—— CLINICAL INVESTIGATION ——

Epidemiological Survey of Intraocular Inflammation in Japan

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Abstract

Purpose: To report the frequency and trend of intraocular inflammation based on a survey of new ophthalmology patient visits to university hospitals throughout Japan during 2002.

Methods: A questionnaire was sent to the departments of ophthalmology in 110 university hospitals nationwide to survey the total number of new patients who visited the outpatient clinics for the first time between 1 January and 31 December 2002, and also the number of patients diagnosed with intraocular inflammation during this period.

Results: The surveys completed by 41 university hospitals were analyzed in this study. During 2002, a total of 151 299 new ophthalmological patients presented at the 41 institutions, and 3060 (2.2%) of the new patients were diagnosed as having intraocular inflammation. The most frequent intraocular inflammatory disease identified was sarcoidosis (13.3%), followed by Vogt-Koyanagi-Harada (VKH) disease (6.7%), Behçet disease (6.2%), bacterial endophthalmitis (3.8%), herpetic iridocyclitis (3.6%), diabetic iritis (1.6%), human leukocyte antigen-B27-associated uveitis (1.5%), acute retinal necrosis (1.3%), ocular toxoplasmosis (1.1%), ocular toxocariasis (1.1%), uveitis associated with human T lymphotropic virus-1 (also known as HAU) (1.1%), and others. Infectious intraocular inflammation accounted for 16% of all uveitis cases.

Conclusions: Through the collaboration of a large number of institutions, some aspects of the epidemiology of intraocular inflammation in Japan were elucidated. However, the disease concept and diagnostic criteria remain ambiguous for a considerable number of diseases within the spectrum of intraocular inflammation, and the possibility that such factors may bias the present findings cannot be denied. In the future, a prospective survey based on well-defined, common diagnostic criteria is required to obtain more precise epidemiological data. **Jpn J Ophthalmol** 2007;51:41–44 © Japanese Ophthalmological Society 2007

Key Words: epidemiology, intraocular inflammation, Japan, uveitis

Introduction

Statistical analyses of the incidence of intraocular inflammation have been reported in numerous Japanese and overseas studies.[1–8] The factors that affect the epidemiology of

intraocular inflammation include endogenous factors such as age, sex, ethnic background, medical history, and immunogenetic background, as well as exogenous factors such as climate, public health, dietary habits, and causative pathogens. The exogenous factors in particular may change over time, and periodic implementation of epidemiological surveys of intraocular inflammation is important. On the other hand, it is not easy to define and control clinically the individual factors of intraocular inflammation. Since there are great differences among institutions in the quality and quantity of tests performed for the purpose of diagnosis,

epidemiological studies of a single institution or a limited number of districts are inadequate for evaluating the general status of intraocular inflammation.

A working group of the Japanese Ocular Inflammation Society conducted a survey to delineate the status of intraocular inflammation in university hospitals nationwide. The results of the survey are reported in this article.

Materials and Methods

A questionnaire was sent to the departments of ophthalmology in 110 university hospitals nationwide to survey the total number of patients who visited the outpatient ophthalmology clinics for the first time during the 1-year period between 1 January and 31 December 2002. The number of patients diagnosed as having intraocular inflammation during this period, together with the identified diseases, were investigated.

Explanatory notes were provided in the survey questionnaire giving specific instructions on the vocabulary for diagnosis. For example, while "acute anterior uveitis" is a commonly used diagnostic term, the diagnostic criteria for this entity remain ambiguous, and respondents were requested to register this diagnosis as "unclassified intraocular inflammation." Cases of acute anterior uveitis with identified underlying causes were to be preferably registered using the terms of the underlying diseases; therefore, cases of intraocular inflammation associated with diabetes, ankylosing spondylitis, or human leukocyte antigen (HLA)-B27 were registered as diabetic iritis, ankylosing spondylitis-associated uveitis, or uveitis associated with HLA-B27, respectively. While intermediate uveitis is treated as an independent clinical entity in America and Europe, this disease is relatively rare in Japan, and definitive diagnostic criteria are not well established. Therefore this disease was registered also as "unclassified intraocular inflammation." Postoperative intraocular inflammation such as bacterial endophthalmitis after intraocular surgery was included as endophthalmitis as well as endogenous bacterial endophthalmitis. Other than these explanatory notes here described, the use of specific national or international guidelines was not required in this study.

Results

Among the 110 institutions contacted, 68 indicated willingness to participate in the questionnaire survey, and, finally, 44 institutions responded. Three institutions were excluded owing to incomplete entries, and eventually the data of 41 institutions were included in the analysis. During the year 2002, a total of 151 299 new patients presented as ophthalmology outpatients in the participating 41 institutions; 3060 (2.2%) were diagnosed as having intraocular inflammation. The proportion of patients diagnosed as having intraocular inflammation ranged widely, from 0.6% to 7.8% of the new patients.

Table 1. Diagnostic frequencies in 2002 for new patients with intraocular inflammatory diseases in 41 Japanese university hospitals

Disease	Number of patients (%)
Sarcoidosis	407 (13.3)
Vogt-Koyanagi-Harada disease	205 (6.7)
Behçet disease	189 (6.2)
Bacterial endophthalmitis	115 (3.8)
Herpetic iritis	110 (3.6)
Posner-Schlossman syndrome	57 (1.9)
Diabetic iritis	48 (1.6)
HLA-B27-associated uveitis[1]	46 (1.5)
Acute retinal necrosis	41 (1.3)
Ocular toxoplasmosis	36 (1.1)
Ocular toxocariasis	35 (1.1)
HTLV-1-associated uveitis[2]	35 (1.1)
Fungal endophthalmitis	32 (1.0)
Intraocular lymphoma	32 (1.0)
Collagen disease-associated uveitis	31 (1.0)
Cytomegalovirus retinitis	24 (0.8)
Ocular tuberculosis	20 (0.7)
IBD-associated uveitis[3]	18 (0.6)
Juvenile uveitis except for JRA[4]	17 (0.5)
Fuchs heterochromic iridocyclitis	15 (0.5)
JRA-associated uveitis[4]	15 (0.5)
Others	341 (11.1)
Unclassified intraocular inflammation	1191 (38.9)
Total	3060 (100)

HLA, human leukocyte antigen; HTLV, human T lymphotropic virus; IBD, inflammatory bowel disease; JRA, juvenile rheumatoid arthritis.
[1–4]Refer to these references for relevant information.

The distribution of specific intraocular inflammatory diseases in Japan is shown in Table 1. The most frequent intraocular inflammatory disease identified was sarcoidosis (13.3%), followed by Vogt-Koyanagi-Harada (VKH) disease (6.7%), Behçet disease (6.2%), bacterial endophthalmitis (3.8%), herpetic iridocyclitis (3.6%), diabetic iritis (1.6%), HLA-B27-associated uveitis (1.5%), acute retinal necrosis (1.3%), ocular toxoplasmosis (1.1%), ocular toxocariasis (1.1%), human T lymphotropic virus (HTLV)-1 associated uveitis (1.1%), and others. Unclassified intraocular inflammation constituted 39% of all cases. Infectious intraocular inflammation accounted for 16% of all cases. Sarcoidosis, VKH disease and Behçet disease are conventionally the three major intraocular inflammatory diseases in Japan, and these three diseases combined accounted for 26% of all intraocular inflammation cases. When the frequency of the diseases was analyzed by area, the average frequency in five institutions in the Kyushu area accounted for 5.1% of HTLV-1 associated uveitis and 2.7% of the uveitis associated with toxoplasmosis. These frequencies greatly exceeded the national average, which was 1.5% and 1.1%, respectively. Especially, the frequency of uveitis associated with HTLV-1 in the Kyushu area is significantly greater than the national average ($P < 0.0001$, Mann-Whitney test). The other diseases showed approximately equal geographic distribution.

Discussion

Recent epidemiological studies of intraocular inflammation in Japan showed an increase in the number of institutions treating sarcoidosis as the most prevalent uveitis.[1,5] In the present national survey, sarcoidosis also had the highest frequency of 13.3%. In Japan, a diagnosis of sarcoidosis has to satisfy the diagnostic criteria of the Ministry of Health, Labour and Welfare;[9] hence, many cases that are strongly suspect based on ocular findings do not lead to a definitive diagnosis of sarcoidosis. Among the unclassified cases that constituted 39% of all intraocular inflammations in this survey, there are probably a large number of cases in which ocular findings were strongly suggestive of sarcoidosis but the results of systemic investigations did not satisfy the Ministry's diagnostic criteria. VKH disease, which occupies the second place in frequency in our study, showed no marked variations in case rate with the passage of time. On the other hand, a few reports have indicated a tendency for the number of patients with Behçet disease in Japan to decrease,[10,11] and the incidence remained at 6.2% in the present survey. Among infectious intraocular inflammation cases, the frequency of intraocular inflammation caused by herpes virus was high. This was probably a consequence of the establishment and widespread use of reliable diagnostic methods such as polymerase chain reaction.

There was no marked variation in the geographical distribution of intraocular inflammatory diseases overall, but a relatively high proportion of HTLV-1-associated uveitis and ocular toxoplasmosis was observed in the Kyushu area compared with other areas in Japan. The increase in HTLV-1-associated uveitis is probably due to a high prevalence of HTLV-1 virus carriers in the southern part of Kyushu.[12] The increase of ocular toxoplasmosis may be related to dietary habits, including the consumption of uncooked chicken, and other regional factors. On the other hand, while HTLV-1-associated uveitis was previously reported to be localized mainly in South Kyushu,[5,13,14] our survey has demonstrated that this disease is by no means rare in other areas outside Kyushu.

As shown above, this preliminary survey has elucidated the overall trend of intraocular inflammation in Japan. However, several issues were also highlighted. Since the present questionnaire survey is a retrospective study based on clinical charts, the final diagnoses at various institutions were not based on a standard set of tests. Consequently, the survey results might have been affected. For example, when a patient with acute anterior uveitis was diagnosed, it was unclear whether the underlying causes such as HLA, diabetes, or ankylosing spondylitis were investigated. In addition, since the institutions surveyed were university hospitals, serving mainly as referral centers, milder cases that are more likely to be diagnosed and treated at general clinics were not included in this statistical analysis. For example, Posner-Schlossman syndrome is an entity for which appropriate treatments usually control the intraocular inflammation and intraocular pressure within a relatively short time. It is likely that the actual number of patients affected by Posner-Schlossman syndrome far exceeds the figure recorded in this survey.

In the future, to develop a more accurate epidemiological study of intraocular inflammation in Japan, a prospective survey based on well-defined, common diagnostic criteria is indispensable.

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