

Gullian- Barre Syndrome in Pregnancy – A Case Report and Review of the Literature

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Abstract

The immune-mediated Gullian- Barré syndrome (GBS) is an acute demyelinating polyradiculopathy (AIDP) which typically presents as progressive, fairly symmetric muscle weakness accompanied by absent or depressed deep tendon reflexes. It has been linked to various infectious agents, such as *Campilobacter jejuni* and typically presents 2-4 weeks following a respiratory or gastrointestinal illness. With an estimated incidence in the general population of 0.75-2:100,000, its occurrence in pregnancy does not differ. Diagnostic criteria consist of clinical, laboratory and electrophysiological tests. Treatment of pregnant and non-pregnant patients with GBS usually does not differ and it is mainly composed of supportive care and monitoring of respiratory, cardiac and hemodynamic functions. Disease modifying treatments such as plasmapheresis and intravenous immunoglobulin (IVIg) are relatively safe in pregnancy. Timing and mode of delivery are based on obstetric indications and depend on maternal and fetal status. As such, if a pre-term delivery is indicated a course of antenatal corticosteroids should be considered. Therefore, GBS in pregnancy should be handled by a multidisciplinary team involving neurologists, obstetricians and anesthesiologists.

We present a case report of an otherwise healthy woman diagnosed with GBS in pregnancy. Patient presentation, diagnosis, treatment and outcome as well of review of the literature will be discussed.

Keywords: Gullian- Barré syndrome; Pregnancy

Introduction

The immune-mediated Gullian- Barré syndrome (GBS) is an acute demyelinating polyradiculopathy (AIDP). It has been linked to various infectious agents. Incidence in the general population is estimated at 0.75-2:100,000 occurrences and is no different in pregnancy [1]. Although rare, it carries a high maternal risk such as the need for ventilation support and higher mortality rates (10%) [2].

Due to the disparity of cases in the obstetric population, no guidelines have been established for the diagnosis and treatment of this condition. Our aim was to summarize the available information in the literature and present the available recommendations.

Typically, GBS presents 2-4 weeks following a respiratory or gastrointestinal illness, with complaints of finger dysesthesias and weakness in the proximal muscles of the lower extremities. This weakness may progress over hours to days to involve the arms, truncal muscles, cranial nerves, and respiratory muscles [3,4]. Commonly there is a delay in presentation and in pregnancy it can be accounted for the non-specific symptoms that might mimic the normal physiological changes of pregnancy [5].

The diagnostic evaluation is based upon both the clinical presentation, laboratory and electrophysiological investigations. Such diagnostic criteria have been determined by the National Institute of Neurological Disorders and Stroke (NINDS) [6]. Both clinical and laboratory evaluation can be useful in diagnosing GBS in pregnancy. A lumbar puncture reveals an elevated cerebro-spinal fluid (CSF) protein with normal white blood cell (WBC) counts [7]. Nerve conduction studies (NCS) and electromyography (EMG) show an evolving multifocal demyelinating polyneuropathy.

As mentioned, GBS typically presents within 30 days of an infection. This is thought to trigger an autoimmune response directed against the peripheral nervous system. Treatment of GBS is composed

of supportive care with close monitoring of respiratory, cardiac and hemodynamic functions. Deep vein thrombosis prophylaxis and physical therapy are essential. Plasmapheresis or administration of intravenous immunoglobulin (IVIg) are recommended as well. Management of GBS in the pregnant population requires a multidisciplinary approach involving neurologists, obstetricians and anesthesiologists and generally does not differ from the treatment of non-pregnant population. It raises many concerns/ issues regarding both maternal and fetal outcomes, mode of delivery and the use of anesthesia and analgesia.

We present a case report of an otherwise healthy woman diagnosed with GBS in pregnancy. Patient presentation, diagnosis, treatment and outcome as well of review of the literature will be described.

Case Report

K.C, a G2P1, otherwise healthy woman was diagnosed with GBS at her 33rd gestational week. Obstetric history has a previous indicated preterm vaginal delivery of twins at 31 weeks of gestation due to severe preeclampsia. Current pregnancy is low risk and included the following tests recommended by the Israeli Obstetric and Gynecologic association: Dating the pregnancy by a first trimester ultrasound, nuchal and integrated serum biomarker screening, glucose challenge

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test, an early ultra-sonographic anatomical survey (14-16 weeks) and a late scan (22-24 weeks) as well as a routine follow-up on fetal growth and well-being. Laboratory parameters taken as a routine screen included blood counts, urine cultures, thyroid function tests, serology for TORCHS (which was negative in the 1st trimester of the index pregnancy).

By her 30th gestational week she reported numbness and paresthesia of the 4th and 5th digits of her right hand which progressed to the left hand and tip of the toes of both feet. The paresthesia continued to ascend towards her elbows and knees accompanied by pain in both upper limbs which appeared the following week. At 32 weeks she sought medical care. At her initial presentation the patient was assured the symptoms could be accounted for the physiological changes of pregnancy.

Due to the clinical manifestation and based on her personal history of anemia and negative serology for CMV – both vitamin B12 levels and anti CMV immunoglobulin levels were obtained, revealing a CMV seroconversion with low avidity (anti CMV IgG positive and IgM negative) and low levels of Vitamin B12 (92 pcmol/l). Thorough history taking revealed a recent vaccination with dTaP (Vaccination against pertussis is recommended by the health ministry in the 3rd trimester) as well as a child with a recent flue like illness.

Entering her 33rd gestational week she was referred to the ER for a neurological consult due to weakness, complaining she was about to fall while descending down the stairs. A thorough neurological examination showed decreased deep tendon reflexes (which were completely absent by the next days) and a mild muscle weakness in the extremities. She was hospitalized at the Neurology department for monitoring and further evaluation. The first nerve conduction study was inconclusive. Due to the inconclusive results as well as the low levels of vitamin B12 and an atypical presentation, the differential diagnosis was either GBS or vitamin B12 deficiency. At first she was treated with supportive care monitoring her respiratory and cardiovascular status. By the next week and a half, the weakness became more significant, to a point where she was unable able to walk 5 steps unaided and get up from a sitting to a standing position by herself. Facial nerve weakness developed without bulbar or autonomic signs or symptoms.

CSF analysis, which was obtained at week 34, revealed elevated protein without an elevation in WBC counts. Treatment with IVIG was initiated. By the second day of treatment progression ceased and she completed a total of five days of IVIG treatment after which she was discharged with no further deterioration, with recommendations for physical therapy and neurologic follow-up. At 39 weeks she spontaneously delivered a healthy female neonate weighing 3255 grams. Since labor progressed quickly she did not require any analgesia. The neonate's urine tested negative for CMV, ruling out vertical transmission.

Four months postpartum, neurological follow up reveals mild peripheral weakness and an occasional mild paresthesia. The neonate's neurological and physical examination is unremarkable, and she normally achieves developmental mile-stones.

Discussion

GBS typically presents as an acute monophasic paralyzing illness provoked by a preceding infection, with a rare non-significant difference in incidence among pregnant women compared to the non-pregnant population. A search of the English literature was conducted using the key words "Gullian- Barré syndrome" and "pregnancy" and a total number of 42 papers which were retrieved (a full comprehensive

reference list can be submitted), describing 54 cases of GBS in pregnancy (including ours). Search was limited to the last 20 years in order to demonstrate maternal and fetal outcomes in recent years. We evaluated information regarding the causative agents, treatments, need for support, pregnancy outcomes and mode of delivery as well of analgesia/anesthesia methods.

Our patient did not present with the classical features of GBS which include a progressive, fairly symmetric muscle weakness accompanied by absent or depressed deep tendon reflexes. Paresthesia in the hands and feet accompanies weakness in more than 80% of patients followed by dysautonomia (70%) which manifests as tachycardia, urinary retention, blood pressure fluctuation. Pain, located in the back and extremities can be the presenting symptom in the acute phase in up to 66% of patients [8-12]. The wide variation and clinical presentation often results in a delay of diagnosis, especially as some changes mimic the normal physiological changes of pregnancy. Our patient presented at 30 weeks of gestation and was accurately diagnosed three weeks later.

As clinical suspicion rises there are typical laboratory and electrophysiological investigations that might aid in making the diagnosis. Typical CSF findings are elevated protein levels with normal WBC counts, which are present in over 75% of patients [13]. These changes were also presented by our patient. Typical NSC and EMG findings of NCS aid in the diagnosis and also provide information regarding the prognosis. The first electrodiagnostic findings can support the diagnosis of GBS, acute motor axonal neuropathy or acute motor and sensory axonal neuropathy. The fact that our patient had both inconclusive NSC and low levels of vitamin B12 have led to a wider differential diagnosis. Since nerve conduction abnormalities progress overtime, serial neurophysiologic studies are required. Antibodies (IgG) directed against GQ1b, a ganglioside component of nerve, might be detected in the serum, but are not measured routinely due to limited clinical utility. The NINDS have developed diagnostic criteria for GBS and they are applicable in about 80-90% of patients [14].

GBS occurs as a result of an abnormal immune response directed towards the peripheral nerves. It has been postulated that molecular mimicry causes the abnormal response [15]. The causative agent can be identified in two-thirds of cases [16]. *Campylobacter jejuni* is the most common pathogen associated with GBS in the non-pregnant population followed by cytomegalovirus (CMV) [17,18]. Literature review revealed a causative agent (mostly CMV) in 17 of the cases.

An attempt to identify the causative agent is important since both *Campylobacter jejuni* and CMV are associated with a more severe clinical course and a delayed recovery. Moreover, it can aid in the estimation of disease progression as well as in planning pregnancy management such as timing and mode of delivery and surveillance due to the implications of a possible CMV infection on the developing fetus.

Treatment of pregnant and non-pregnant patients with GBS is predominantly symptomatic and composed of supportive care manifested as close monitoring of respiratory, cardiac and hemodynamic functions and disease modifying treatments such as plasmapheresis or IVIG. Up to 30% of patients need ventilation support [19]. Dysautonomia occurs in 70% of patients, with tachycardia most common followed by urinary retention, hypertension with hypotension, arrhythmia and loss of sweating. Therefore, heart rate and blood pressure monitoring are recommended. Any sign of cardiovascular instability of the pregnant women should be corrected and its implication on the fetus should be recorded by fetal monitoring. Disease modifying treatment with plasmapheresis

is thought to remove circulating antibodies and complement factors. Potential risks are hypotension, fluid overload, sepsis and deranged clotting factors [20]. There are no differences in the risks between non-pregnant and pregnant women [21]. It is a relatively safe treatment in pregnancy also implemented in other conditions, mainly thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. IVIG, as effective as plasmapheresis [22], is recommended for non-ambulatory patients who start treatment within two-four weeks of the onset of their symptoms [23]. Side effects are rash, aseptic meningitis, acute renal failure and hypersensitivity leading to stroke. Our review found 25 cases treated either with plasmapheresis or IVIG. Interestingly, there is a tendency towards IVIG treatment recently, probably due to the relatively convenient mode of administration.

Prophylaxis with low molecular weight heparin and supportive stockings for the prevention of deep vein thrombosis are of extreme importance as pregnancy itself possess a higher risk for thromboembolic events. Nosocomial infections, such as pneumonia and urinary tract infection occur in up to 30% of patients [10]. These infections tend to be more severe in the pregnant woman and might lead to complications such as preterm delivery, sepsis, pulmonary and cardiovascular instability with high maternal morbidity and mortality. Therefore, the treatment of GBS in the pregnant women should be comprised of a multidisciplinary approach involving neurologists, obstetricians and anesthesiologists.

Timing and mode of delivery are important decisions to make in the pregnant women diagnosed with GBS. A close follow up regarding disease progression and maternal hemodynamic status as well as fetal well-being might determine the timing of delivery. Any pregnant woman presenting with worsening hemodynamic status should be a candidate for indicated pre-term delivery and a course of antenatal steroids should be administered in order to enhance fetal lung maturity. The clinician should weigh maternal risks against the risk of fetal immaturity. In the cases reviewed in the literature, mode of delivery was either vaginal delivery, cesarean section or instrumental delivery. Accordingly, GBS itself is not an indication for cesarean section and an operative vaginal delivery should be performed according to obstetric indications [24].

There has been no consensus in literature regarding the appropriate anesthetic technique for cesarean section in the presence of GBS. The first report raising the suspicion of GBS triggered by use of regional anesthesia was reported in 1985 [25]. The hypothesis that chemical or mechanical disturbances provoked GBS remained unproven. One should be aware that the use of succinylcholine in patients with GBS might lead to hyperkalemia and eventually to cardiac arrest. Regional anesthesia (epidural or spinal) and general anesthesia are techniques used by various authors [26]. Therefore, the choice of analgesia as well as anesthesia for cesarean section in pregnant women with GBS should be carefully evaluated because both are potentially high risk in this population [24].

In a large retrospective study recently published [27], a total of 47 cases were described. The authors concluded that the risk of GBS increases in the 3rd trimester and first 2 weeks after delivery. Due to variety of clinical presentation, one should have a high clinical suspicion. Their cases, as does ours, highlight the role of a multidisciplinary follow up on women diagnosed with GBS.

Conclusion

Although a relatively rare medical condition to encounter in pregnancy, GBS poses a clinical challenge requiring a multidisciplinary

approach. A prompt evaluation should be undertaken in patients presenting with the typical clinical features. There is a great clinical significance to the identification of the causative agent as it tends to affect the clinical course of the disease as well as its prognosis and in case of a CMV infection can also be of grave consequences to the fetus.

Treatment is comprised primarily of supportive care with close respiratory and cardiac monitoring and should be followed, when needed, by either plasmapheresis or IVIG, both relatively safe in pregnancy.

Timing of delivery should rely mainly on the maternal status and if a pre-term delivery is indicated a course of antenatal corticosteroids should be considered. GBS is not an indication for caesarian delivery and mode of delivery should be tailored individually, mostly based on obstetric indications. Anesthesia should be performed according to maternal status and a thorough anesthesiologist consult. A close postpartum follow up of both mother and infant are warranted.

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