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Presentation delay in patients affected with exudative age-related macular degeneration

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Abstract *Background:* Presentation delay (i.e. duration of visual symptoms before initial presentation) is an established critical parameter for visual prognosis in patients with exudative age-related macular degeneration (ARMD) considering the natural history of the disease and the limitations of current treatments. The purpose of this study was to determine the duration of presentation delay and its evolution in two periods 4 years apart. *Methods:* Presentation delay in 1598 patients affected with exudative ARMD was retrospectively reviewed during two similar 8-month periods in 1994 and 1998 in a tertiary referral center. *Results:* The proportions of patients examined either within 1 month, between 1 and 3 months, and between 3 and 6 months after onset of symptoms, respectively, increased between 1994 and 1998 from 23% to 33%, from 27% to 32.5%, and from 14% to 18.5%. The proportions of patients examined between 6 and 12 months and after 12 months decreased from 16% to 12% and from 20% to 4%, respectively. Furthermore, the proportion of patients presenting with a first eye involvement during the first month following the onset of symptoms rose from 42% in 1994 to 52% in 1998. All these differences were statistically significant. *Conclusion:* This first specific review of presentation delay in exudative ARMD showed a significant decrease in this parameter between 1994 and 1998 that should be taken into account when assessing the overall evolution of visual outcome. Further studies are warranted to ascertain that these findings reflect a global improvement in the management of macular diseases.

Introduction

Age-related macular degeneration (ARMD) is the leading cause of blindness in people over 50 years of age in western countries. Severe visual loss occurs mostly in patients affected with the exudative form of the disease [5]. As the percentage of people over 50 years of age continues to grow, ARMD is becoming a major public health problem in developed countries.

At present, the only proven effective treatments for exudative ARMD are laser photocoagulation and photodynamic therapy (PDT) with verteporfin. According to randomized clinical trials [3, 13, 14, 15, 16,17], laser photocoagulation is beneficial only in eyes with well-defined (or classic) choroidal neovascularization (CNV) on fluorescein angiography (FA). Verteporfin PDT achieved stabilization of visual acuity (VA) in predominantly well-defined subfoveal CNV [21]. However, well-defined CNV represents only a minority of eyes with exudative ARMD [7].

Several previous studies established the relationship between a shorter duration of visual symptoms (VS) prior to initial presentation (i.e. a shorter presentation delay) and the possibility of benefiting from laser photocoagulation treatment [9, 10, 13]. Considering that the natural history of predominantly well-defined CNV is associated with a progressive decrease of VA [1, 2, 3, 8, 13, 14, 15] and that the effectiveness of verteporfin PDT is

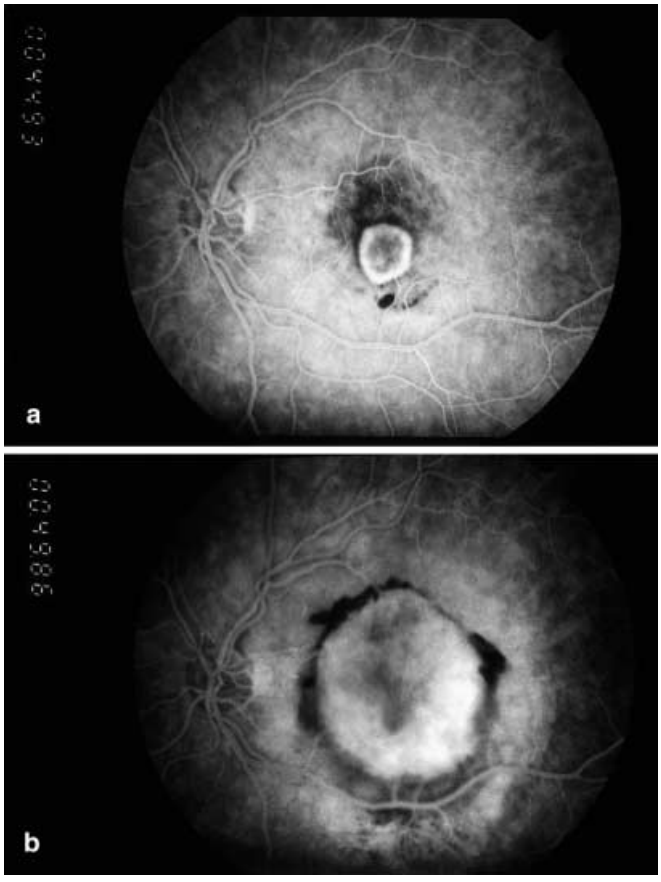

Fig. 1a, b Presentation delay and visual prognosis. Case 1. A 70-year- old patient presented because of a decrease in visual acuity (VA) in his left eye 3 weeks earlier. VA in this eye was 20/60. Fluorescein angiography (FA) showed a well-defined (classic) subfoveal CNV membrane (**a**). Immediately afterwards, the patient had a life-threatening myocardial infarction and Visudyne photodynamic therapy could not be performed. Three months later, VA in the left eye had dropped to 20/200, and a major extension of the CNV membrane was disclosed by FA (**b**)

mainly limited to achieving stabilization of VA [21], it also seems desirable to perform such treatment as early as possible (Fig. 1).

Therefore, any modification of presentation delay can alter the visual prognosis of affected patients. The aim of this study was to analyze the duration of presentation delay and its evolution between 1994 and 1998 at the Eye University Clinic of Créteil.

Materials and methods

Duration of VS prior to initial presentation in our clinic (presentation delay) was retrospectively reviewed in all patients affected with exudative ARMD during two 8-month periods four years apart: 1 February to 30 September 1995 and the same period in 1998. The Eye University Clinic of Créteil serves mainly as a tertiary referral center but also as a primary care provider. The organization of the Macula Department in our clinic remained unchanged between these two periods. In particular, the overwhelming majority of the patients referred to our center are examined and studied with FA within 24 h of following their referral, and this was the case in both 1994 and 1998.

Early signs of exudative ARMD were defined according to the international classification system [20]. Exclusion criteria were the following: (1) treatment by laser photocoagulation in the posterior pole before referral; (2) presence of any other cause of CNV, such as degenerative myopia, angioid streaks, chorioretinal inflammatory diseases, hereditary retinal disorders, or presumed ocular histoplasmosis syndrome; (3) date of onset of visual symptoms unknown or imprecise.

The duration of VS was recorded in the patient's charts, which included a form filled out at their first presentation. That information was compared with the data provided in the letter from the referring ophthalmologist. In the case of disagreement between these two sources, the longer duration of VS was selected.

The data were analyzed using standard statistical methods. The relationships between categorical variables were examined using Pearson's chi-square technique. Differences were considered significant when the probability of their occurrence by chance was less than 5%.

Results

Eight hundred forty-eight patients were studied in the group of patients presenting for the first time in our department between 1 February1994 and 30 September 1994 (group A). Seven hundred fifty patients were studied in the group of patients examined between 1 February 1998 and 30 September 1998 (group B).

In group A, 195 of the 848 patients (23%) were examined within the first month following the onset of VS, 228 (27%) between 1 and 3 months after the onset of VS, 119 (14%) between 3 and 6 months, 137 (16%) between 6 and 12 months, and 169 (20%) were examined after more than 1 year.

In group B, 248 of the 750 patients (33%) were examined within the first month following the onset of VS, 244 (32.5%) between 1 and 3 months after the onset of VS, 138 (18.5%) between 3 and 6 months, 90 (12%) between 6 and 12 months, and 30 patients (4%) were examined after more than 1 year (Fig. 2).

All the differences observed between group A and group B were statistically significant: the increased proportions of patients examined within one month ($P<0.001$), between 1 and 3 months ($P<0.02$), and between 3 and 6 months ($P<0.02$) after the onset of VS, as well as the decreased percentages of patients examined 6–12 months ($P<0.02$) and more than 1 year ($P<0.001$) after the onset of the VS.

In group A, of 195 patients examined during the first month after the onset of the VS, 82 (42%) were presenting for a first eye involvement and 113 (58%) for a second eye involvement. In group B, of 248 patients examined during the first month after the onset of VS, 129 (52%) were presenting for a first eye involvement and

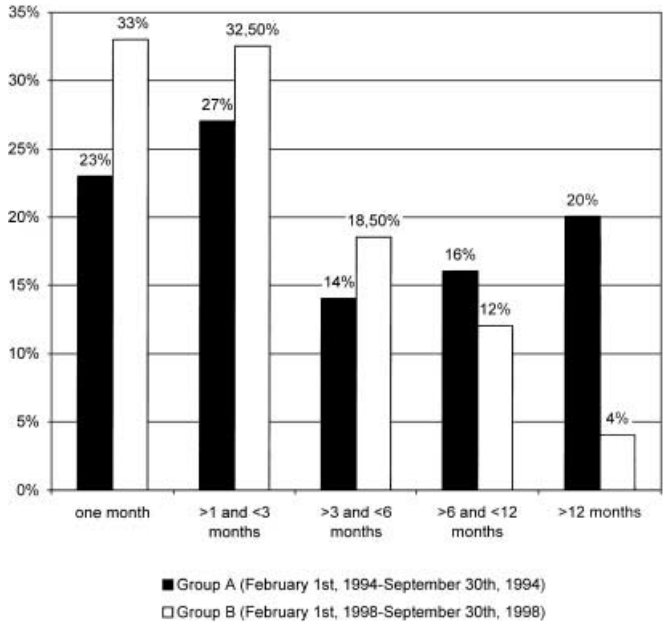

Fig. 2 Duration of visual symptoms at the time of presentation to a referral center in patients with exudative ARMD

119 (48%) for a second eye involvement. The increased proportion of patients presenting with a first eye involvement during the first month following the onset of symptoms attained statistical significance ($P<0.05$).

Discussion

Duration of VS before clinical examination and FA (i.e., presentation delay) is a well-known major parameter in determining visual prognosis in eyes affected with exudative ARMD. In 1979, Grey et al. [10] found that 83% of the eyes examined within 15 days of the onset of VS were potentially treatable with laser photocoagulation, compared with 43% of those examined between 3 and 4 weeks after onset. This rate decreased to 30% in eyes examined between 3 and 4 months, 10% in eyes examined between 5 and 6 months and only 1% in eyes examined more than 1 year after the onset of VS. Many other studies established that progressive and severe visual loss occurs during the natural course of all types of CNV in ARMD [1, 2, 3, 8, 11, 13, 14, 15, 16, 17, 19].

Data from the Macular Photocoagulation Study (MPS) Group trial published in 1982 concerning patients with extrafoveal CNV alone suggested that only 5% of the presenting patients met that criterion [13]. This finding is corroborated by a study by Pauleikhoff et al. [18], who detected only 6% of treatable lesions on FA performed in patients with late ARMD. Data provided by the follow-up of patients included in the observation groups of the MPS [13, 14, 15} showed that well-defined CNV which originates eccentrically has a tendency to expand preferentially toward the fovea. The growth of these membranes is more important at the early stage of proliferation. Other studies [12, 22] reported that a well-defined CNV membrane could expand at a rate of 9 to 10 µm per day. Gelfand et al. [9] also found that presentation delay is a major parameter in determining potential suitability for laser photocoagulation treatment according to the MPS eligibility criteria. Therefore, all factors and means resulting in a shorter presentation delay before retinal examination must be considered. In this regard, self-monitoring of the central vision of each eye on a regular basis has already been recommended for patients at risk for the development of exudative ARMD [6].

However, despite all these data, no detailed analysis of presentation delay in exudative ARMD is presently available. In fact, several factors are probably involved in the control of presentation delay: the patient's information and awareness of visual symptoms, the ophthalmologists' concern for exudative ARMD and their referral pattern, and the access to specialized eye care. Assessing the exact role of each of these factors in the decrease of presentation delay observed herein between 1994 and 1998 is extremely difficult. As the data stressing the importance of early retinal and angiographic examination go back to the late 1970s, most ophthalmologists were already well aware in 1994 of the importance of early referral of patients with symptoms of CNV. There was no significant change in the therapeutic means and guidelines for exudative ARMD between the two periods studied that could account for a major change in the referral pattern (the data establishing the effectiveness of verteporfin PDT were published in 1999 [21]).

It seems logical to expect that patients present earlier when the second eye becomes involved, which is the case for other ocular conditions such as retinal detachments. Therefore, the higher proportion of patients presenting for a first eye involvement during the first month in 1998 than in 1994 may suggest that people aged over 50 years are becoming better informed and more sensitive to visual symptoms and to their quality of eyesight. In order to confirm this hypothesis, the data provided by our study should be compared with corresponding data from other ophthalmologic referral centers in Western Europe.

The slight difference in the number of patients with exudative ARMD examined during the second period studied (750 in 1998 vs 848 in 1994, an 11.5% decrease) may be accidental or may be related to some unidentified local factors such as an increased number of retinal consultants and angiographic centers in our country or greater selectivity in referral. However, despite this decrease in the total number of examined patients, our results show that the number of patients examined at any point before 6 months after onset of VS was higher in 1998.

This work is preliminary and limited in scope. However, it provides the first specific review of the duration of VS prior to retinal examination in patients with exudative ARMD and provides the background for future studies to evaluate the potential impact of new diagnostic modalities and treatment approaches such as verteporfin PDT. Modifications of presentation delay, such as identified in this report, should be taken into account when assessing the overall evolution of visual outcome in exudative ARMD. Further multicentric studies are warranted to ascertain that our findings reflect a global improvement in the awareness and the management of macular diseases.

In summary, a significant decrease in presentation delay, which has already been established as a critical parameter for visual prognosis in patients with exudative ARMD considering the natural history of the disease and the limitations of current treatments, was observed between 1994 and 1998. This decrease should be taken into account when assessing the overall evolution of visual outcome. Further multicentric studies are warranted to ascertain that these findings reflect a global improvement in the awareness and the management of macular diseases.

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