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# Successful implantation and immediate activation of Vagus Nerve Stimulation (VNS) during pregnancy in a patient with intractable epilepsy: A case illustration and review of the literature

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ABSTRACT

While Vagus Nerve Stimulation (VNS) is proven to be a safe and effective adjunctive therapy in the general population with medically intractable seizures, little is published about its implantation during pregnancy. Here we illustrate the case of a 21 year old primigravid woman with medically refractory seizures who underwent safe and successful VNS implantation and immediate activation of the device in her 32nd week of pregnancy, resulting in dramatically improved seizure control and subsequent delivery of a healthy baby.

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## 1. Introduction

Seizures during pregnancy can be a challenging clinical problem to manage and may be associated with devastating consequences. The prevalence of epilepsy in pregnant women is 0.7% according to population-based studies [1]. Literature reports that seizure frequency may alter during pregnancy and labor with some women with epilepsy experiencing increase seizure frequency [2,3]. Furthermore, seizures may cause obstetric complications such as placental abruption, premature labor and delivery, and superficial abdominal hematomas secondary to fall [1]. Pregnant women with epilepsy are also at increased risk for spontaneous abortion, induction of labor, caesarean section, and postpartum hemorrhage [1]. During 2006–2008, 14 women in the United Kingdom suffering from epilepsy died during pregnancy due to their seizure activity [2]. Abe et al. report that the incidence of major congenital malformation in women without epilepsy is 1.6–2.2%, whereas that in WWE is higher, at 2.8–3.6%. Women with epilepsy who take AEDs during pregnancy have an incidence of 4.2–6.7% of major congenital malformation, and seizures may become refractory to previous AED regimens that were effective prior to pregnancy [1].

One potential adjunctive treatment for women with refractory seizures during pregnancy is vagal nerve stimulation (VNS). The exact mechanism of vagal nerve stimulation is not definitive however its use may play a role in the brainstem reticular formation and nucleus solitarius tracts by modifying electrical stimuli [4]. This electrical stimuli modification may interfere with the stereotypical electrical activity distinctive of a seizure [5,6].

VNS placement during pregnancy may be effective for seizure control in patients with refractory seizures during pregnancy by allowing for superior seizure control at lower AED doses. This may result in improved perinatal outcomes and decreased risk of major congenital malformations. This technique, however, is poorly described in the existing literature and there is presently only a single case report of VNS implantation during pregnancy [7]. The device can be activated on demand when an external programmer device is placed on the skin above the generator/battery allowing for at will activation and inactivation.

Here we describe a case in which VNS implantation was safely and successfully performed in a patient with pharmacoresistant epilepsy during her 32nd week of pregnancy, resulting in a dramatic reduction of seizures and an uncomplicated delivery of a healthy baby.

## 2. Case presentation

A 21 year old female in her 3rd trimester of pregnancy presented with refractory epileptic seizures since childhood. Imaging showed left frontotemporal focal cortical dysplasia. EEG showed focal interictal epileptiform discharges, and continuous EEG monitoring showed subclinical focal electrographic seizures. At the time of presentation she was having 3–7 clinical seizures per week, some of which secondarily generalized, despite a regimen of 4 AEDs (gabapentin, lacosamide, oxcarbazepine, and zonisamide), all at therapeutic levels. Her history was significant for failure of many other AEDs, including levetiracetam. In order to improve her seizure control and therefore lessen the risk of injury to the patient as well as the fetus, the decision was made to pursue VNS implantation, as adding or increasing AEDs at that point could

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be associated with adverse effects on the fetus or, more likely, failure to achieve seizure control.

Multiple studies have shown that when the first AED fails to result in seizure freedom, the chance of each successive AED addition has a progressively lower chance of leading to seizure freedom. In a large prospective trial by Brodie et al., with a follow-up range of 2–26 years, 49% of patients became seizure free on the first AED, followed by an additional 13% with the addition of a second AED, and an additional 4% with the addition of a third AED [8]. VNS, however, has been shown to be very efficacious in cases of medically intractable epilepsy in which the addition of another AED would be of very little benefit [9]. VNS in focal epilepsy has been shown in multiple large case series to lead to a >50% reduction in seizures in 50–64% of patients at 1–5 year follow-up, and another group of large studies showed 20% of patients to have a >75% reduction in seizures at 1 year follow-up [10,11]. In our patient, the VNS implantation procedure was performed by a neurosurgeon under general anesthesia, and the obstetrics team was present in the OR throughout the procedure. Due to the urgent need for seizure control, the device was activated in the OR immediately after implantation rather than implementing the usual 2-week waiting period (which is typically employed in order to allow postsurgical healing of the vagus nerve). Follow-up continuous EEG monitoring after VNS implantation did not show any seizure activity, and the patient was discharged after 3 days without any complications. After VNS placement, the patient's seizure frequency significantly decreased to one every few weeks, whereas it had been 3–7 per week prior to the procedure. She delivered a healthy baby boy at 37 weeks by cesarean section without any complications.

## 3. Discussion

Pregnant patients with refractory epilepsy have a higher incidence of obstetric complications including hyperemesis gravidarum, preterm delivery, pregnancy-induced hypertension, preeclampsia, cesarean delivery, placental abruption, and perinatal mortality [12,13]. In addition, the use of antiepileptic medications (especially polytherapy) is associated with an increased risk of fetal malformations if given early in pregnancy, and when given late in pregnancy can be associated with long term adverse cognitive effects in a child [12,13]. Vagal nerve stimulation has been used in the United States since 1997 and offers a viable adjunctive treatment for medically refractory seizures [14–16]. Although VNS does not usually result in complete seizure freedom, VNS as an adjunct to medical therapy does appear to provide a significant reduction in seizures and a significant improvement in quality of life [17]. Studies have consistently shown the utility of VNS in treating medically refractory epilepsy, but only a few cases of women who have been treated with VNS during pregnancy have been described [7].

Husain et al. [18] described a pregnant patient who began receiving VNS therapy for depression 3 years prior to her pregnancy. She continued receiving VNS therapy throughout her pregnancy, labor, and delivery, which enabled the sustained remission of her depression. The pregnancy was uneventful; a healthy daughter was delivered at full term [18]. Houser et al. [7] reported a 19-year-old primigravid woman with refractory epilepsy since childhood in whom the VNS was implanted approximately 2 months before conception. Her seizure control improved, and she underwent a term spontaneous delivery complicated by mild preeclampsia [7]. Galbarriatu and colleagues [19] published a report describing a patient who became pregnant with a VNS already implanted. There were no complications during pregnancy or delivery, and her AEDs were reduced [19]. Salerno G and colleagues reported the case of a young woman affected by childhood-onset partial epilepsy, obesity, and depression, in which VNS malfunction was detected during pregnancy. Although the device functioning was not optimal during the critical period of organogenesis, no morphological abnormalities of the fetus were detected [20].

In all of the cases reported above, the VNS had been implanted before conception. Our case, however, describes a patient with medically refractory epilepsy who underwent safe and successful VNS implantation during her 3rd trimester of pregnancy, with immediate activation of the device, without complications, and resulting in dramatically improved seizure control and subsequent delivery of a healthy baby.

## 4. Conslusion

VNS implantation and therapy for medically refractory seizures is a viable option and can be safe and effective during pregnancy. Further long term studies and follow ups are warranted to investigate its possible outcome on fetuses and pregnant mothers who undergo this treatment.

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