Treatment of Vogt-Koyanagi-Harada’s Disease During Pregnancy

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Background: Caution should be exercised in treating patients with autoimmune diseases during pregnancy.

Cases: We successfully treated three cases of Vogt-Koyanagi-Harada’s disease (VKH disease) during pregnancy.

Observations: In the second trimester (14–27 weeks) of 1 patient, inflammation was mild and could be treated by topical corticosteroid. There is the possibility that her immune response had been modified by pregnancy. Systemic corticosteroid in a high dose was administered to the two cases in the second and third trimesters of pregnancy (28–41 weeks). The severity of inflammation in these 2 patients was similar to that in nonpregnant women. Inflammation subsided immediately without recurrence in all cases. No abnormality was found during the deliveries or in the babies.

Conclusions: Treatment for VKH disease during pregnancy should be chosen according to the severity of inflammation, the stage of pregnancy, and the maternal and fetal conditions.

Key Words: Corticosteroid, trimester of pregnancy, Vogt-Koyanagi-Harada’s disease.

Introduction

Vogt-Koyanagi-Harada’s (VKH) disease is a systemic disease that affects various organs and involves melanocytes.1 The clinical findings of this disease are bilateral panuveitis with serous retinal detachment, pleocytosis in the cerebrospinal fluid (CSF), headache, hearing loss, alopecia, poliosis, and vitiligo. It is believed to be an autoimmune disease. In particular, patients show abnormal cellular immunity against melanocytes.3 However, the exact mechanism of the disease process is not yet clear. It is known that the immune responses of pregnant women differ from those of nonpregnant women. During pregnancy, cellular immunity is generally suppressed, but the immunological influence of pregnancy on VKH disease has not yet been fully clarified. There has been some evidence, in several case reports, that the clinical course of VKH disease was modified by pregnancy (Table 1). We report here three cases of VKH disease during pregnancy.

Case Reports

Case 1

The patient was a 26-year-old woman with sudden onset of bilateral blurring of vision on January 12, 1984, in the 19th week of pregnancy. On the next day, the patient was first examined by an ophthalmologist. Her vision had decreased OU, but headache and hearing loss were not observed. Her visual acuity was 0.1 (0.2Xcyl + 1.00D AX180°), OD and 0.5 (n c), OS. There was moderate inflammation in the anterior chamber and bilateral serous retinal detachment in the posterior pole with optic disc edema. Pleocytosis was present in CSF. Based on these findings, she was diagnosed as having VKH disease and treatment with systemic corticosteroid (intravenous drip infusion of prednisolone 200 mg) was initiated.
on January 24, 1984. At this time she was in the 21st week of pregnancy. Bilateral serous retinal detachment gradually disappeared and her visual acuity recovered to 1.0 (n c), OU. The corticosteroid was tapered and stopped after 2 months. The remainder of her pregnancy was uneventful and the patient delivered a healthy baby on June 18, 1984.

Case 2

The patient was a 33-year-old woman with sudden onset of bilateral decreased vision on April 27, 1994, in the 28th week of pregnancy. The patient first visited us on May 2, 1994. She complained of bilateral blurred vision, but no headache or hearing loss. Her visual acuity was 0.04 (0.4X 1 3.5D), OD and 0.02 (0.2X 1 3.5D), OS. There was moderate inflammation in the anterior chamber and bilateral serous retinal detachment at the posterior pole (Figure 1). Fluorescein angiography (FAG) showed leakage and pooling of the dye in the posterior pole (Figure 2). Lumbar puncture on May 10 demonstrated 27 cells/3 mm². A working diagnosis of VKH disease was established, and the patient was treated with intravenous drip infusion of corticosteroid (prednisolone 200 mg/day) beginning on May 12, 1994, in her 31st week of pregnancy. After 2 weeks, bilateral serous retinal detachment had almost disappeared (Figures 3 and 4). The corticosteroid was gradually tapered. Her visual acuity was 1.0 (n c), OD and 0.9 (1.0X + 0.5D), OS on June 15. Her delivery was on July 15, 1994. There were no abnormal signs in her delivery or in the baby. No recurrence of VKH disease has been observed.

Case 3

The patient was a 24-year-old woman who was first examined by us in her 17th week of pregnancy on April 23, 1996, for the complaint of bilateral blurred vision accompanied by headache and hearing loss. Her visual acuity was 0.4(1.5X 2 1.5Dcyl 2 0.5D AX180°), OD and 0.6 (1.5X 2 1.25Dcyl 2 0.37D AX180°), OS. There was mild inflammation in the anterior chamber and bilateral serous retinal detachment at the posterior pole. Lumbar puncture on April 30 demonstrated 252 cells/3 mm². The patient was diagnosed with VKH disease. Because the inflammation was mild without visual loss and she was in the 17th week of pregnancy, the patient was treated only with topical corticosteroid. Her visual acuity was 1.5

Table 1. Vogt-Koyanagi-Harada (VKH) Disease During Pregnancy, Corticosteroid Therapy, Delivery, and Outcome

<table>
<thead>
<tr>
<th>Reported by</th>
<th>Stage of Pregnancy</th>
<th>Type of Therapy</th>
<th>Type of Delivery</th>
<th>Outcome of VKH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sato et al⁶</td>
<td>10 wk</td>
<td>Topical</td>
<td>Normal</td>
<td>Cure</td>
</tr>
<tr>
<td>Lance¹¹</td>
<td>3 mo</td>
<td>Systemic</td>
<td>Abortion</td>
<td>Recurrence</td>
</tr>
<tr>
<td>Yamagami et al¹²</td>
<td>7 mo</td>
<td>Systemic</td>
<td>Normal</td>
<td>Cure</td>
</tr>
<tr>
<td>Nohara et al⁸</td>
<td>12 wk</td>
<td>Close observation</td>
<td>Normal</td>
<td>Cure</td>
</tr>
<tr>
<td>Watase et al¹³</td>
<td>26 wk</td>
<td>Systemic</td>
<td>Normal</td>
<td>Cure</td>
</tr>
<tr>
<td>Taguchi et al⁷</td>
<td>3 mo</td>
<td>Topical</td>
<td>Normal</td>
<td>Cure</td>
</tr>
</tbody>
</table>

Figure 1. Pretreatment fundus in a 28-week pregnant patient (case 2). Note subretinal edema at posterior pole.

Figure 2. Pretreatment fluorescein angiography shows leakage of dye from choroid into subretinal space at posterior pole in case 2.
VKH DURING PREGNANCY

(n c), OU on May 3. Bilateral serous retinal detachment had almost disappeared by May 7. Her delivery was on July 25, 1996. There were no abnormal findings in her delivery and the baby was healthy. No recurrence of VKH disease has been seen.

Discussion

Vogt-Koyanagi-Harada’s disease is an organ-specific autoimmune disease affecting melanocytes. Cellular immunity plays an important immunological role in this disease. Recent studies of lymphocytes at the sites of inflammation have provided important insight into the mechanisms of VKH disease. Cytokines, especially interleukin (IL)-6 and IL-2, play an important role during inflammation, primarily by regulating the diverse functions of lymphocytes and monocytes.

During pregnancy, cellular immunity is generally suppressed, but the immunological influence of pregnancy on VKH disease has not yet been fully clarified. It is known that the immune responses of pregnant women are different from those of non-pregnant women. For example, the number of T cells decreases and the amount of IgG and IgM increases in pregnant women, although the number of lymphocytes in the peripheral blood does not change. Cellular immunity is also known to be suppressed during pregnancy. For a pregnancy to continue, the mother must tolerate the fetal tissue that is foreign to her immune system.

There are thought to be various protective mechanisms preventing immune attack. Th2 cells that produce IL-4 and IL-10 are activated, IL-10 suppresses Th1 cells that produce IL-2 and interferon-γ, and natural killer cells are suppressed. It is known that the chronic inflammation of autoimmune disease is remitted during pregnancy. We reported three cases of VKH disease during pregnancy. All cases had typical VKH signs, such as bilateral nonrhegmatogenous retinal detachment at the posterior pole, anterior uveitis, and pleocytosis in the cerebrospinal fluid. Inflammation disappeared after treatment with steroids and has not recurred in all cases. Case 3 in the second trimester of pregnancy was treated only with topical corticosteroid. Uveal inflammation was mild in this case, probably due to increased production of endogenous corticosteroid, which suppressed cellular immunity during the first and second trimesters of pregnancy. Uveal inflammation was rather mild and inflammation disappeared quickly after topical treatment in this patient. She has had no recurrence of the disease. Sato et al. and Taguchi et al. reported 2 patients in the first trimester of pregnancy with VKH disease.

These patients were treated with topical corticosteroid because systemic steroid therapy could have possibly induced abortion or some abnormality in the baby. Nohara et al. also reported a patient with VKH disease in the first trimester of pregnancy. This patient was placed under close observation without systemic or topical corticosteroid treatment. About 1 month later, VKH disease spontaneously subsided.

The clinical course of our case 1 in the second trimester of pregnancy was not different from that of VKH disease in a nonpregnant woman. In our second case, surface markers of CSF cells and peripheral blood lymphocytes (PBLs) were analyzed by flow cytometric analysis. It was shown that the frequency of CD45RO-positive CD4-positive cells (memory T cells) in CSF cells was significantly

Figure 3. In posttreatment fundus of case 2, subretinal edema at posterior pole has disappeared.

Figure 4. Posttreatment fluorescein angiography shows leakage of dye from choroid into subretinal space at posterior pole has disappeared in case 2.
higher than that of PBLs (data not shown). This finding is similar to that in nonpregnant women with VKH disease.\(^9\) We explained the possible side effects of systemic and topical corticosteroid therapy during pregnancy to our patients. Fortunately, they were treated successfully with systemic corticosteroids without any undesirable effects. In case 2 we performed FAG. Recent reports state that no data are available on the use of FAG during pregnancy. Fluorescein crosses the placenta in humans but FAG does not result in a high rate of birth anomalies or complications when performed on pregnant patients. Some ophthalmologists who have used this procedure indicate that FAG should be reserved for vision-threatening lesions and should be performed only in the late stage of pregnancy.\(^10\) Based on their data and after consulting an obstetrician we performed FAG on this patient.

Lance et al\(^11\) reported on two pregnant women with VKH disease. Their symptoms of VKH disease were mild during pregnancy without corticosteroid treatment, but they developed recurrent symptoms after termination of their pregnancies. The authors suggested that the changes in immunity and humoral constituents during pregnancy accounted for the remission. Yamagami et al\(^12\) and Watase et al\(^13\) reported on patients with VKH disease in the second trimester of pregnancy. These 2 patients were treated with systemic corticosteroid, resulting in complete remission of symptoms. No abnormal findings have been reported in their delivery or in their babies. It is possible that systemic corticosteroid therapy for a pregnant woman in the second and third trimester of pregnancy will induce pituitary dysfunction in the baby.\(^14\)

There is a possibility that the immune function and the severity of inflammation of VKH disease will be influenced by the stage of pregnancy. It is known that cellular immunity is suppressed, production of inflammatory cytokines is low and corticosteroid production is high in early pregnancy. The inflammation of VKH disease in the first and second trimester of pregnancy may be very mild due to these immunological changes. In this period the baby is susceptible to various undesirable effects of drugs and so systemic corticosteroid should not be given to a pregnant woman. However, in the third trimester of pregnancy, systemic corticosteroid therapy will be effective and useful for the suppression of inflammation. The important points are the stage of pregnancy and the severity of the inflammation. We can conclude that the treatment for VKH disease in pregnancy should be chosen according to the severity of the inflammation, the stage of pregnancy, and the maternal and fetal conditions.

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