HLA antigens in donovanosis (granuloma inguinale)

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Abstract

**Objective**—To compare the frequencies of HLA antigens in patients with donovanosis and in controls.

**Design**—HLA Class I, Class II and DQ antigens were detected in patients with genital ulceration caused by donovanosis and in a control group.

**Setting**—City Health STD Clinic, King Edward VIII Hospital, Durban, South Africa.

**Participants**—Sixty (47 men, 13 women) patients with donovanosis.

**Results**—HLA B57 was detected in nine of 60 (15%) with donovanosis and 75 of 1478 (5.1%) controls (RR = 3.3, χ² = 11.0, p = 0.001, p corrected = 0.026).

**Conclusions**—A possible link between donovanosis and HLA B57 could be explained by co-existing alleles or immune response genes in linkage disequilibrium altering disease susceptibility.

Introduction

Donovanosis is a genital ulcerative disease (GUD) found in diverse geographical locations where poor socio-economic conditions prevail and is commoner in dark-skinned races. Donovanosis is generally regarded as a sexually transmitted disease (STD) but the modes of infection and transmission are not yet established with certainty. The causative agent, *Calymmatobacterium granulomatis*, has been isolated from faeces, and transmission through auto-inoculation is suggested. The organism possesses a capsule and is similar to klebsiella strains but its biochemical and bacterial characteristics are not well defined.

Although previously thought to be uncommon in Southern Africa, donovanosis has recently emerged as a significant cause of GUD in Durban. In 1988, 171 cases were diagnosed by the presence of Donovan bodies on direct microscopy using the RapiDiff technique, a simple bench diagnostic staining method.

Most bacterial STDs are readily transmitted from male to female and female to male. However, variable transmission rates of infection with *C granulomatis* are reported from different populations. The prevalence of disease amongst regular sexual partners varies from 1% in the USA and 1% in Papua New Guinea to 50% in India. The apparent racial predominance amongst blacks and variability in transmission suggests that host susceptibility factors may be relevant in the disease process.

No clear association between a single HLA antigen and a particular STD has been described but donovanosis has been suggested as one STD with a reasonable chance of such a link. We therefore investigated the frequency of HLA antigens amongst Zulu patients with donovanosis attending a STD clinic in Durban.

Patients and Methods

Sixty Zulu patients (47 men, 13 women) attending the City Health STD Clinic at King Edward VIII Hospital, Durban with genital ulcerative lesions of donovanosis were entered into the study. Donovanosis was diagnosed by the detection of Donovan bodies on tissue smears stained with RapiDiff and examined by direct microscopy. Specific (TPHA) and non-specific (RPR) serological tests for syphilis were performed. Laboratory facilities for identifying herpes simplex virus, chancroid and lymphogranuloma venereum infections were unavailable.

The control group consisted of 1478 normal subjects who were either staff or randomly selected blood donors of the same ethnic origins as the patients. HLA Class I antigens were determined in all patients and control subjects by a two-stage microlymphocytotoxicity test with 180 sera consisting of: 1. local sera requested for use in international histocompatibility workshops; 2. local sera verified with international workshop sera; 3. sera exchanged with other laboratories worldwide.

Similarly 120 sera were used to define the Class II antigens on B-lymphocyte enriched lymphocyte suspension prepared with the aid of straws packed with nylon wool. Class II antigens were determined in 53 patients and 513 controls except that HLA DQ antigens were tested in 129 controls.

Statistics

Differences in HLA frequencies were tested for significance with the χ² test and the probability
Corrected by multiplying the p value by the number of comparisons made, that is, the number of antigens tested. Relative risks were calculated according to the formulae recommended by Woolf.  

**Results**  

The frequencies of HLA A and B antigens in the patients and controls are shown in table 1 and of HLA DR and DQ antigens in table 2. HLA B57 was detected in nine of 60 (15%) with donovanosis and 75 of 1478 (5-1%) controls (RR = 3.3, \( \chi^2 = 11.0, p = 0.001, \) p corrected = 0.026). HLA A23 was detected in three of 60 (5%) with donovanosis and 281 of 1478 (19-0%) controls (RR = 0.2, \( \chi^2 = 7.5, p < 0.01, \) p not significant after correction).

Positive serological tests for syphilis (TPHA and RPR) were detected in 14 (10 men and four women).

**Discussion**  

There are few reports linking HLA antigens and STDs. Amongst Chinese prostitutes in Singapore, HLA AW19 and HLA B17 were associated with syphilis and gonorrhoea and HLA A11 and HLA B15 conferred relative resistance. Behcet's disease, although not a STD, does cause genital ulceration and is associated with HLA B5. The development of disease may be related to early sexual intercourse or adolescent infection. Our findings of a possible link between HLA B57 and donovanosis and a trend towards resistance to disease with HLA A23 could be explained by co-existing alleles or immune response genes in linkage disequilibrium altering disease susceptibility.

Donovanosis is a STD about which little is known despite its recognition in the nineteenth century. It differs from most bacterial STDs in having a long incubation period and a variable transmission rate to regular sexual partners thereby suggesting inherent differences in host susceptibility. The causative organism *C. granulomatis* shares some features of klebsiella strains including a prominent capsule but its bacterial characteristics are still not yet clearly defined. Klebsiella extracts are more likely to interact with HLA B27 than other HLA antigens producing an altered-self major histocompatibility complex that may trigger reactive arthritis. Donovanosis has only recently been recognised as a significant cause of GUD amongst the local Zulu population. Whether this reflects a new epidemic or increased awareness following the introduction of a rapid diagnostic test is uncertain. Elsewhere in South Africa donovanosis occurs in East Transvaal amongst the Swazi but is otherwise uncommon.

The highest prevalence of donovanosis worldwide is in Dutch New Guinea and Papua New Guinea. However, HLA B57 was not identified amongst
natives of the Highlands and Coastal Areas. Further studies of HLA status and Donovanosis are required amongst population groups from endemic areas to clarify possible immunopathological mechanisms of disease and assess the role of genetic factors.

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