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New-Onset Seizure in Pregnancy: Case Report and Literature Review

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Summary. New-onset seizures during pregnancy are a rare but quite challenging situation. Seizures in pregnancy result from three categories of conditions: pre-existing or new-onset epilepsy, new onset of seizures due to a non-pregnancy-related condition, and neurologic conditions either specific to or occurring quite frequently during pregnancy, especially eclampsia. Electroencephalography (EEG) and neuroimaging help to differentiate between these conditions. However, neuroimaging and treatment of pregnant patients with seizures are challenging due to the lack of randomized controlled trials in pregnant women. This article presents a clinical case of a 31-year-old primigravida woman at 29 weeks of gestation diagnosed with new-onset epilepsy which manifested with bilateral tonic-clonic seizure and slow pathological waves on the EEG with no neurologic deficits or magnetic resonance imaging abnormalities.

Keywords: epilepsy, pregnancy, new-onset seizures.

INTRODUCTION

Epilepsy is one of the most common neurological diseases and affects over 70 million people worldwide. Infants and older adults are at the highest risk of developing a seizure disorder, but the disease can occur at any age [1]. The prevalence of epilepsy is between 4 and 10 per 1000 people in the developed world; consequently, epilepsy is one of the most common neurological disorders affecting women of reproductive age [2]. Seizures during pregnancy mostly occur in women who were already diagnosed with epilepsy before pregnancy, but sometimes some women may have new-onset seizures during pregnancy, although this situation is quite rare [3]. Causes of seizures in pregnancy can be grouped into three categories. The first and most common cause is the exacerbation of a previously diagnosed epilepsy [4]. Sometimes seizures occur only during pregnancy and women are seizure-free between pregnancies – this rare condition is termed gestational epilepsy. Another rare type of epilepsy is gestational onset epilepsy; in this case, women have the first seizure during pregnancy and since then spontaneous recurrent seizures continue to occur even after labour [3]. The second category is new-onset seizures caused by a condition that is not related to pregnancy, such as brain tumours, cerebrovascular events, infections, or metabolic derangements. The third category includes disorders specific to or often occurring during pregnancy, the best and most common example being eclampsia [4]. The occurrence of seizures during pregnancy is a challenging situation. There is a risk not only to the health of women, but also to their unborn offspring, as there is much evidence that seizures in pregnancy are associated with miscarriage, stillbirth, preterm delivery, gynaecological bleeding, caesarean delivery, developmental delay, and congenital malformation [5]. Making an accurate diagnosis is extremely important, since therapy must be directed to the underlying disorder, as well as to seizure control [6]. In this article, we present a clinical case of new-onset seizure in pregnancy: gestational onset epilepsy.

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CASE REPORT

A 31-year-old primigravida woman at 29 weeks of gestation presented to the emergency department after a wit-

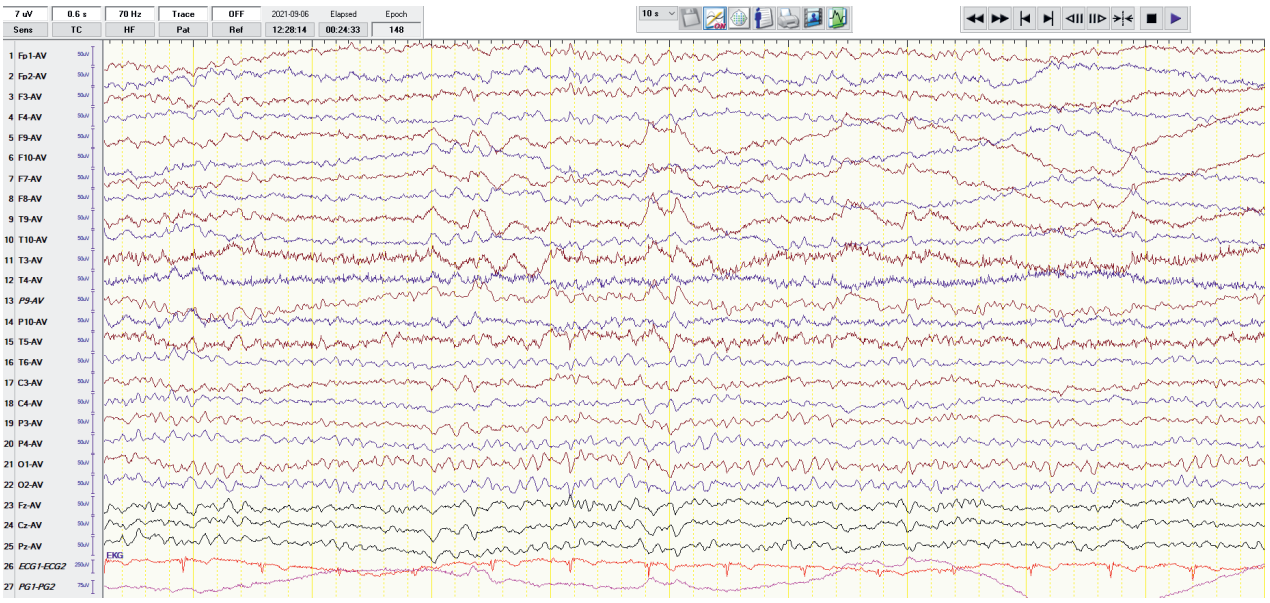

Fig. 1. **EEG (Day 1): slow waves in the left temporal region**

nessed loss of consciousness and seizure-like activity. According to her mother, it was 2:00 am and she was sleeping when she suddenly heard a strange, roar-like noise in her daughter's room. When the mother came into the room, she saw that her daughter's eyes were rolled back and she was rigid, after a few seconds jerking body movements were observed, which lasted for several minutes. The patient urinated at the end of the seizure. She regained consciousness but was very confused until she arrived at the hospital.

The patient's medical history included another episode of loss of consciousness a year ago, this episode was the first in her life – she was standing and eating when she suddenly lost consciousness and fell on her back. The episode was observed by the patient's husband who denied jerking body movements, incontinence or tongue biting. A computed tomography (CT) was performed which showed no abnormalities. Blood samples were taken and the results showed anemia – hemoglobin 99 g/L (reference range 120-150) and low potassium level 3.51 mmol/L (3.5-5.5). The patient also had a history of migraine without aura, which was diagnosed in adolescence and treated with triptans. There were no migraine attacks during pregnancy. At 24 weeks of gestation, the patient was diagnosed with gestational anemia (hemoglobin 89 g/L) and treated with tardyferon 160 mg per day. The patient denied using illicit drugs or alcohol. She had no history of central nervous system infection, head trauma, or other chronic diseases.

Upon arrival at the emergency department, the patient complained of general weakness, headache, and nausea. On examination, she was fully alert and oriented and had

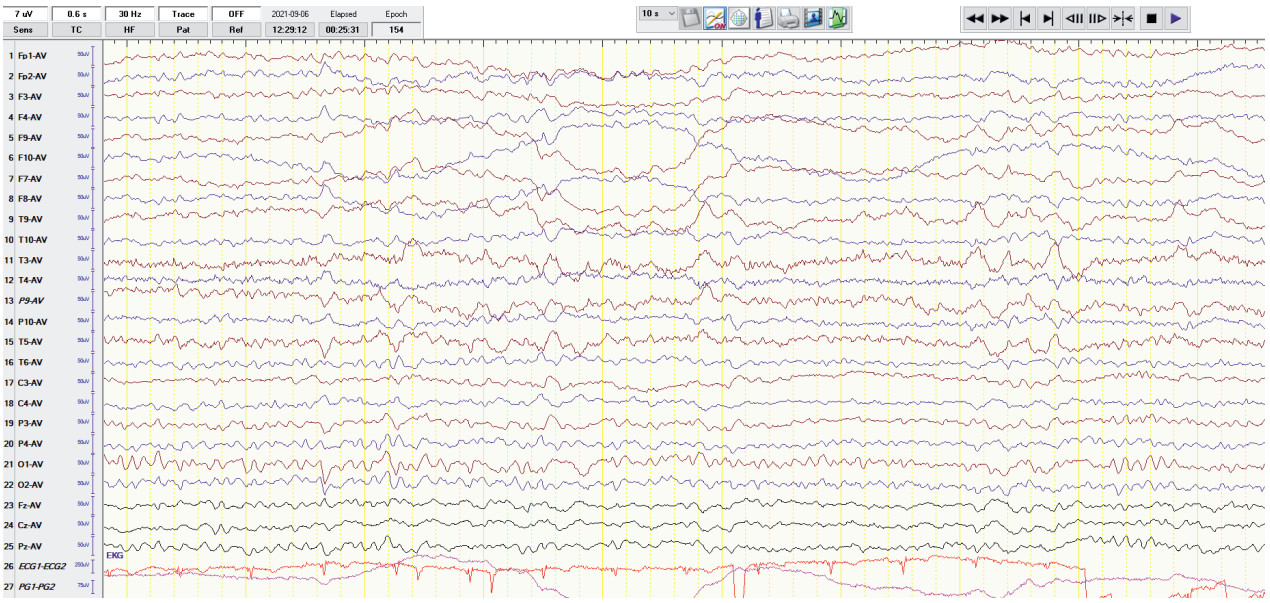

Fig. 2. **EEG (Day 4): slow activity in the left temporal region became more prominent**

no neurologic deficits. Her blood pressure was 127/85 mmHg, pulse 71 beats per minute, temperature 36.0 C. External fetal monitoring showed a reactive heart tracing. Urine sample was obtained, the results showed proteinuria 0.1 g/L (0.15), leukocyturia 500 /μL (25). Blood test results: white blood cell count 11.03×10^9/L (4.0-9.8), platelet count 195×10^9/L (140-450), hemoglobin 103 g/L (117-145), C-reactive protein 10.8 mg/L (5), creatinine 63 μmol/L (49-90), normal potassium, sodium, calcium, magnesium, thyroid-stimulating hormone levels and normal liver chemistry test. On the day of admission, electroencephalography (EEG) was performed, it showed variable slow pathological theta waves in the left temporal region, typical epileptiform potentials were not observed (Fig. 1). Magnetic resonance imaging (MRI) T1-weighted images showed no visual tumour or other abnormalities, however, there were many motion artifacts and the imaging was not completed because the patient did not tolerate the investigation. Since brain imaging was not completed, it was decided to repeat MRI in the future. On day 4, EEG was repeated, and slow pathological waves in the left temporal region became more prominent (Fig. 2). Therefore, the patient was diagnosed with epilepsy and treatment with levetiracetam 500 mg per day was initiated. In the last 5 months, no seizures were observed. At 41 weeks of gestation, labour was induced. A female infant of 2720 g was born with Apgar scores of 5 and 7, with signs of meconium aspiration syndrome.

DISCUSSION AND LITERATURE REVIEW

New-onset seizures during pregnancy are quite rare. A study of a large cohort in China demonstrated a relatively low risk of gestational onset epilepsy – 2.1% (22/1041) of women with epilepsy and reproductive history developed their first seizure during pregnancy. 4 (18.2%) new-onset seizures occurred in the first trimester, 10 (45.4%) in the second trimester, and 8 (36.4%) in the third trimester [5]. A retrospective study in the United States of America found that of 84 women who had at least one seizure during pregnancy, 11 (13.1%) had never had seizures before pregnancy and 5 (6%) of these women had their first unprovoked epileptic seizure confirmed by epileptiform activity on the EEG [2]. Yakunina et al reported similar results – in this study, the percentage of gestational onset focal epilepsy was 3.4% (4/116) [7]. In other studies, the proportion was higher. Melikova studied 70 pregnant women with focal epilepsy and 8 (11.4%) of them presented with a first-time epileptic seizure during pregnancy [8]. In another study from Azerbaijan, 112 pregnant women with epilepsy were evaluated and 12 (10.7%) had their first seizures during pregnancy [3]. The different proportions of gestational onset epilepsy recorded in these studies may be due to different populations, different inclusion criteria, for example, in some studies only women with focal epilepsy were investigated. In addition, the higher prevalence of new-onset epilepsy during pregnancy may be a result of under-recognized focal seizures before pregnancy. The diagnosis of epilepsy is not always definite at the onset of symptoms, especially when seizures occur not so often and some types of seizures may be underdiagnosed [3].

First-time seizures in pregnancy are a serious condition. It is extremely important to examine the patient attentively and make an accurate diagnosis, as the correct diagnosis leads to successful treatment [4]. In the first trimester, metabolic alterations should be ruled out first, then medications should be reviewed, and toxicology tests can also provide valuable information. In the second trimester, syncope is a probable cause of unclear loss of consciousness. In the third trimester, eclampsia, posterior reversible encephalopathy syndrome, and stroke occur more often than in early pregnancy, so these diagnoses are worth consideration. Brain tumours, infections, and sudden events associated with vascular malformations can occur in any trimester [9]. Possible causes of seizures in pregnancy are listed in Table [4, 6, 10].

In most cases, pregnant women with seizures must be considered as having eclampsia and treatment should be initiated immediately until further investigations prove an alternative diagnosis [4]. Eclampsia manifests as generalized tonic-clonic seizures in a pregnant woman with preeclampsia. Symptoms of preeclampsia include new-onset arterial hypertension after 20 weeks of gestation, proteinuria, renal dysfunction, liver dysfunction, central nervous system disturbances, pulmonary edema, and thrombocytopenia. Eclampsia before 20 weeks is uncom-

Table. **Causes of seizures during pregnancy**

- Epilepsy
- Eclampsia
- Posterior reversible encephalopathy syndrome (PRES)
- Reversible cerebral vasoconstriction syndrome (RCVS)
- Thrombotic thrombocytopenic purpura
- Hypertensive encephalopathy
- Cerebrovascular events
  - Arterial thrombosis
  - Cerebral venous thrombosis (CVT)
  - Intracerebral or subarachnoid hemorrhage
  - Hypoxic ischemic encephalopathy
  - Cavernous venous malformation
- Infectious encephalitis or brain abscess
- Brain tumour
- Congenital brain anomalies
- Head trauma
- Hypoglycemia, hyperosmolar nonketotic hyperglycemia, hypocalcaemia, hyponatremia
- Systemic infection
- Liver or renal failure
- Drug overdose or withdrawal
- Antiphospholipid syndrome
- Systemic lupus erythematosus

mon but some cases have been reported in gestational trophoblastic disease [11]. The first-line treatment to prevent recurrent seizures is magnesium sulfate. The initial loading bolus is 4-6 grams intravenously over 15 to 20 minutes with a maintenance dose of 1-3 grams an hour, depending on renal function [12]. After hemodynamic stabilization, further investigation, including the collection of the patient's medical history, blood and urine laboratory tests, and fetal evaluation, is obligatory to differentiate eclampsia from other possible seizure disorders. Electroencephalography and brain MRI or CT will help to differentiate between these conditions [10].

Brain imaging should be done in every pregnant woman having new-onset seizures. The only exception is classical eclampsia [13]. If the probable diagnosis is eclampsia, but there are persistent neurologic deficits, prolonged loss of consciousness, recurrence of seizures despite magnesium sulfate therapy, seizures occur 48 hours after delivery or before 20 weeks of gestation, CT or MRI of the head should be considered [12]. If PRES, RCVS, or CVT are suspected, not only native CT or MRI scan of the brain but also cerebrovascular imaging should be done to verify the diagnosis [13]. Often, clinicians are concerned about the ionizing radiation and iodinated contrast that are associated with CT scans. However, maternal head CT results in very minimal fetal irradiation [14]. It has been estimated that fetal radiation dose is less than 0.1 mGy, and the risk of anomalies, growth retardation, or abortion has not been reported at radiation doses below 50 mGy [15]. Head CT remains the most available neuroimaging method for initial diagnosis and should not be rejected if there are obvious indications for this examination. Iodinated contrast media belongs to FDA category B because there are no adequate and well-controlled studies in pregnant women. However, retrospective studies have not found any clinically important effect on infant thyroid function, and no adverse effects have been observed in animal reproduction studies [14]. MRI is generally preferred over CT since it does not use ionizing radiation. At present, no adverse effects of MRI on the fetus have been observed, so the potential risks are only theoretical. Although the risks are theoretical, it is still recommended for pregnant women that the specific absorption rate be less than 2 W/kg to reduce tissue heating effects. In addition, the exposure should be as short as possible to minimize any effect of acoustic noise on fetal hearing [16]. Based on the accessible literature, the administration of gadolinium-based contrast agents (GBCA) is not recommended, especially in the first trimester during organogenesis, unless the expected benefits outweigh the possible harms. However, to date, no studies have reported any adverse effects when human fetuses are exposed in utero [17].

Epilepsy management during pregnancy requires special consideration. Maintaining maternal seizure control must be balanced against the teratogenic and neurocognitive risks to the fetus. Provoking factors such as stress, sleep deprivation, and hormonal changes can also influence the neurologist's decision of whether or not to initiate treatment with antiepileptic drugs after a seizure [2]. It is widely known that valproate greatly increases the risk of congenital malformations (CM). Some earlier studies have shown that carbamazepine, phenytoin, and phenobarbital are associated with similar risks of CM as valproate. However, newer investigations using more precise analytical techniques have found a weaker link between these antiseizure drugs and CM. In recent years, evidence has accumulated indicating a significantly increased incidence of cleft lip/craniofacial deformities due to exposure to topiramate in the first trimester, especially at high doses. On the other hand, several well-conducted studies have shown that lamotrigine (LTG) and levetiracetam (LEV) do not significantly increase the risk of CM [18]. LTG is a suitable option if it is started before conception, however, it is not a suitable alternative to start during pregnancy, because there is increased clearance in pregnant women and it is difficult to reach therapeutic concentrations, and rapid titration increases the risk of rash, so LTG cannot be started quickly. Unlike LTG, LEV can be started immediately at a therapeutic dose and has a broad spectrum of action for different seizure types [19]. Neurologists must also consider the higher risk of teratogenicity in the first trimester and the relatively higher risk of fetal harm from seizures in later trimesters [2].

In conclusion, most epileptic seizures during pregnancy occur in women with pre-existing epilepsy, however, up to 11.4% are diagnosed with gestational onset epilepsy. But not all women who develop seizures have epilepsy. When a pregnant woman has a new onset of seizures, we need to differentiate between the various causes of the seizures, including eclampsia or mass lesions. Neuroimaging is often necessary for differential diagnosis. There is a lack of longitudinal and prospective studies to sustain evidence-based imaging studies during pregnancy. However, the potential risks are mainly theoretical, and head CT or MRI are not contraindicated during pregnancy and should not be withheld in urgent situations. Treatment of pregnant patients with seizures is also challenging due to the lack of randomised controlled trials in pregnant women. In addition, there is a risk of fetal harm from seizures, so neurologists must consider the risk of seizure recurrence and, if the risk of recurrence is considered to justify treatment, choose an antiseizure drug with the lowest risk of teratogenesis. It is well established that lamotrigine and levetiracetam do not significantly increase the risk of congenital malformations. In our case, the patient presented with a first-time bilateral tonic-clonic seizure, an unclear episode of loss of consciousness a year ago, non-specific MRI findings, and slow pathological waves on the EEG, which led to the diagnosis of new-onset epilepsy. The main diagnostic tool, in this case, was the detection of pathological waves on EEG. Due to the risk of seizure recurrence, levetiracetam was prescribed. Further research on neuroimaging and antiseizure medication during pregnancy could improve diagnostic accuracy, management, and lead to better outcomes and safety for the mother and fetus.

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PIRMAS PRIEPUOLIS NĖŠTUMO METU: ATVEJO PRISTATYMAS IR LITERATŪROS APŽVALGA

Santrauka

Naujai atsiradę priepuoliai nėštumo metu yra reta, bet gana sudėtinga situacija. Priepuoliai nėštumo metu atsiranda dėl priežasčių, kurias galima priskirti trims kategorijoms: anksčiau diagnozuota arba naujai atsiradusi epilepsija, naujai atsiradę priepuoliai dėl su nėštumu nesusijusių būklių ir nėštumui specifiškos arba dažnai nėštumo metu pasitaikančios būklės, ypač eklampsija. Elektroencefalografija (EEG) ir neurovizualiniai tyrimai padeda diferencijuoti šias būkles. Tačiau nėščių pacienčių, patiriančių priepuolius, neurovizualiniai tyrimai ir gydymas kelia daug iššūkių, kadangi trūksta su nėščiomis moterimis atliktų klinikinių atsitiktinių imčių tyrimų. Straipsnyje pateikiame klinikinį atvejį, kai 31 metų 29-ą savaitę pirmą kartą nėščiai moteriai buvo diagnozuota naujai atsiradusi epilepsija, pasireiškusi abipusiais toniniais-kloniniais traukuliais ir EEG fiksuotu lėtu patologiniu aktyvumu, be neurologinio deficito ar anomalijų magnetinio rezonanso tyrime.

Raktažodžiai: epilepsija, nėštumas, naujai atsiradę priepuoliai.

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