European Journal of Ophthalmology / Vol. 15 no. 5, 2005 / pp. 607-609

Immune recovery uveitis and human leukocyte antigen typing: A report on four patients

G. MODORATI, E. MISEROCCHI, R. BRANCATO

Department of Ophthalmology and Visual Sciences, Immunology and Uveitis Service, University Hospital San Raffaele, Milano - Italy

PURPOSE. To report the typing of human leukocyte antigen (HLA) in four human immunodeficiency virus–positive (HIV) patients with immune recovery uveitis (IRU).
METHODS. The medical history of four consecutive patients who presented at the Ocular Immunology and Uveitis Service (University Hospital San Raffaele, Milan, Italy) with definite diagnosis of IRU is reported. The HLA typing was tested in all patients.
RESULTS. All patients presented the clinical and ophthalmological characteristics of IRU. The HLA typing analysis showed the presence of HLA B 8-18 in all patients.
CONCLUSIONS. The data obtained from these patients indicate the presence of the same HLA typing (B 8-18). The clinical relevance of such association needs to be further evaluated. (Eur J Ophthalmol 2005; 15: 607-9)

Key Words. Immune recovery uveitis, HLA, Cytomegalovirus, HIV

Accepted: March 14, 2005

INTRODUCTION

Immune recovery uveitis (IRU) is a chronic intraocular inflammatory syndrome occurring in selected patients with inactive cytomegalovirus (CMV) retinitis taking highly active antiretroviral therapy (HAART) who experienced increase in CD4-T lymphocyte count (1-4).

The typical manifestations of this inflammatory syndrome are blurred vision, visual loss, and floaters. The uveitis is typically characterized by inflammation of the posterior segment of the eye rather than anterior, with vitritis, papillitis, and macular edema (1-4).

This syndrome is now believed to be the leading cause of visual loss in patients with acquired immunodeficiency syndrome (1-4). The pathogenesis of this disorder remains unclear and controversial. In particular, why IRU occurs in only a few of these patients is unknown. The aim of the present study was to evaluate the HLA typing in four consecutive patients with IRU.

METHODS

All patients with clinical characteristics of IRU referred to the Immunology and Uveitis Service (San Raffaele Hospital, Milan, Italy) in 2000 were included in the study. IRU was defined as ocular inflammation (vitritis, macular edema, and mild anterior uveitis) associated with clinical immune recovery in patients with acquired immunodeficiency syndrome and inactive CMV retinitis who responded to HAART and CD4 T-lymphocytes levels >60 cells/mm^3 (4). Eight HIV–positive patients with history of previous CMV retinitis treated with HAART who did not develop IRU were used as a control group.

RESULTS

All patients underwent a complete ophthalmologic evaluation. The HLA typing analysis showed the pres-

Presented as a poster at the 2003 IOIS meeting.

1120-6721/607-03$15.00/0

TABLE - PATIENT CHARACTERISTICS, TREATMENT AND ONSET OF CMV RETINITIS, TYPE OF HAART, AND HLA TYPING

Patient no.	Sex	Age, yr	CD4/µL pre/post HAART	CMV retinitis onset	Treatment of CMV retinitis	IRU onset	HLA-B
1	M	43	100/211	Nov. 1999	DHPG/Fosc	March 2000	B 8-18
2	F	34	34/662	June 1995	DHPG	Apr. 2000	B 8-18
3	F	27	200/680	May 1997	DHPG	Sept. 2000	B 8-18
4	M	22	120/514	Oct. 1998	DHPG	Oct. 2000	B 8-18

CMV = Cytomegalovirus; HAART = Highly active antiretroviral therapy; HLA = Human leukocyte antigen; IRU = Immune recovery uveitis; DHPG = Ganciclovir; Fosc = Foscarnet

ence of HLA B 8-18 in all patients. The characteristics of patients, immune reconstitution, timing of retinitis diagnosis, timing of IRU diagnosis, and the HLA-B typing for the four patients evaluated are reported in Table I. HLA typing in the control group showed no presence of HLA B 8-18.

DISCUSSION

The pathogenesis of IRU is unknown and unexplained. However, the uveitis may represent an immunologic reaction to CMV antigens in the eye made possible by HAART-mediated improvement in immune status (1-4).

A similar inflammatory immune recovery phenomenon involving other organs has been reported with other pathogens such as necrotizing lymphadenitis related to Mycobacterium avium complex infections (2-5). Nussenblatt and El-Bradley have hypothesized that the amount of viral replication is important in the pathogenesis of IRU, and that it is possible that the mode of treatment for CMV retinitis may influence the rate of IRU (6, 7). The occurrence of IRU appears to be variable, and the reasons for this variability are unclear (1-4).

In a study of 82 patients with CMV retinitis treated with HAART, only 33 (40.2%) were considered responders to HAART. Among this group only 6 patients (18.1%) developed IRU (2).

To date, the largest series in the literature fail to reveal similarities among patients with IRU (1-4).

In order to better understand why only a specific cohort of patients is susceptible to IRU, we decided to explore a possible genetic predisposition for this immunologic disorder. The results of our study show that all patients with IRU have HLA B 8-18.

The major histocompatibility complex (MHC), a group of genes located on chromosome 6 in humans, is a major factor controlling each individual's immune response. Therefore an attempt to demonstrate a possible correlation between the MHC and IRU was our logical approach. Previous studies in MHC showed significant levels of association between HLA B 27 and anterior uveitis, and between HLA A 29 and birdshot retinochoroidopathy (8).

In our experience, among 23 patients with CMV retinitis treated with HAART who showed a rapid increase in CD 4 cells, the prevalence of IRU was 17.4% (4 patients). All these patients with IRU showed the same HLA B 8-18.

Despite the small number of cases we hypothesize a possible genetic predisposition to develop IRU.

Further studies are needed to confirm our preliminary results in order to determine the role of HLA in the pathogenesis of IRU.

The authors have no proprietary interest in any aspect of the article

Reprint requests to:
Giulio Modorati, MD
Department of Ophthalmology and Visual Sciences
University Hospital San Raffaele
Via Olgettina 60
20132 Milan, Italy
giulio.modorati@hsr.it

REFERENCES

1. Karavellas MP, Lowder CY, MacDonald JC, Avila CP Jr, Freeman WR. Immune recovery vitritis associated with inactive cytomegalovirus retinitis: a new syndrome. Arch Ophthalmol 1998; 116: 169-75.
2. Nguyen QD, Kempen JH, Bolton SG, Dunn JP, Jabs DA. Immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis after highly active antiretroviral therapy. Am J Ophthalmol 2000; 129: 634-9.
3. Robinson MR, Reed G, Csaky KG, Polis MA, Whitcup SM. Immune-recovery uveitis in patients with cytomegalovirus retinitis taking highly active antiretroviral therapy. Am J Ophthalmol 2000; 130: 49-56.
4. Karavellas MP, Azen SP, MacDonald JC, et al. Immune recovery vitritis and uveitis in AIDS. Clinical predictors, sequelae, and treatment outcomes. Retina 2001; 21: 1-9.
5. Zamir E, Hidson H, Ober RR, et al. Massive mycobacterial choroiditis during highly active antiretroviral therapy: another immune recovery uveitis? Ophthalmology 2002; 109: 2144-8.
6. Nussenblatt RB, Lane HC. Human immunodeficiency virus disease: changing patterns of intraocular inflammation. Am J Ophthalmol 1998; 125: 374-82.
7. El-Bradley MH, Cheng L, Song MK, Torriani FJ, Freeman WR. Long-term results of treatment of macular complications in eyes with immune recovery uveitis using a graded treatment approach. Retina 2004; 24: 376-82.
8. Gery I, Nussenblatt RB. Immunologic basis of uveitis. In: Pepose JS, Holland GN, Wilhelmus KR, eds. Ocular Infection and Immunity. St. Louis: Mosby-Year Book, 1998: 141-56.