

Brief Communication

THE STUDY OF CLASS I HLA TYPES IN PATIENTS WITH ULCERATIVE COLITIS AND ITS COMPARISON WITH HEALTHY PERSONS

Ulcerative Colitis (UC) is an inflammatory bowel disease which its causing factors are unknown, but it is known that immunological reactions¹ are active in this disease and increase in severity with progression of the disease. It is strongly considered to have an important role for genetic factors in the development of inflammatory bowel disease by evaluation of genetic epidemiology, and the association between human leukocyte antigens (HLA) and ulcerative colitis is of particular importance. Ulcerative colitis is a disease with remission and relapse courses, and a percentage of patients with chronic disease will be affected by colon cancer.

The aim of this work is to study the class I HLA antigens in patients with ulcerative colitis and its comparison with healthy persons and also define the correlation between human leukocyte antigens and different forms of ulcerative colitis (mild, moderate, severe). Family history of the disease has a strong role and the correlation between genetic and inflammatory bowel disease has been shown by many studies.^{2,3,4}

The method of performing this study was case-control, 100 patients with ulcerative colitis whom their disease were diagnosed and documented as UC by clinical observation, colonoscopy, and pathological tests, and stool examination for possible existence of mono-cellular parasites particularly *Entamoeba histolytica* that were performed 3 times, were negative, and 6 months had passed from the onset of their disease, were evaluated for class I HLA antigens by serologic techniques and microcytotoxicity method, and were compared with a normal control group.

For the control group, 100 persons whose health were confirmed by an internist, were referred to the laboratory and HLA typing test was performed, exactly the same as the earlier method and the obtained results, were documented.

The accuracy and precision of the method had been

confirmed previously.

In the control group, 51 of 100 healthy persons were male and 49 were female with mean age 45 and 42 years respectively.

In the patients group, 44 of 100 patients with ulcerative colitis were male with mean age of 37 and 56 of 100 were female with mean age of 41 years.

From 100 patients with UC, 46 had mild ulcerative colitis, 40 moderate, and 14 patients had severe UC.

From 100 patients, 15 had a family history of UC and 85 patients had no such history. 48 types of class I HLA antigens (A, B, C) were assessed both in patients and control groups, and the highest frequency in the control group was related to HLA A2 (28%), BW6 (56%), and CW4 (23%) antigens, and in 100 patients with UC, the highest frequency was related to A2 (41%), B5 (22%), B35 (23%), Bw2 (19%), CW4 (50%) and CW6 (56%) antigens.

The chi-square test was performed for any antigen in all three phases of ulcerative colitis.

The evaluation of results obtained from typing of class I HLA antigens in patients and its comparison with healthy persons shows that with regard to antigen type, there is an increase in percentages of HLA-A2, A28, A24, B5, B18, B27, B35, B51, BW4, CW1, CW2, CW3 and CW4 antigens and there has also been a relative decrease in percentages of A1, A3, A9, A11, A26, A29, B12, B14, B21, B38, B49, and B60 antigens. Comparing with healthy persons among the mentioned antigens, A2 (28%), BW6 (56%), and CW4 (23%) have the highest frequency and A30 and A31 with 0% have the least frequency in healthy persons. And in patients with ulcerative colitis, A2 (41%), B35 (23%), BW6 (56%), and CW4 (50%) antigens had the most frequency, and A26, B14, B17 and B55 with 0% had the least frequency. The chi-square test shows that the frequency percentages of A3, A9, A23, A24, B5, B12, B15, B22 and B51 antigens have significant difference in all three phases of ulcerative colitis (p -value<0.05) and no significant difference has been seen in other class I HLA antigens in triple phases of UC disease. Considering more and significant expression of group B antigens,

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it is clear-cut that there is a relationship between these antigens and severity of colon inflammation and can play an important role in the development of ulcerative colitis.

By performing chi-square and Fisher exact test, it is seen that the frequency percentages of class I HLA B21, B53, and CW4 antigens have significant difference in males and females and no significant difference is seen in other antigens between females and males. Considering the age, we saw the highest frequency in the third and fourth decades of life. Regarding the relationship between inflammatory bowel disease and activity of immunologic reactions,^{5,6} the significant increase of A3, A9, A23, A25, B5, B15, B22 and B51, in the severe phase of colitis compared to mild and moderate phases can indicate the further relationship of UC with genetics. For this, it is suggested that genetic studies be performed in patients with ulcerative colitis as well as current studies on this disease have focused on genetic factors.^{7,8}

Comparing our obtained results with results in other scientific centers it is seen that there is similarity in increase of A2, BW4, B27, B37 and B5 antigens, and decrease in A1 antigens^{9,10} But about A3, A11, B25, B13, and B15 antigens there is a difference in their frequency in comparison to other studies,^{11,12,1} The most probable cause of genetic heterogeneity, can be due to changes in effective factors in the immune system of the body and in the environment.

Ultimately, it is suggested that by performing HLA typing in patients with ulcerative colitis and the evaluation of antigens expressed by them, and also defining the percentage of expressed antigens and comparing them to that of healthy persons, we can evaluate the state of the disease and response to treatment in more extent.

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REFERENCES

1. Dermott R: Immunology of inflammatory bowel disease. *Current Opinion in Gastroenterology* 14: 289-294; 1998.
2. Pera A, Sostegni R, Daperno M, Ercole E, Laudr C, Rocca R, et al: Genotype-phenotype relationship in inflammatory bowel disease. *European Journal of Internal Medicine* 11: 204-209, 2000.
3. Cho JH, Brant SR: Genetics and genetic markers in inflammatory bowel disease. *Current Opinion in Gastroenterology* 14: 283-288, 1998.
4. Yamamoto-Furusho JK, Uscanga LF, Vargas-Alarcon G, Ruiz Morales JA, Higueral L, Cutino T, Rodriguez-Perez JM, Villarreal Grza Granados J: Clinical and genetic heterogeneity in Mexican patients with ulcerative colitis. *Hum Immunol* Jan; 64(1): 119-23, 2003.
5. Ikeda Y, Akbar F, Matsui H, et al: Characterizations of antigen-presenting dendritic cells in the peripheral blood and colonic mucosa of patients with ulcerative colitis. *Eur J Gastroenterol Hepatol* 13(7): 841-50, 2001.
6. Rutgeert S, Paul, Severine, Vermeire: Serological diagnosis of inflammatory bowel disease. *The Lancet* 356: 23/30, Dec, 2000.
7. Perri F, Annese V, Piepoli A, Napolitano G, Lombardi G, Ciavarella G, et al: HLA antigens and PANCA define ulcerative colitis as a genetically heterogeneous disorder. *Ital J Gastroenterol Hepatol* Feb; 30(1): 56-61, 1998.
8. Uyar FA, Imeryuz N, Saruhan-Diresneneli G, Ceken H, Ozdogan O, Sahin S, Tozun N: The distribution of HLA-DRB alleles in ulcerative colitis patients in Turkey. *Eur J Immunogenet* 25(4): 293-6, 1998.
9. Hiwatashi N, Kikuchi T, Masamune O, Ouchi E, Watandbe H, Goto Y: HLA antigens in inflammatory bowel disease. *Tohoku J Exp Med* 131(4): 381-5, 1980.
10. Seki S, Sugimurd K, Ota M, Matsuzawa J, Katsuyama Y, Ishizuka K, Mochizuki T, Suzuki K, Youeyama O, Mizuki N, Honmo T, Inoko H, Asakura H: Stratification analysis of MICA triplet repeat polymorphisms and HLA antigens associated with ulcerative colitis in Japanese. *Tissue Antigens* 58(2): 71-76, August, 2001.
11. Biemond I, Burnham WR, D'Amaro J, Langman MJ: HLA-A and -B antigens in inflammatory bowel disease. *Gut* 7(8): 934-41, 1986.
12. Giardiello FM, Lazenby AJ, Yardley JH, Bias WB, Johnson J, Alianiello RG, Bedine MS, Bayless TM: Increased HLA A1 and diminished HLA A3 in lymphocytic colitis compared to controls and patients with collagenous colitis. *Dig Dis Sci* 37(4): 496-9, 1992.
13. Amano K, Seko A, Sugiyama H, Takahashi T, Watanabe T, Iguchi H, Nagano T, Osumi Y, Fuwa Y, Ngai K, et al: Ulcerative colitis in female siblings with an identical human leukocyte antigen haplotype (A24, BW52, DR52 and DQW1). *Intern Med* 32 (4): 298-301, 1993.