Multifocal Acquired Demyelinating Sensory and Motor Neuropathy in Pregnancy, a Case Report

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Abstract

In this report we describe a case of MADSAM during pregnancy. MADSAM is a multifocal asymmetric demyelinating neuropathy that causes muscle weakness and sensory loss. The disease is caused by an autoimmune response of unknown origin. MADSAM has been described in literature but the effect of pregnancy on the course of MADSAM and vice versa remains uncertain. As far as we know this is the first report of MADSAM during pregnancy.

Keywords: Demyelinating neuropathy; Pregnancy; Multifocal acquired demyelinating sensory and motor neuropathy; MADSAM; Lewis-Sumner syndrome; Chronic acquired demyelinating neuropathy

Introduction

Multifocal acquired demyelinating sensory and motor polyneuropathy (MADSAM) was first described in 1982 by Lewis and colleagues and is also known as the 'Lewis-Sumner syndrome.' It is characterized by an asymmetric multifocal pattern of sensory and motor loss caused by an auto-immune mediated inflammation. This results in demyelination of motor and sensory neurons. The classification of MADSAM has been in relation to chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multifocal acquired demyelinating neuropathy (MADSAM). The classification of MADSAM in relation to chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) has repeatedly been discussed. Most experts consider MADSAM a variant or atypical form of CIDP, since the treatment response resembles that of CIDP patients.

Diagnostic findings include sensory nerve conduction abnormalities, characteristic motor neuron conduction blocks in (arm) nerves with diminished reflexes in about 90% of cases. Complete or partial conduction blocks are most common in the median and ulnar nerves. The disease has a slow progressive course. Studies show that about one to two-thirds of MADSAM patients respond to corticosteroids and 50-80% has a good response to intravenous immunoglobulin (IVIG) [8-10].

Literature on chronic inflammatory demyelinating neuropathy (CIDP) in pregnancy is scarce. To our knowledge no reports are written describing the course of MADSAM during pregnancy. In this case report we describe a pregnant woman with MADSAM.

Case

A 34-year-old, gravida 1, gestational age 31 weeks, was referred to the hospital by her midwife with questions concerning sphincter rupture in her family history. On further evaluation, her medical history revealed diagnosis of MADSAM at the age of 28. Her main complaints at the time of diagnosis were progressive tingling and loss of strength of the right hand. Neurological examination showed muscle weakness and loss of vibration sense in the right hand and the right wrist. The right biceps tendon reflex, right triceps tendon reflex and left achilles tendon reflex were absent (Table 1). Since her diagnosis with MADSAM, the disease had progressed very slowly with the exception of a flu episode with fever two years later. At that time symptoms of tingling and loss of strength became temporarily more intense, but recovered within approximately seven days.

About five years after diagnosis, just before conception, there were only complaints of feeling of tingling, cramps and weakness of the right hand. No specific preconception advice was given to her by her neurologist or the general practitioner. She had been under the obstetric care of a mid-wife.

During evaluation at the obstetric department at a gestational age of 31 weeks, she explained that her disease had progressed during pregnancy with tingling in both hands and cramping of the right hand and both feet and legs. In addition, she experienced episodes of involuntary bending of the right knee throughout the day, possibly due to loss of strength. Evaluation by the neurologist revealed progression of MADSAM disease with diffuse weakness of the right hand and weakness of the left hand. Fine motoric skills of the right hand were significantly reduced compared with the left hand. It had become very difficult to write. Reflexes of the upper limbs were all absent. In the lower limbs, minimal weakness was found. Sense of vibration was partially lost in the right lower leg. Despite progression of the disease, no specific treatment for MADSAM was given in terms of corticosteroids or IVIG. She started physiotherapy and regular massaging of the affected areas to relieve symptoms.

As part of her pre-partum evaluation, the anesthesiologist was asked to assess anesthetic options in case this would become necessary during delivery. With regard to pain medication during delivery, the anesthesiologist advised not to use epidural, but instead use remifentanil when necessary. In case of caesarean section, spinal anesthesia was thought to be safer than general anesthesia.

At 40 weeks pregnancy, neurologic symptoms were stable, but her blood pressure increased to 160/100 mmHg. There were no symptoms of pre-eclampsia and laboratory results came back normal. She was admitted to the hospital for observation and started on nifedipine.
About 100 cases of MADSAM neuropathy [8] have been described to date, none of which describe the course during pregnancy. The effect of pregnancy on the course of MADSAM therefore remains uncertain. A small study of 15 pregnancies in 9 patients with CIDP has been published however. Contrary to multiple sclerosis (MS), another demyelinating polyneuropathy, this study shows an increased exacerbation risk primarily in the third trimester and the postpartum period [13,14]. For MS we know that pregnancy can result in relative disease suppression due to the T-cell modulatory effect of pregnancy [15]. This T-modulatory effect results in tolerance for the fetal semi-allograft while not suppressing the immune system and exposing the body and fetus to infection [16]. Specific generated regulatory T-cells are capable of regulating coincidental autoimmune responses through linked suppression [16]. CIDP is known to involve not only cellular but also humoral immunity [17], making a similar suppressive mechanism unlikely. Instead, the altered state of immunity in pregnancy has been blamed for the exacerbation risk of CIDP [18]. We believe that this same pathogenesis may cause exacerbations in pregnant patients with MADSAM.

Our patient noticed progression of symptoms with tingling in both hands and cramping of the right hand and both feet and legs during the second half of pregnancy. Evaluation by the neurologist also revealed progression of MADSAM disease. The need for invasive therapeutic intervention should be weighed against its potential risk for mother and fetus. Treatment options include immunotherapy, corticosteroids and intravenous immunoglobulins (IVIG) with response rates comparable to CIDP [9]. About one to two-thirds of the patients respond to steroids and 50-80% has a beneficial response to IVIG [8-10]. IVIG is well tolerated in most patients, but effects on pregnant women are unknown. Their most important but rare side effects are thromboembolic events and anaphylaxis [15,19].

Auto-immune disease is known to increase the risk for hypertension and preeclampsia but studies providing such relationship usually describe disorders with known increased cardiovascular risk profiles such as systemic lupus or diabetes [20,21]. Research reviewed that hypertensive disorders may result from the presence of agonistic autoantibodies that are directed to a specific epitope on the angiotensine II type I receptor (AT1R) [21]. However, this phenomenon has not been described for CIPD, MADSAM or other autoimmune demyelinating diseases. Whether MADSAM increases the risk of hypertension and/or placental dysfunction remains to be seen.

Muscles and reflexes At time of diagnosis Before pregnancy During pregnancy Post-partum

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Muscle strength measured in MRC grade. MRC: Medical Research Council ranging from 0 (=no movement, no contraction) to 5 (=normal)

Table 1: Neurological examination at time of diagnosis, before pregnancy, during pregnancy and post-partum.
In the weeks before delivery, hypertension made induction of labor a necessity to prevent maternal and fetal complications as per national protocol [22]. Since CIDP affects peripheral motor and sensory neurons and not the autonomous nerve system, uterine contractions should not be affected and vaginal delivery is possible and induced in our patient.

In our patient, the direct post-partum period was complicated with excessive hemorrhage due to uterine atony. About 5% of all deliveries is complicated by post-partum hemorrhage of which uterine atony is the most frequent cause. Numbers on the risk for post-partum hemorrhage in CIDP or MADSAM are not available, but based on its peripheral nature expected to be comparable to the population risk.

Literature on anesthesia in CIDP patients, let alone MADSAM, is scarce. A 1999 report describes that spinal anesthesia is acceptable for cesarean section delivery in CIDP-patients when precautions have been taken [23]. As discussed above, our patient was evaluated by an anesthesiologist in an outpatient setting to prevent turmoil and doctors delay in case pain relief would become necessary during the delivery. The anesthesiologist advised remifentanyl, because of very limited experience with the use of epidural for patients with MADSAM. There are no studies that describe the use of general anesthesia in patients with MADSAM. We do know that the use of general anesthesia in patients with CIDP may result in prolonged muscle blockade [24]. Increased risk of complications associated with general anesthesia has been described for patients with Guillain-Barré syndrome. A depolarizing muscle relaxant may induce hyperkalemia and cardiac arrest in cases with significant denervation [25]. Considering the known risks of general anesthesia for other demyelinating neuropathies, spinal anesthesia was thought to be the safest procedure of choice when cesarean section would be needed.

In the weeks after the delivery, patients' neurologic symptoms decreased quickly to the level present before conception. As discussed above, it had not been the first time our patient experienced a temporary relapse. It is well established that excessive physical (and emotional) stress can elicit a relapse, which is reversible once the stressor is gone [13].

Based on the limited knowledge of the course of CIDP and, more in general, on auto-immune disease, we feel that MADSAM patients ought to be under specialist care. Pre-, intra- and post-partum monitoring of patient and fetus should to be performed by a gynaecologist. Especially the third trimester and the post partum period might be vulnerable periods for relapses. It remains unclear whether there is a relationship between MADSAM and hypotension or placental dysfunction.

References
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