients of various age groups.*

	LL form			TT form		
Age	No. cases	HB_sAg	anti-HB_s	No. cases	HB_sAg	anti-HB_s
<20	15	20	46.6	6	16.1	50
21–40	65	23	30.7	39	15.3	43.5
>40	55	27.2	65.4	42	7.1	73.8

TABLE 5. *Frequency of "e" antigen and e-antibody in leprosy patients in three different surveys.*

	HB_eAg positivity (%)			anti-e positivity (%)		
	LL	TT	Controls	LL	TT	Controls
Nuti, *et al.*,[12,13]	0	0	0	8.1	3.5	10.6
Chiron, *et al.*,[5]	6.0	6.8	1	40.1	43.7	6.0
Terencio, *et al.*,[18]	4	—	0	13.0	—	0

patients of e-antigen (very surprisingly the e-antigen was found also in the 4% of HB_sAg negative patients ([5])), their conclusions are in accord with the concept that the impaired cell-mediated immunity which characterizes LL patients seems to play no role in the distribution of hepatitis B virus markers in leprosy.

SUMMARY

Serum samples from 222 Somalian patients, 135 with the lepromatous form of leprosy and 87 with the tuberculoid form of the disease, were examined for the presence of the surface antigen (HB_sAg), the "e" antigen (HB_eAg), and their corresponding antibodies (anti-HB_s and anti-e).

HB_sAg was present in 24.4% of the LL cases and in 11.5% of the TT patients while anti-HB_s was found respectively in 46.6% and 58.6%. The e-antigen was not found in any case of leprosy; anti-e was detected in 8.1% of the LL patients and in 3.5% of the TT cases.

The rate of HBV seropositivity (HB_sAg plus anti-HB_s) was the same in the LL patients (71.1%) and in the TT patients (70.1%) and that could reflect the conditions of life in their closed community.

The analysis of results obtained in Somalia has shown the presence of a difference in the distribution of HB_sAg among leprosy patients, with an increased antigenemia in the lepromatous form which was statistically significant ($p < 0.05$). No differences, however, were found between the leprosy patients and healthy controls.

These observations seem to indicate that patients with lepromatous leprosy do not have an increased susceptibility to infection by hepatitis B virus.

RESUMEN

Se buscó la presencia del antígeno de superficie (HB_sAg), del antígeno "e" (HB_eAg), y de los anticuerpos correspondientes (anti-HB_s y anti-e) en el suero de 222 pacientes de Somalia, 135 con lepra lepromatosa y 87 con lepra tuberculoide.

El antígeno HB_s estuvo presente en el 24.4% de los casos LL y en el 11.5% de los casos TT mientras que el anticuerpo anti-HB_s se encontró, respectivamente, en el 46.6% y en el 58.6% de los casos. El antígeno e no se encontró en ninguno de los casos de lepra pero el anticuerpo anti-e se detectó en el 8.1% de las formas LL y en el 3.5% de las formas TT.

La frecuencia de seropositividad HBV (antígeno HB_s más anticuerpo anti-HB_s) fue la misma en los pacientes LL (71.1%) que en los pacientes TT (70.1%) y eso, pudo ser un reflejo de las condiciones de vida en esa comunidad cerrada.

El análisis de los resultados obtenidos en Somalia ha demostrado diferencias en la difusión del antígeno HB_s entre los pacientes con lepra, con una antigenemia aumentada en los pacientes lepromatosos la cual fue estadísticamente significante ($p < 0.05$). Sin embargo, no se encontraron diferencias entre los pacientes con lepra y los controles sanos.

Estas observaciones parecen indicar que los pacientes lepromatosos no presentan una incrementada susceptibilidad a la infección por virus de la hepatitis B.

RÉSUMÉ

On a examiné des échantillons de sérum provenant de 222 malades somaliens, dont 135 atteints de la forme lépromateuse de la lèpre et 87 avec la forme tuberculoïde de la maladie. Cette étude a été réalisée en vue de détecter la présence de l'antigène de surface (HB_sAg) et de l'antigène "e" (HB_eAg), de même que les anticorps correspondants (anti-HB_s et anti-e).

La présence d'antigènes HB_sAg a été relevée dans 24,4% des échantillons provenant de malades atteints de la forme LL et dans 11,5% de ceux provenant de malades TT, alors que l'anticorps anti-HB_s n'a été observé respectivement que chez 46,6% et 58,6% des malades atteints de l'une et l'autre de ces deux formes. On n'a pas détecté d'antigène "e" dans les cas de lèpre. Néanmoins, des anticorps anti-e ont été observés chez 8,1% des malades de la forme LL et chez 3,5% de ceux souffrant de la forme TT.

Le taux de positivité sérique pour HBV (HB_s Ag plus anti-HB_s) a été trouvé identique chez les malades LL (71,1%) et chez des malades TT (70,1%). Ceci pourrait témoigner des conditions de vie dans une communauté fermée.

L'analyse des résultats obtenus en Somalie ont montré l'existence d'une différence dans la diffusion de l'antigène HB_sAG parmi les malades de la lèpre, avec une antigénémie accrue chez les malades de la forme lépromateuse, augmentation qui était statistiquement significative ($p < 0.05$). Aucune différence n'a cependant été trouvée entre les malades de la lèpre dans leur ensemble et les témoins en bonne santé.

Ces observations semblent indiquer que les malades souffrant de lèpre lépromateuse ne présentent pas une suceptibilité accrue à l'infection par le virus de l'hépatite B.

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