HLA-B27 associated rheumatologic diseases in Indonesia

Mardjuadi, A.

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Chapter 7

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Summary

Ankylosing spondylitis (AS) and reactive arthritis (ReA) are frequently complicated by extra articular manifestations like acute anterior uveitis (AAU). AS and ReA belong to the group of spondyloarthopathies (SpA). Both SpA and AAU show a strong association with the class I HLA molecule HLA-B27 and are therefore known as “B27 associated diseases”.

Rheumatologists in Indonesia were well aware of the fact that SpA was far more seen in ethnic Chinese living in Indonesia than in native Indonesians of the Malayan race. It was supposed that HLA-B27 would occur more frequently in Chinese than in native Indonesians. The study by Muslichan, however, showed that in native Indonesians the frequency of HLA-B27 was about twice that in Chinese.

In chapter 2 a study is described about the prevalence of HLA-B27 among Chinese and native Indonesians with SpA, in comparison with the frequencies of HLA-B27 in the healthy Indonesian population. This study shows that the frequency of HLA-B27 in native Indonesian SpA patients (8%) does not differ from the frequency in healthy native Indonesians (9%). Native Indonesians were thus the only people in the world in which SpA was not found to be associated with HLA-B27. The Chinese Indonesian SpA patients, however, showed HLA-B27 in an increased frequency (62%) if compared to healthy Chinese controls (4%).

Searching an explanation for the fact that in native Indonesians SpA is not associated with HLA-B27, we studied whether native Indonesians had a particular HLA-B27 subtype. This study, which is described in chapter 3, revealed that 89% of 18 healthy native Indonesians which were HLA-B27 positive, had the subtype B*2706. This subtype was found in none of eight native Indonesian SpA patients. These patients had B*2705 or B*2704. Of eight healthy Chinese Indonesians which were HLA-B27 positive, 62% had the subtype B*2706. This subtype was completely absent in the 23 Chinese SpA patients studied, since these patients had the subtypes B*2704 or B*2707. It could thus be concluded that HLA-B*2706 is not associated with SpA and that the high frequency of B*2706 among the HLA-B27 positive native Indonesians is responsible for the fact that in this population no association between HLA-B27 and SpA was observed.

HLA-B*2706 was neither by us in Indonesia, nor by Lopez-Larrea et al. in Thailand or Ren et al. in Singapore, observed in patients with SpA. To study whether HLA-B*2706 might protect against the disease we described in chapter 4 two families in which some members were HLA-B*2704/B*2706 heterozygote. Some of such heterozygotes had SpA, demonstrating that HLA-B*2706 is not protective against the disease.

Since Chinese and native Indonesians differ in far more aspects than just their HLA-B27 subtype, we studied whether the clinical features of SpA differed in these two racial groups. From the results which are given in chapter 5 can be learned that the clinical features of AS, the frequency of peripheral joint involvement and the age of onset of complaints was about equal for both groups and not different from those observed in other parts of the world.

Finally we reached in chapter 6 a helping hand to the rheumatologist in Southeast Asia dealing with patients suspected from SpA. They should not hesitate to (sub)type their patients for HLA-B27 and HLA-B*2706 or at least pay attention to the racial background of the patient, since SpA is rare among people of pure Malayan race, while this is not the case in people from Chinese or Caucasian descent.

This thesis deals only with the problems concerning the association between HLA-B27 and its
subtypes and SpA. It is good to keep in mind that other, up to now unknown, genetic factors are probably of even greater pathogenetic importance, while certainly half of the etiology is of environmental, probably bacteriological kind.