Long-term Impact of Treated Congenital Toxoplasmosis on Quality of Life and Visual Performance

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Background: Long-term evolution of congenital toxoplasmosis is not documented. We assessed the outcome of treated congenital toxoplasmosis in a cohort of adult individuals who had undergone ante- and postnatal treatment to provide information for pediatricians and parents on the evolution of the disease.

Methods: We conducted a questionnaire study on 126 adults with congenital toxoplasmosis (mean age: 22.2 years; age range: 18–31 years) monitored regularly until the time of inclusion. The main outcome measures were quality of life (Psychological General Well-Being Index) and visual function (VF14 questionnaire), and the outcomes were correlated with disease-specific factors.

Results: Of the 102 patients (80.9%) who were finally included in the study, 12 (11.8%) presented neurologic effects and 60 (58.8%) manifested ocular lesions; in the latter category, 13 individuals (12.7%) had reduced visual function. The overall global quality-of-life score (74.7 ± 14.2) was close to the expected normal range for the general population (73.7 ± 15.3). Overall, visual function was only slightly impaired (M = 97.3; 95% confidence interval, 95.8–98.8). Although disease-independent critical life circumstances were associated with a reduced Psychological General Well-Being Index, this index was not influenced by any of the clinical characteristics of congenital toxoplasmosis. Neurologic pathologies, reduced visual acuity, foveal location of the retinal lesion, and squinting contributed to decreased visual function at follow-up.

Conclusions: Our data reveal that treated congenital toxoplasmosis has little effect on the quality of life and visual function of the affected individuals. These encouraging findings may help to alleviate the anxiety of affected individuals and their parents.

Key Words: congenital toxoplasmosis, Psychological General Well-Being Index, VF14, visual performance, quality of life

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Maternal infection with *Toxoplasma gondii* during pregnancy may have disease consequences for the fetus, ranging from the subclinical level to severe neurologic or ocular abnormalities. Among the latter, chorioretinitis is the most common manifestation. Although the majority of infected newborns show no clinical signs at the time of birth, they are at risk for developing visual impairment from newly acquired retinal lesions during childhood or adolescence.[1–3] The effect of these lesions on sight depends upon their topographical relationship to the macula and the optic disc. New lesions or recurrences may occur unpredictably and at any time long after birth.[4] Neurologic lesions may lead to severe handicaps[5] and intellectual impairment.[6]

The lack of precise information relating to the medical and psychosocial outcomes of congenital infection increases the anxiety of parents and health professionals. In adults, the outcome of the disease has been addressed in only 1 study.[7] Hence, very little information is available on long-term evolution of treated congenital toxoplasmosis (TCT).

In this study, we report on the long-term quality of life and visual function of a cohort of 102 adult patients with TCT. They were identified by mass antenatal screening, were treated ante- and postnatally, and were monitored at a single center in France.

METHODS

Study Design

This prospective study was carried out on a series of patients with TCT. Infection was confirmed during the pregnancy of their mothers or within the first months of life. The patients were born between March 1983 and June 1991, and were contacted at the end of January 2009 by the toxoplasmosis reference center of Lyon, France. At follow-up, they had a mean age of 22.2 years (range: 18–31.2 years).

Inclusion Criteria

To be eligible for inclusion in this study, the patients had to have a minimal age of 18 years and to have been monitored regularly since the time of birth in the same center. Only patients with maternal seroconversion detected through mass screening of pregnant women were included. To avoid an overestimation of severe cases, referred patients were not enrolled in the study.

Procedure

The patients were informed of the aim of the study and were invited to participate by completing 2 questionnaires. Visual acuity and clinical state of the eyes of all the patients had been assessed during their regular control visits, the last at the end of follow-up within the year before inclusion. For patients who had not had their ophthalmological control visits in Lyon, clinical information from their private ophthalmologists was included.

Measurements

Baseline Characteristics

Maternal seroconversion during pregnancy had been established, ante- and postnatal treatment had been undertaken, and ocular history had been fully documented. Additional sociodemographic information concerning the patients was available.

Clinical Information During the Follow-up Period

From the time of birth until the end of the follow-up period, data relating to postnatal treatment, recurrences, and organ mani-

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festations (such as neurologic problems) had been collected prospectively. Ophthalmologic status had been assessed every 3 months during the first year of life, and every 6 to 12 months thereafter until the end of the follow-up period, using a standardized form.[3] To obtain a reliable rating for the ocular findings, this was assessed independently by 2 ophthalmologists. Differences were resolved by consensus. Information relating to visual acuity was recorded for each eye. A value of less than 0.2 on the Snellen scale was defined as poor vision. The number of retinal lesions were recorded; as their localization may affect the field of vision or visual acuity,[8] they were rated as affecting the foveal center or other regions. The number of recurrences per eye was divided into 2 categories: none versus one or more. The absence or presence of squinting was documented.

Follow-up Information

Quality of Life

Quality of life was assessed according to the Psychological General Well-Being Index (PGWBI), which is a 22-item, self-reporting system (free authorization from the MAPI Research Institute). Patients rated their well-being during the past 2 weeks. The responses were scored from 1 to 5, and totaled between 22 and 110. A higher score indicates a feeling of well-being. The index is subdivided into 6 categories: anxiety, depressed mood, positive well-being, self-control, general health and vitality. The PGWBI has been shown to be a reliable measure of well-being. The internal validity in this study was very good for most of the subdivisions, with alpha-values above 0.80; the 2 exceptions were self-control (alpha-value = 0.66) and general health (alpha-value = 0.70). The total score was highly consistent (Cronbach alpha-value = 0.94). Data pertaining to our population were assessed on the basis of information provided by MAPI for a European survey of persons who were under 30 years of age.

Functional Visual Status

The functional visual status was estimated using a validated French version of the Visual functioning (VF14) questionnaire,[9,10] with the authorization of Prof. Gresset, University of Montreal, Canada. This self-reporting system addresses difficulties experienced by the patients in performing vision-related daily tasks, such as reading, sporting activities, or driving a car. The questions can be answered on a scale from 0 (unable to perform the task) to 4. The overall range of the scale lies between 0 and 100, with higher scores indicating less functional impairment. For our population, the Cronbach alpha-value was 0.90.

Statistical Analysis

The data were entered in an Excel sheet and double-checked by an independent observer. The data analysis was conducted using an SPSS system (Version 16, SPSS Incorporation, Chicago, IL). Descriptive information is presented as absolute numbers or as mean values together with standard deviations. The association of sociodemographic factors, clinical characteristics, and actual circumstances with quality of life and visual function was analyzed by using Spearman rank correlation.

Ethical Approval

The study was approved by the local Institutional Ethical Committee. All patients had given their written consent to participate in the study. The study was conducted in strict accordance with the Declaration of Helsinki.

RESULTS

Patient Flow Chart

Between 1983 and 1991, consecutive patients with TCT were evaluated prospectively. During this period, serology was compulsory in France at the first antenatal visit and for the 6 subsequent visits. The addresses of 4 persons could not be traced, and 13 patients did not respond to the initial invitation. Of the 109 patients who responded, 7 refused to participate. Therefore, the data from 102 patients were analyzed (Figure, Supplemental Digital Content 1, http://links.lww.com/INF/A735).

Patient Characteristics

Of the 102 patients, 44 were women. Eighty-seven of the individuals were living in a partnership or were married. Due to the young mean age of the patients (22.2 ± 3.4 years), 96 patients were as yet childless, 4 patients had 1 child, and 1 patient had 2 children. Among them, 27.5% had completed a high school education and 48% had obtained a university degree. Due to the large number of individuals who had undergone a high school education, 56.8% were not yet employed. The remaining persons were engaged in jobs at middle (36.3%) to higher educational level (6.9%).

Clinical Characteristics

Eight persons had been infected during the first trimester of maternal pregnancy, 53 during the second, and 41 during the third. Earlier gestational age at maternal seroconversion was associated with a higher risk of neurologic signs, but no association with eye lesions was found. Eighty-one mothers had undergone treatment during pregnancy, and all but one of the patients had undergone postnatal therapy. Twelve of the patients had neurologic effects (intracranial calcifications: n = 11; hydrocephalus: n = 2; seizures: n = 1). Of the 102 patients, 60 (58.8%) showed ocular lesions, but these were only associated with reduced visual function in a few instances (12.7%) (Table 1). The localization of the most central lesions did not follow a specific pattern or predilection in either eye. Too few cases of recurrences were reported (11.8%) to assess the effect of this factor on the quality of life.

TABLE 1. Ophthalmological Characteristics and Neurological Problems of the Patients

	Absolute Number (%)
No. ocular lesions	
None	42 (41.2%)
1	25 (24.5%)
2	17 (16.7%)
3 or more	18 (17.6%)
Lesions in both eyes*	26 (25.5%)
Persons with reduced visual acuity†	13 (12.7%)
Localization of lesion (independent of eye)	
Fovea	16 (15.7%)
Other region	44 (43.1%)
None	42 (41.2%)
Recurrences	
Without recurrences	90 (88.2%)
One recurrence	12 (11.8%)
Squinting	6 (5.9%)
Microphthalmia	3 (2.9%)
Cataract	1 (0.9%)
Neurological findings	
Intracranial calcifications	11 (10.8%)
Hydrocephalus	2 (1.9%)

*One person had central lesions in both eyes.
†As defined by a best-corrected Snellen score below 16 of 20.

TABLE 2. Quality of Life in Our Cohort Compared With That in an Age-matched General Population

	Study Cohort (n = 102)		General Population (Age-matched)*	
	Mean	Standard Deviation	Mean	Standard Deviation
Anxiety	71.2	19.3	72.2	19.6
Positive well-being	64.7	17.0	64.0	18.7
Vitality	64.7	15.2	68.0	18.5
Depressed mood	85.9	17.9	83.5	17.1
Self-control	80.7	16.0	82.5	17.2
General health	84.7	16.1	78.4	18.4
Global score	74.7	14.2	73.7	15.3

*European general population according to MAPI Institute; none of the differences attained statistical significance ($P > 0.05$).

Quality of Life and Visual Function

The overall global score for quality of life was good, and the general state of health was rated as being very good. The means for positive well-being and vitality were lower than the means for the other subdimensions. However, these data are consistent with those reported for the general population (Table 2). Visual function (VF14) was similarly very good (M = 97.3; 95% confidence interval, 95.8–98.8). Our data revealed that in patients with TCT, quality of life correlated moderately with visual function ($r = 0.421$; $P < 0.001$).

Association of Clinical Characteristics With Quality of Life and Visual Function

With respect to sociodemographic variables, women had a poorer quality of life than men. However, visual function was not poorer in women (Table, Supplemental Digital Content 2, http://links.lww.com/INF/A736, which represents correlation of sociodemographic and clinical characteristics with quality of life [global score] and visual function [VF14]). Level of education was not associated with either quality of life or visual function. With regard to early clinical variables, only the existence of neurologic problems had a negative effect on visual function. However, neurologic symptoms were not correlated with quality of life. The current clinical variables were correlated with poor visual function. Impairments in visual acuity, squinting, and foveal lesions were highly correlated with a patient's own assessment of his/her visual function ($r > 0.35$ at minimum). The current clinical variables were not correlated with quality of life. Distressful current circumstances had a negative effect on quality of life. An impairment in visual function tended to be associated with living under distressful current circumstances.

DISCUSSION

Our study is the first of its kind to demonstrate that TCT does not compromise the overall long-term quality of life or visual performance of affected patients. The global PGWBI scores did not differ from those that have been documented for an age-matched general European population. Women had moderately lower scores than men, which also correlates with findings for the general European population.[11] Patients with ocular lesions, even with posterior-pole involvement, did not have lower scores in general. The lowest score in both questionnaires was reported by a 24-year-old female patient who had microcephaly, cerebral calcification, bilateral retinal lesions (one of which involved the optic nerve), and epilepsy that was poorly controlled by medical treatment. The sole patient with bilateral macular involvement had average scores in both questionnaires (PGWBI: 78.2; VF14: 71.2). He admitted to being fearful of the possible occurrence of new ocular events. Nevertheless, he was able to pursue a normal professional life, although his visual acuity did not reach the level requisite for a driving license. Summarizing these results, it can be argued that some cases with moderate limitations in visual function and quality of life can be found, whereas the majority of cases are minimally or not affected by TCT in the long term. Health-related outcomes in previously published studies showed more severe impairments than those presented in this study. However, these studies related to referred cases that underwent neither antenatal treatment nor postnatal therapy for more than one-month duration, with shorter follow-up times[6,12,13] or to institutionalized handicapped children.[14] To date, only 1 study has monitored patients for a period as long as 20 years.[7] In this series, 9 of the 11 patients (81.8%) had chorioretinitis, and 3 of the patients were blind in 1 eye. In our cohort, only 1 case of cataract was reported, although the frequency of this condition in other studies involving patients ranged between 17%[15] and 40%.[14] We found no evidence of limited cognitive function in our cohort because the educational level was comparable with or even higher than that of the general population. None of the individuals were living in an institution for handicapped persons. At the age of 14 to 15 years, the school performances of the TCT patients did not differ from those of other uninfected children who were recruited through the same nationwide program.[7] Roizen et al[16] reported that vision impairment might affect cognitive testing. In our study, most of the mothers had undergone antenatal treatment and almost all of the infants were treated for 1 year after birth.

Whether the outcomes in our patients are comparable with those in untreated women and children is debatable, because the role of ante- and postnatal treatment in reducing sequelae has not yet been demonstrated in controlled studies.[17] Weak evidence of an association between early antenatal treatment and a reduced risk for mother-to-child transmission has been reported.[18] Cortina-Borja et al recently published an observational prospective cohort study suggesting that prenatal treatment reduced the risk of severe neurologic sequelae in infants.[19] Conversely, prenatal treatment does not appear to reduce the risk for chorioretinitis.[17] Nevertheless, the possibility of a beneficial effect is supported by the findings of a study in which 120 American children were treated for one year with pyrimethamine and sulfadiazine. After a follow-up period of 10.5 (±4.8) years, the outcome was overridingly favorable.[20] Moreover, a remarkable abatement of severe and active symptoms of disease was observed only a few weeks after initiation of the treatment. When the therapy was initiated at the time of birth and continued for 12 months, the outcome was better than that in untreated children.[20] Another study reported little progression of the disease in infants who had been treated from the time of birth.[21] Recurrences developed in 11.7% of cases, whereas new lesions were detected in 70% of the infants who had undergone no treatment during the first year of life.[22]

The duration of the follow-up period may also influence the results and could particularly bias the incidence of ocular involvement and recurrences.[3] Of the 12 recurrences reported in our cohort, 10 were diagnosed after the first decade, among them 3 at the age of 19 years. *Toxoplasma* strain genotypes may also play an as yet undetermined role and may explain differences in the frequencies of eye lesions between European and South American cohorts of patients.[23] In Europe, most isolates are of the type II genotype,[24] whereas in South America, types I/III, intermediate, or atypical genotypes predominate.[25] However, genetic diversity cannot account for intra-European differences.

The findings of our study indicate that the disease will most probably be confined to the eyes, with the possibility of late-onset chorioretinitis and unpredictable relapses in adulthood. Nevertheless, patients without neurologic abnormalities generally fare well, irrespective of their ocular status, their low vitality, and poor sense of well-being related to toxoplasmosis-independent events. The localization of an ocular lesion is not a reliable gauge of visual performance, as it tends to overestimate an impairment.[26] In conclusion, long-term outcome of TCT is rather good.

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