Epidemiology of endogenous uveitis in north-eastern Italy. Analysis of 655 new cases

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ABSTRACT.

Purpose: **To report the results of a retrospective analysis among endogenous uveitis patients in the north-eastern area of Italy.**

Methods: **The authors reviewed a series of 655 new cases treated between October 1986 and December 1993. The incidence of endogenous uveitis was calculated based on a 100,000 patient population.**

Results: **The average incidence was 11.40/100,000. The majority of patients were between the ages of 20 and 70 years (74.43%). A probable diagnosis was determined in 55.57% of cases; anterior uveitis was diagnosed in 58.01% of cases, posterior uveitis in 26.11%, panuveitis in 12.98%, and intermediate uveitis in 2.9% of cases. The authors observed recurrences in 25.49% of cases. While the first cases are almost equally distributed in the various months, the recurrences seem to be significantly more frequent in the cold (from November to February; mean air temperature<8°) and transitional months (October and from March to May; mean air temperature from 8°C to 18°C) than in the warm months (from June to September; mean air temperature >18°C). Respectively p=0.003 and p=0.029.**

Conclusion: **The incidence in this series is lower than in other European and American studies. Despite the high rate of idiopathic cases in this study, the authors support that the presentation of single case experiences may allow improved multi-centric analysis and a greater understanding of the epidemiology of uveitis.**

Key words: endogenous uveitis – epidemiology – incidence – uveitis entities.

Uveitis accounts for approximately 10% of all severe visual disorders in the western world (Nussenblatt 1990). As new disease entities have been described in literature, interest in uveitis has also increased. There are only few earlier population-based studies on the incidence of uveitis (Darrell et al. 1962; Miettinen 1977; Vadot 1984; Nussenblatt 1990; Palmares et al. 1990; Tran et al. 1995; Saari et al. 1995; Pivetti–Pezzi et al. 1996; Päivönsalo-Hietanen et al. 1997).

Selected forms of uveitis have been found to have a definite geographical distribution such as onchocerchiasis, histoplasmosis, and Behçet's syndrome (Perkins 1976). As a consequence, studies on the incidence of uveitis within a community are important in order to enable rational investigation and management of the disease. Despite advances in diagnostic accuracy, many cases of intraocular inflammation continue to defy diagnosis. Thus epidemiological studies in uveitis may be extremely important in an effort to better understand the etiology of the disease and the classification of its subtypes.

The authors conducted a retrospective analysis among patients treated at the Eye Clinic at the University of Verona in Italy. The Eye Clinic is a provider of in-patient and out-patient care as well as a major referral center for an area of approximately 789,000 inhabitants.

Patients and Methods

The authors reviewed a series of 655 in-patient and out-patient new cases of endogenous uveitis treated at the Eye Clinic at the University of Verona between October 1986 and December 1993. Among these patients, 167 cases of recurrences were observed. Demographic data and pattern of uveitis were utilized for computer analysis.

Uveitis was recorded, according to the International Uveitis Study Group Classification System, based on the anatomical location of the inflammation: anterior uveitis (iris and ciliary body), posterior uveitis (choroid and retina), intermediate uveitis (peripheral retina and pars plana of the ciliary body), and panuveitis (inflammation of the entire uvea) (Bloch-Michel & Nussenblatt 1987). HIV-positive patients were not included in this series.

The incidence rate of different forms of uveitis for a 100,000 patient population per year was calculated using population statistics of the city of Verona, the county of Verona, and the hospital district of the University. The total number of patients treated at the Eye Clinic, between October 1986 and December 1993, was 18,244. During the period of this study, the combined city and county population increased from 783,886 to 798,533 inhabitants (Table 1).

Table 1. Annual incidence rates for a 100,000 patient population.

	Mean population	Cases	Incidence
1987	783,320	93	11.87
1988	784,965	115	14.65
1989	786,883	74	9.40
1990	789,606	90	11.39
1991	789,917	81	10.25
1992	790,158	104	13.16
1993	793,692	72	9.07
Average	788,363	89.86	11.40

Table 2. Systemic pathologies of patients.

Pathology	Number of patients
Hypertension	26
Diabetes mellitus	22
Juvenile rheumatoid arthritis	14
Rheumatoid arthritis	12
Tubercolosis	8
Psoriasis	7
Chronic tonsillitis	6
Sarcoidosis	6
Duodenal ulcer	5
Hypothyroidism	4
Gout	3
Chronic sinusitis	2

Table 3. Etiology vs. anatomic location of endogenous uveitis.

	Anterior No.	Intermediate No.	Posterior No.	Panuveitis No.	Number of patients No.	Number of patients %
Idiopathic	220	7	36	28	291	44.42%
Toxoplasmosis	0	0	103	13	116	17.7%
Viral (herpes simplex and zoster)	72	0	5	0	77	11.75%
Tuberculosis	24	0	17	5	46	7.02%
Behçet disease	3	0	2	15	20	3.05%
Local infections	5	1	6	3	15	2.29%
Fuchs' heterochromatic dystrophy	14	0	0	0	14	2.14%
Pars planitis	0	11	0	0	11	1.68%
Juvenile rheumatoid arthritis	11	0	0	0	11	1.68%
Mycosis	1	0	0	9	10	1.53%
Rheumatoid arthritis	9	0	0	0	9	1.37%
Vogt-Koyanagy-Harada syndrome	0	0	0	9	9	1.37%
Posner-Schlossman syndrome	9	0	0	0	9	1.37%
Psoriasis arthritis	6	0	0	0	6	0.91%
Phacoanaphylaxis	6	0	0	0	6	0.91%
Sarcoidosis	0	0	2	3	5	0.76%
Total	380	19	171	85	655	
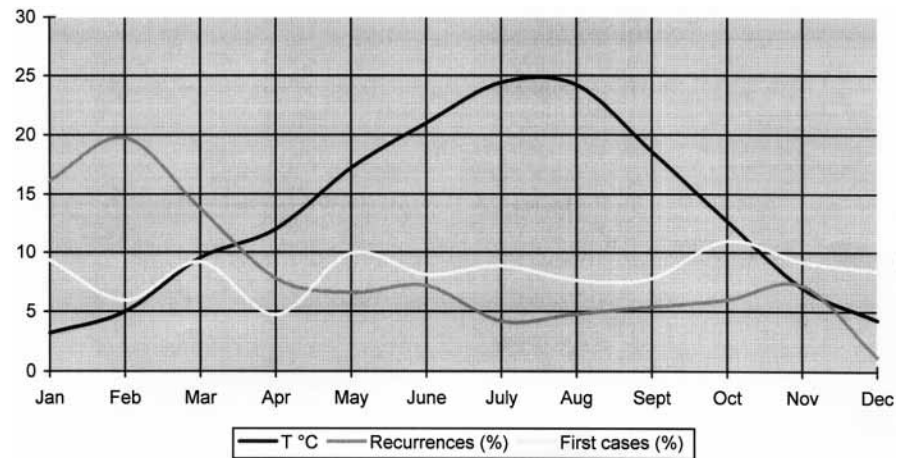
Fig. 1. Monthly distribution of first cases and recurrences and mean air temperature.

Results

Incidence

The authors observed 655 new cases of endogenous uveitis, with the average number of cases per year ranging from 72 in 1993 to 115 in 1988. Uveitis patients represented 5.8% of all in-patient and 16.7% of all out-patient cases. The patient follow-up period varied from two weeks to one year. The average incidence of endogenous uveitis in this study was 11.40/100,000. The annual incidence rates among a population are reported in Table 1.

Seasonal distribution

We grouped the months of the year into cold (November, December, January, February), transitional (March, April, May, October) and warm (June, July, August, September) seasons according to the mean air temperature in north-eastern Italy. We considered cold the months whose mean air temperature was below 8°C, warm above 18°C and transitional between 8°C and 18°C. We found 215 cases (32.82%) in the cold months, 228 cases (34.81%) in the transitional months and 212 cases (32.36%) in the warm ones. This seasonal distribution of cases, analyzed with chi-square test for 3×2 frequency table, was not statistically significant (p=0.72) (Fig. 1).

Sex

Among the 655 cases, 341 (52.06%) were male and 314 were female (47.94%). The ratio is comparable to the male/female ratio of the general population in Italy (ISTAT 1981).

Age

The average age of the population in this study was 44.36 years (male: 44.13 years; female: 44.6). The distribution of risk of uveitis varied for each decade of age. Most patients were between the ages of 20 and 70 years (74.43%); the highest proportions were found in the decades between 20 to 29 years (112 patients; 17.09% of the total) and 50 to 59 years (110 patients; 16.73% of the total). Similar percentages were observed among three different decades: patients between

Table 4. Etiology in young and adult patients.

	Young (≤18 years)	Adult
Idiopathic	40%	46%
Toxoplasmosis	8%	14%
Viral (herpes simplex and zoster)	–	15%
Tuberculosis	7%	6%
Juvenile rheumatoid arthritis	6%	–
Behçet disease	–	4%
Fuchs' heterochromatic dystrophy	8%	1.5%

30 to 39 years (86 patients; 13.13% of the total), patients between 40 to 49 years (91 patients; 13.89% of the total), and those between 60 to 69 years (89 patients; 13.59% of the total). Twenty-two patients were younger than ten years (3.36%), 12 patients were between 80 and 89 years (1.83%), and 2 patients were older than 90 years (0.3%).

Patient history

The distribution of refraction error includes: 347 emmetrope patients (52.98% of the total), 157 myope (23.97%), and 151 hyperope patients (23.05%). Systemic pathologies of the patients are reported in Table 2. Monocular presentation was more frequently noted (73.4%) than the bilateral (26.6%).

Etiology

Probable diagnosis was determined in 364 cases (55.57%). The etiology of 291 cases (44.42%), almost all anterior uveitis, could not be found and were thus classified as idiophatic. Table 3 reports the etiology of the whole series of 655 new cases.

The etiology distribution differed between young (≤18 years of age) and adult patients (Table 4).

With regard to the anatomical location, there were 380 cases (58.01%) of anterior uveitis, 171 (26.11%) posterior uveitis; 85 cases (12.98%) panuveitis, and 19 cases (2.9%) of intermediate uveitis (Table 5).

Besides the series of 655 new cases of endogenous uveitis, during the period from October 1986 to December 1993, the authors also observed 187 cases of exogenous uveitis, caused primarily by trauma, surgical trauma, or exogenous infection of the uveal tract.

Recurrences

The authors observed 167 cases of recurrences (25.49%, 82 male and 85 female). Of these cases, 74 (44.31%) recurred in the cold months, 57 (34.13%) in the transitional months and 36 (21.56%) in the warm months. This difference was statistically significant (p=0.0015). We compared the distribution of cases between seasons. We found that the number of recurrences in the cold and transitional months was significantly higher than in the warm seasons (p=0.0003 and p=0.029 respectively). The different number of recurrent cases between the transitional and warm seasons, instead was not statistically significant (p=0.13). (Fig. 1).

Complications

In this series, the uveitis episode was complicated by glaucoma in 25 cases, cataract in 17 cases, cystoid macular edema (CME) in 10 cases, band keratopathy in 5 cases, and tractional retinal detachment in 2 cases. Table 6 reports the correlation between uveitis etiology and associated complications.

Discussion

The annual incidence rate of uveitis in this study was 11.40/100,000 population which is essentially lower than in earlier population-based studies. The annual incidence rate of uveitis was 17/100,000 population in USA (Darrell et al. 1962) and in France (Vadot 1984), 19.6/100,000 population in northern Finland (Miettinen 1977) and 22.6/100,000 in south-western Finland (Saari et al. 1995; Päivönsalo-Hietanen et al. 1997). Thus the incidence of uveitis in this study was only one-half of that reported in south-western Finland. In our study obviously many cases of anterior uveitis may have been treated by private ophthalmologists or other eye centers in this area and therefore our material may reflect more the same distribution of uveitis as seen in other tertiary referral centers in Italy and in southern Europe.

The distribution of risk of uveitis was different in each decade of age. Most patients in this series were between the ages of 20 and 70 years (74.43%) which is consistent with the findings of Saari (Saari et al. 1995).

In this series, the etiology was established in 55.57% of cases, while in 44.42%, the etiology could not be determined. Although these results support several reported surveys (Pivetti-Pezzi 1987; James et al. 1979; Bloch-Michel et al. 1980), they differ with others such as

Table 5. Comparative classification of uveitis in various studies.

	Present study Verona, Italy	Palmares et al. Northern Portugal	Tran et al. Switzerland	Pivetti-Pezzi et al. Italy
No. of patients	655	450	435	1417
Anterior uveitis	58.01%	60%	62%	49%
Posterior uveitis	26.11%	24%	20%	22%
Panuveitis	12.98%	12%	7%	16%
Intermediate uveitis	2.9%	4%	11%	12%

Table 6. Correlation between etiology of endogenous uveitis and complications.

	Retinal detachment	Cystoid macular edema	Cataract	Glaucoma	Band keratopathy
Vogt-Koyanagy-Harada	1	/	/	/	/
Behçet	1	2	2	/	/
Pars planitis	/	5	2	1	2
Juvenile rheumatoid arthritis	/	3	/	/	3
Arthritis	/	/	/	2	/
Fuchs'	/	/	8	8	/
Viral	/	/	/	9	/
Sarcoidosis	/	/	/	1	/
Tuberculosis	/	/	5	4	/
Total	2	10	17	25	5

Bardelli et al. (1982), Friedman & Schwartz (1981) and Pivetti-Pezzi et al. (1996).

As regards as the distribution of our uveitis cases according to different anatomical location, this is very similar to those reported from other Southern European countries and from Switzerland (Palmares et al. 1990; Tran et al. 1995; Pivetti-Pezzi et al. 1996) (Table 5).

In anterior uveitis, it is often difficult to determine a specific diagnosis, primarily because the eye responds in a very similar manner in a large range of systemic diseases and infections for a given human population in a given environmental setting. It is easier to classify posterior uveitis due to the fact that the appearance of the fundus often correlates well with a specific diagnosis. In this study, the most common cause of posterior uveitis was toxoplasmosis which is consistent with other studies in western countries (Tran et al. 1995).

Intermediate uveitis still remains frequently underdiagnosed, particularly in young adults. The study of Henderly et al. (1987) reported a percentage of 15.4% of intermediate uveitis, an exceptionally high rate compared to the low figures of Perkins (4.6%) (1976), Schlaegel (4.6%), Palmares (4.0%) (1990), and those found in this study (2.9%). Other surveys, as well as the present study, show a very low prevalence of sarcoidosis (0.4% of all cases) (Pivetti-Pezzi et al. 1996). The authors suspect that this disease is underdiagnosed due to the difficulty of diagnosing a sarcoidosis ocular involvement, the low incidence of sarcoidosis in Italy (Blasi & Pezza 1989), and the fact that a systemic and costly diagnostic approach is sometimes necessary.

The Eye Clinic in Verona is a direct-care facility and a referral center. As stated by Tao Tran V, (Tran et al. 1995), this circumstance may explain the great number of anterior uveitis cases and the proportionally small number of posterior uveitis and panuveitis cases compared to other studies (Henderly et al. 1987). These centers may consult almost exclusively referred patients thus resulting in a bias towards more complicated posterior uveitis or panuveitis. The higher occurrence of posterior uveitis and panuveitis in Japan may be explained by the high incidence of Beçhet's uveitis and Vogt-Koyanagi-Harada in that country (Sugita et al. 1993).

Although patient history data was of significant importance in determining probable diagnosis (Table 2), systemic diseases such as hypertension and diabetes, frequently found in patient case records, are unlikely to be correlated to uveitis episodes due to their high incidence in the general population.

Uveitis tends to recur, as shown also in this study (25.49% of cases); therefore, it appears extremely important to monitor uveitis patients at least twice a year after the acute phase. The out-patient care of the Day Hospital System was found to be useful and practical as a delivery care system for uveitis patients.

While the seasonal distribution of the first cases, analyzed with chi-square test for 3×2 frequency table, was not statistically significant (p=0.72), differently from what is seen in south-western Finland (Päivönsalo-Hietanen et al. 1998), we found that the number of recurrences in the cold and transitional months was significantly higher than in the warm seasons (p=0.0003 and p=0.029 respectively).

Conclusion

The incidence of endogenous uveitis in this study was 11.40/100,000/year. Diagnosis was determined in 55.57% of the cases. There was no correlation found between the rate of uveitis and sex or refractive errors. The occurrence of endogenous uveitis was determined to be low under 10 and over 90 years of age, most frequently occurring between the ages of 20–29 and 50–59 years. While the distribution of first cases was not so different between seasons, during the cold and transitional months, the rate of recurrences was significantly higher than during warm months. The proportion of recurred uveitis was demonstrated to be significant among the total number of endogenous uveitis cases. The most frequent complications included glaucoma, cataract, and CME. Band keratopathy and retinal detachment were noted less frequently.

Despite the possible limitations and the high rate of idiopathic cases in this study, the authors support that the presentation of single case experiences from various uveitis centers may allow improved multi-centric analysis and a better understanding of the factors which influence the incidence and prevalence of uveitis in different countries.

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