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# SARCOIDOSIS AND TUBERCULOSIS IN THREE PATIENTS: CONNECTION WITH HLA?

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Infectious and genetic factors have been considered as potential causes in sarcoidosis (SA). Pathological similarities between SA and tuberculosis (TB) suggest M. tuberculosis antigen(s) as causative agent(s). In our previously published analysis of the Human Leukocyte Antigens (HLA) both in patients with SA and TB in the same ethnic group from Poland we revealed that in Stage II of SA, HLA-B5,-B8, -DRB1*15, -DQA1*01 were found significantly more frequently, whereas HLA-B13, -B35, -DQB1:*02,-*03,-*05, -DQA1*03 were less common than in healthy individuals. In TB, HLA-B15, -DRB1:*16,-*14, -DQB1*05, -DQA1*03 were detected more often and HLA-A2, -DRB1*11, -DQB1*02, -DQA1:*02,-*05 were less frequent than in controls. In Stage II of SA, HLA-B5, -B8, -DRB1:*15,-*11, -DQA1*0102 were statistically more frequent and HLA-B13, -B15, -DRB1:*16,-*04,-*14, -DQB1:*03,-*05,-*06, -DQA1*03 were less frequent than in TB. The occurrence of other tested antigens in both populations was comparable. Thus the HLA antigens may be important in the etiopathogenesis of TB in patients with SA. Therefore we evaluated the frequency of HLA class I and II by PCR amplification with sequence-specific primers (PCR-SSP) in three female patients with pulmonary SA (Stage II), who developed TB on corticosteroids (CS) therapy. SA was previously diagnosed in each case by histopathological evidence of non-caseating granuloma in lymph nodes. All patients (average age 54 yr) had chronic SA with several recurrences of the disease. TB occurred during the last relapse of SA in each tested case. M. tuberculosis culture was positive in all cases. None of these patients had a previous history of TB. During TB, the CD4/CD8 ratio, radiological picture and pulmonary function tests (gasometry, spirometry, plethysmography, DLCO and 6MWT) were similar to those present while active SA, whereas the clinical symptoms were more like in TB. PPD test was negative. All patients underwent effective anti-tuberculosis treatment. Analysis of HLA revealed: 1st case: HLA-A:*01,-*26, -B:*15,-*40, DRB1:*07,-*13, DQB1:*02,-*03, DQA1:*05,-*05; 2nd case: HLA-A:*02,*24, -B:*15, *40, DRB1:*03,-*07, DQB1:*02,-*02, DQA1:*02,-*05, and 3rd case: HLA-A:*01,-*24 -B:*, DRB1:*11,-*16, DQB1:*03,-*05, DQA1:*01,-*05. In summary, all three patients had a similar occurrence of HLA connected with high risk for developing SA (6 alleles: DRB1*11, DQB1*05, DQA1*01, 3xDQA1*05) or TB (7 alleles: 3xB*15, DRB1*16, 2xDQB1*03, DQB1*05) and 17 alleles with comparable frequency in both diseases. However, 9 out of these 17 alleles were more frequently found in patients with SA than TB in our previously mentioned HLA genotyping study. Therefore, SA in these three women developed at first, and afterwards additional environmental factors, e.g.,

CS, age, or lifestyle stress may have provoked TB. There is a possibility that the occurrence of HLA antigen more characteristic for TB than SA causes the development of TB in our patients with SA.