Journal of Neuroimmunology 321 (2018) 24–28

Contents lists available at ScienceDirect

Journal of Neuroimmunology

journal homepage: www.elsevier.com/locate/jneuroim

Does pregnancy affect women with multiple sclerosis? A prospective study in Western China

Wanlin Lai[a], Masako Kinoshita[b], Anjiao Peng[a], Wanling Li[a], Xiangmiao Qiu[a], Xi Zhu[a], Shixu He[a], Lin Zhang[a], Lei Chen[a,*]

[a] Department of Neurology, West China Hospital, Sichuan University, No. 37 Guo Xue Xiang, Chengdu, Sichuan 610041, PR China
[b] Department of Neurology, Utano National Hospital, National Hospital Organization, 8 Ondoyama-Cho, Narutaki, Ukyoku, Kyoto 616-8255, Japan

ARTICLE INFO

Keywords:
Multiple sclerosis
Pregnancy
Natural history
Annualized relapse rate (ARR)

ABSTRACT

Objectives: Pregnancy is considered to be protective for multiple sclerosis (MS) but little is known about Asian MS women. Our study aimed to investigate whether pregnancy affects the course of MS and whether MS affects pregnancy in a Chinese cohort.

Methods: We established a database (2009–2016) of 94 females with MS in the Department of Neurology at West China Hospital. From this database, we enrolled females who had been pregnant before or after the clinical onset of MS and consecutively followed up the patients and their offspring for at least one year after delivery. We registered their demographic, clinical and pregnancy-related information, as well as the annualized relapse rate (ARR) and Expanded Disability Status Scale (EDSS) score.

Results: We enrolled 55 females with MS and 126 pregnancies. Among them, 14 females had 15 deliveries after MS onset. In these 15 full-term pregnancies after MS onset, the average ARR decreased from 0.46 ± 0.52 in the year before pregnancy to 0.07 ± 0.26 (P = .034) during pregnancy and no drug exposure were observed during pregnancy. The average EDSS score at one year after delivery (1.50 ± 1.72) was higher than that at conception (0.77 ± 1.35; P = .045).

Conclusions: The natural history of MS during pregnancy suggests that full-term pregnancy protects MS females from relapse. However, the disability of MS females may develop after delivery.

1. Introduction

Multiple sclerosis (MS) is a chronic autoimmune-mediated inflammatory demyelinating disease of the central nervous system. MS mainly occurs in young adults with a higher incidence in females than in males (F:M, 2–3:1) (Voskuhl and Gold, 2012). Thus, most female patients of childbearing age and their families worry about pregnancy problems. Until now, several studies from Europe reported that annualized relapse rate (ARR) of MS decreased during pregnancy and increased after delivery (Nelson et al., 1988; Runmarker and Andersen, 1995; Confavreux et al., 1998; Finkelsztejn et al., 2011; Jesus-Ribeiro et al., 2017).

However, some questions still remain to be answered. First, a few studies observed no changes of relapse rate in these periods (Roullet et al., 1993; Finkelsztejn et al., 2011; Cuello et al., 2017; Jesus-Ribeiro et al., 2017). Second, no data have been obtained from Asia up to now. Third, few of the studies observed the natural history of MS during pregnancy.

Nowadays, as the incidence and prevalence of MS in Asians has increased gradually in epidemiological surveys (Houzen et al., 2008; Cheng et al., 2009; Osoegawa et al., 2009; Alroughani et al., 2014; Etemadifar et al., 2014; Eskandarieh et al., 2016), governments are paying more attention to MS and especially to the reproductive health of female patients. Therefore, we prospectively registered the MS-related clinical data before, during and after pregnancy of female MS patients. Then we tried to figure out whether pregnancy affects the relapse rate of MS in our cohort from Western China.

2. Method

The study was approved by the local ethics committee and written informed consents were obtained from all participants.

2.1. Study subjects

We established a database of females with MS in the Department of

* Corresponding author.
E-mail address: leilei_25@126.com (L. Chen).

https://doi.org/10.1016/j.jneuroim.2018.05.012
Received 21 March 2018; Received in revised form 11 May 2018; Accepted 22 May 2018

Neurology at West China Hospital from January 2009 to June 2016 by prospectively consecutive registration. All the patients in the database accepted magnetic resonance imaging (MRI) and oligoclonal bands (OB) testing and were diagnosed according to the 2010 revisions to the McDonald's criteria (Polman et al., 2011). We excluded females who had never been pregnant or had MS onset (all refer to clinical onset of MS in this article) during their first pregnancy (lack of relapse information before pregnancy as baseline). The rest of the subjects were followed up every month for at least one year after delivery.

We registered demographic characteristics, clinical features, treatments and the ARR of MS, as well as the delivery method, obstetric complications and offspring health of the subjects. A relapse of MS was defined as the appearance or worsening of symptoms of neurologic dysfunction lasting > 24 h. ARR was evaluated one year before pregnancy, during pregnancy and one year after delivery. The Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) score was evaluated at conception, delivery and one year after delivery to assess the disability degree of the subjects. Obstetric complications were diagnosed by the obstetrician. The health condition of the offspring was assessed by neonatologists and paediatricians at birth and at one year after delivery.

2.2. Statistical analysis

Demographic data were reported as number (n) and frequency (%), or mean ± SD. Two sample *t*-tests and Mann–Whitney *U* test were used to compare the average parameters of each two groups. The category variables were analysed using a Chi-square test and the Fisher exact test. ARR during pregnancy and one year after delivery were compared to ARR before pregnancy by Wilcoxon Signed-Rank test. EDSS score at delivery and one year after delivery were compared with EDSS score at conception by paired samples *t*-test. P values < 0.05 were considered statistically significant. Statistical analyses were performed using the Statistical Package for Social Science, version 21 (SPSS, Chicago, IL).

3. Results

3.1. Baseline information of the subjects

We established a database of 94 female patients with MS, among whom 19 (20.2%) females had never been pregnant, 2 (2.1%) females had MS onset during their first pregnancy and 18 (19.1%) females were lost to follow-up. The remaining 55 females with 126 pregnancies (before or after MS onset) were enrolled, including 72 live births and 54 abortions (Fig. 1). The baseline information about MS and pregnancy of the 55 women are shown in Table 1.

3.2. Drug therapy before, during, and after pregnancy

Among the total 55 patients, 52 (94.5%) received treatments for MS after the diagnosis. Of these 52 patients, 36 (65.5%) was treated with corticosteroids, 3 (5.5%) with azathioprine, 2 (3.6%) with mycophenolate mofetil, 2 (3.6%)with immunoglobulin, 1 (1.8%) with interferon, and 14 (25.5%) with Chinese herbs. Among the 14 patients who had delivery after the clinical onset of MS, 11 (78.6%) withdrawn from corticosteroids, 2 (14.3%) from azathioprine and 1 (1.8%) from mycophenolate mofetil for at least six months before pregnancy. Three (21.4%) of the 14 patients never accepted treatment for MS before pregnancy. Thirteen (92.9%) of the 14 women accepted no drug therapy for MS during pregnancy or in the year after delivery, the other one patient received pulsed methylprednisolone for the five relapses after delivery.

3.3. Pregnancy and MS relapse, EDSS score

Among the 55 women, 14 had at least one delivery after MS onset (one had two deliveries). Detailed information about MS relapse and EDSS score is shown in Table 2. The ARR during pregnancy (0.07 ± 0.26; P = 0.034 was much lower than the ARR before pregnancy (0.46 ± 0.52); however, the ARR did not change significantly over the first three months (0.55 ± 1.41; P = 0.492) or the year (0.53 ± 0.92; P = 0.967) after delivery, compared to the ARR before pregnancy. One patient experienced a relapse in the third month during pregnancy. Four patients experienced at least one relapse during the year after delivery although none of them experienced a relapse during the year before pregnancy. Patient No. 5 had three relapses at the 2nd, 5th, 7th month after the first delivery, and two relapses at the 5th day, 6th month after the second delivery. The other three patients had only one relapse during the year after delivery (Table 2).

The average EDSS score at delivery (1.00 ± 1.50; P = 0.334) was not statistically higher than the average EDSS score at conception (0.77 ± 1.35). Nevertheless, the average EDSS score at one year after delivery (1.50 ± 1.72; P = 0.045) was much higher than that at conception. All the assessments of EDSS score at one year after delivery were done at least 5 months after the last relapse during the postpartum year.

3.4. Pregnancy outcomes and offspring

In total, 126 pregnancies occurred before and after MS onset (Table 3), and 72 (57.1%) of them resulted in live births. Most of the live births were naturally born, and no malformations or mental retardations were observed. Fifteen (20.8%) of the live births were delivered after MS onset, and no obstetrical complications were observed from these 15 full-term pregnancies in 14 patients. All of the 15 newborns had an Apgar score of > 7. There were no significant differences between the pregnancies before and after MS onset in number of live births (P = 0.066), abortions (P = 0.734) and caesarean section rate (P = 0.729).

4. Discussion

We prospectively enrolled and followed up on female MS patients with pregnancy before or after MS onset in Western China. We found that the drug therapies for MS in our cohort were different from that in other cohorts. Under such circumstances, our results suggest that full-term pregnancy protects women from MS relapse in a Chinese cohort just like in other European cohorts (Confavreux et al., 1998; Jesus-Ribeiro et al., 2017). However, MS women may develop greater disability after their delivery.

Our study first observed a natural history of MS without drug used during pregnancy while drug exposure occurred in 6% to 68% of the patients in other similar studies (Roullet et al., 1993; De Las Heras et al., 2007; Fragoso et al., 2009; Confavreux et al., 1998). This difference may be explained by that Chinese patients are more worried about the detrimental effects of MS drugs on their babies. Despite a decreased ARR during pregnancy without drug use in our study, several relapses were still observed in our study during pregnancy or after delivery. Therefore, we recommend appropriate MS treatment throughout pregnancy. However, in China, most of the patients were only treated with corticosteroids, and few patients was treated with interferon, immunoglobulin or immunosuppressant together with corticosteroids (Cheng and Xu, 2009). So far there are no standardised international treatments for patients who may become pregnant during the course of MS. Glatiramer acetate seems to be the most probable treatment that could be used throughout pregnancy, since it is the only disease-modifying therapy (DMT) with a Food and Drug Administration (FDA) pregnancy category B rating (no evidence of foetal harm in animal studies) (Voskuhl and Momtazee, 2017).

We found a decrease in ARR of MS during pregnancy, which was in accordance with other previous studies (Nelson et al., 1988; Runmarker and Andersen, 1995; Confavreux et al., 1998; Jesus-Ribeiro et al.,