CASE REPORT

Identifying the aetiology of sudden acute abnormal involuntary movements in a primigravid

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SUMMARY

A 20-year-old primigravid experienced sudden stiffening of the neck, upper and lower extremities and trunk associated with joint pains. She was generally well before hospital admission with no history of attacks, except for her inflammatory bowel disease that was treated more than a year ago. During physical examination, the patient manifested neck flexion deviated to the right, deviation of the eyes downward and to the right, spooning of the upper extremities, exhibition of milkmaid's grip, extension of both lower extremities and jerky speech. She also showed uncontrollable tremors of the neck and occasional flailing of upper extremities. Her preliminary laboratory tests were within normal range. It was worth noting here that her family's medical history was unremarkable. In this article, the process of arriving at the final diagnosis and treatment would be discussed.

BACKGROUND

Abnormal involuntary movements among primigravids are rare and would warrant an extensive investigation to determine the underlying aetiology. Choreoathetoid movement during pregnancy, regardless of its cause, is known as chorea gravidarum.[1] Chorea gravidarum is commonly linked to conditions like lupus, antiphospholipid antibody syndrome, rheumatic fever, Wilson's disease and Huntington's disease.[1] While the prevalence of this condition is rare among pregnant women in developed countries; there are still reports of its presence in many developing countries like the Philippines.[2] Many obstetricians often overlook this rare condition, thus the need to further inform and raise awareness of chorea gravidarum's possible manifestations. Immediate evaluation of this illness could potentially reduce maternal and fetal risks. Proper treatment of its underlying cause might also prevent complications and long-term sequelae among affected patients.

CASE PRESENTATION

In Central Luzon, Philippines, a 20-year-old primigravid was rushed to an emergency room on her seventh week of pregnancy. The patient had sudden involuntary movements worsened by the stiffening of the neck, upper and lower extremities and trunk. She said these had been prompted by severe joint pains of the shoulders, elbows, wrists, knees and ankles. She remained conscious during the attack but already dysarthric. The patient also had irregular facial grimaces and occasional darting of the tongue and clenching of teeth. Balancing her head is difficult due to the tremors in her neck. She was ambulatory but continued to shudder as she walked. There were episodes when she would present violent flailing of the upper extremities and extension of the trunk. At the hospital, she was seen staring blankly while doing an activity and would casually continue it after an attack as if nothing happened. These sudden attacks would not bother her during sleep. She would have joint pains in both upper and lower extremities. She remained ambulatory but had unsteady gait.

The patient had sore throat for 10 days. Her continuous coughing comes with yellowish to greenish phlegm. According to her, she suffered from recurring sore throat infection from childhood that persisted until her teenage years with no known comorbid. She would treat it with erythromycin of unrecalled dose and frequency. The sore throat, she said, usually happens four to five times a year. For her severe vomiting, she had to take metoclopramide (10 mg per tab) one tab as needed.

In 2017, more than a year before her first attack, she was diagnosed with inflammatory bowel disease and was prescribed with mesalazine (500 mg per tab) one tab a day for 2 weeks. She stopped taking the medication 3 months prior to her pregnancy. It was known that the patient has no psychiatric illness; however, the recent death of a family member took a toll on her that caused her despair. Despite that, her family medical history was unremarkable.

Before her admission, she was prescribed with cephalexin (500 mg per tab) one tab thrice a day for 7 days but was later discontinued.

On her physical examination, the patient was awake, afebrile, conscious, coherent and not in cardiorespiratory distress. She is well oriented to time, place and person with intact higher cortical functioning. The cranial nerves were intact. The patient's somatosensory system and motor strength were unremarkable. She is right handed and has normal reflexes. There were no signs of meningeal irritation. The flexor plantar response was normal.

She has no fever prior to her first attack. Her condition dramatically changed during the attack. Her neck flexed to the right, her eyes moved downward and to the right, her upper extremities hyperextended and stiffened, while both wrists were plantarflexed. Her fingers were stiff and forked. She also presented extension and stiffening of both the lower extremities. After an attack, she would have uncontrollable neck tremors and erratic, pitchy speech. There were also a number of times

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when she had random flailing of the upper extremities and slow writhing of the fingers. The patient's grip exhibited increasing and decreasing pressures when asked to squeeze the examiner's hand. She was able to perform tandem gait with fair contralateral swinging of both arms, but she appeared unsteady. At the time of her admission, transvaginal ultrasound showed a single, live, intrauterine pregnancy of 7 weeks and 4 days with normal yolk sac and subchorionic haemorrhage.

INVESTIGATIONS

Laboratory tests

The table 1 below shows the results of the pertinent laboratory tests done on the patient.

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests were requested to determine if there are possible inflammatory processes occurring in the patient. The antinuclear antibody (ANA) and double-stranded DNA (dsDNA) tests helped to either rule in or rule out the possibility of systemic lupus erythematosus. The venereal disease research laboratory (VDRL) test is done as a routine screening to detect any infection caused by syphilis. Antistreptolysin O (ASO) titre and throat swab culture were done in order to establish possible present or recent streptococcal infection. This is important in establishing the diagnosis of rheumatic fever. Serum calcium was obtained to determine if there are any derangements in the calcium stores of the patient. Creatinine kinase-muscle/brain was done to rule out the possibility of myocardial infarction while creatinine kinase-total was requested to determine any possible muscular inflammation due to the recurrent attacks of muscle stiffening. Liver function was tested to determine any derangements in the organ.

MRI of the head

MRI is used to rule in or rule out lesions in the brain that can cause the sudden acute abnormal movements on the patient. The MRI clearly shows any pathological change in the brain that could have caused the patient's condition. Through this test, conditions like haemorrhagic or ischaemic stroke, malignancy and trauma could be prevented.

Results

Normal MRI of the brain.

No evidence of acute infarct or haemorrhage.

No evidence of mesial temporal sclerosis.

Table 1 Laboratory tests and results

Laboratory tests	Results
Erythrocyte sedimentation rate	Normal
C-reactive protein	Normal
Antinuclear antibody	Negative
Double-stranded DNA	Negative
Venereal disease research laboratory	Negative
Antistreptolysin O titre	Elevated
Thyroid function tests	Normal
Liver function tests	Normal
Serum calcium	Normal
Creatinine kinase-muscle/brain	Normal
Throat swab culture	No pathogen
Creatinine kinase-total	Elevated

Magnetic resonance angiography

The magnetic resonance angiography (MRA) was done with MRI to eliminate the possibility of bleeding from a ruptured aneurysm. This imaging is also warranted to look for possible arteriovenous malformations or intracranial arterial diseases.

Results

Developmental variant anatomy: fetal origin of the right posterior cerebral artery.

Hypoplastic right distal vertebral artery.

Normal MRA.

Electroencephalogram

Electroencephalogram (EEG) determined whether the abnormal movements manifested by the patient were seizures or not.

Results

Normal awake EEG recording.

2-D echocardiogram

The 2-dimension (2-D) echocardiogram test was conducted to detect any inflammation of the heart (carditis) in the patient. This helped in establishing the possible diagnosis of acute rheumatic fever.

Results

Normal ejection fraction.

Normal left ventricular dimension with good wall motion and adequate systolic function.

Doppler findings of impaired left ventricular relaxation.

Normal pulmonary artery pressure with mild pulmonic valve regurgitation.

Transvaginal ultrasound

Transvaginal ultrasound was performed to monitor the fetal growth and determine the possible viability of the pregnancy during the patient's treatment.

Results

Single, live intrauterine pregnancy 7 weeks and 4 days by crown rump length

Estimated Date of Delivery: 31 January 2019.

Normal yolk sac.

Subchorionic haemorrhage.

Anteverted uterus.

Normal right ovary with corpus luteum cyst.

Normal left ovary.

ECG

ECG routine test is done to rule out myocardial infarction and to determine if the patient has prolonged PR interval, which is a minor criterion to diagnose rheumatic fever.

Results

Normal ECG readings.

No axis deviation.

No chamber enlargements.

No ST segment elevations or depressions.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for this case were based on the history and physical examination obtained from the patient throughout her

hospital stay. One of the primary differentials considered was a new onset seizure disorder probably secondary to: (1) electrolyte imbalances, (2) structural lesions in the brain and (3) aneurysm. These differentials were ruled out when the serum electrolytes, MRI with MRA, EEG and neurological physical examinations were found to be normal. Other possible causes such as stroke in the young (ischaemic vs haemorrhagic) and space-occupying lesions were also prevented.

The normal values of ESR, CRP, ANA and dsDNA tests shown in table 1 aided in the exclusion of systemic lupus erythematosus and antiphospholipid antibody syndrome. Metabolic causes such as thyrotoxicosis was also disregarded due to unremarkable thyroid function tests. The possibility of neurosyphilis was ruled out due to a non-reactive VDRL screen. The patient was also referred to psychiatry and was cleared of any psychiatric illnesses such as major depressive disorder, generalised anxiety disorder and conversion disorder. However, the presence of elevated ASO titre, history of frequent recurrent throat infection, suspicion of the abnormal movements as Sydenham's chorea and arthralgia in the patient indicated that rheumatic fever could be the most probable aetiology of chorea gravidarum.

TREATMENT

The patient was treated as a case of new onset seizure disorder on the first 3 days of admission. She was given carbamazepine (200 mg per tab) one tab a day and as needed diazepam (2.5 mg) administered intravenously during attacks. She would average around 12 to 15 attacks in the first 3 days of hospitalisation. On the fourth hospital day, she was referred to infectious diseases service and was started on ceftriaxone intravenously for 3 days. There was a decrease in the frequency of attacks to 8–10 in the next 2 days. Diphenhydramine (25 mg per tab) one tab a day started on the third hospital. This helped the patient relax during attacks. On the sixth hospital day, the patient started on penicillin VK (500 mg per tab) three times a day to be taken for 7 days. The patient begun to show overall improvement. The number of attacks per day decreased from 8 attacks to 2 on the first 2 days of penicillin VK administration. The patient was contemplated to take on high dose aspirin, or prednisone, to address the inflammatory effects of rheumatic fever. It was then deferred due to the possible hazardous effects on the developing fetus. She was able to balance her head better and her gait became more stable. The patient became more independent in carrying out her daily routine and had no further attacks for 3 days before she was discharged.

OUTCOME AND FOLLOW-UP

The patient was discharged generally well with no more involuntary movements and steady gait on the ninth hospital day and on the fifth day of penicillin VK administration. She was advised to finish the course of her antibiotic treatment for two more days. She had regular follow-up and was given two doses of benzathine penicillin G (1.2 million units) intramuscular to prevent recurrence of rheumatic fever. The infectious disease service also recommended the patient to complete the 10-year benzathine penicillin G prophylaxis, once every 3 to 4 weeks, to prevent the possible development of rheumatic heart disease. Despite this prophylaxis, the patient would note occasional mild choreathetoid attacks lasting for 3 to 5 min (video 1). She also had regular visits to her obstetrician to monitor the progression of her pregnancy and was advised to undergo congenital anomaly scan on the 20th week of pregnancy to rule out any physical congenital anomalies on the fetus.

Video 1 Patient while having choreoathetoid attacks after hospitalisation.

DISCUSSION

Chorea gravidarum refers to any choreic movements occurring during pregnancy regardless of aetiology.[1] This is characterised by sudden, brief, non-rhythmic, non-repetitive twitching of the limbs usually with concomitant facial grimacing without any specific patterns.[3–5] The onset of this syndrome is commonly preceded by neuropsychiatric symptoms such as emotional lability, mild cognitive changes and, in some cases, psychosis.[1] Choreic movements could affect the patient's ability to eat and ambulate.[1] There are times when these movements become so intense that they predispose the patient to self-injury, rhabdomyolysis and hyperthermia.[1] In 1932, it was reported that there is approximately 1 case of chorea in every 300 deliveries.[6] There has been a steady decline in case reports among developed countries. According to Pathania *et al*, this syndrome has become a rarity in the Western world, however, its prevalence in developing countries remains.[2] At present, the fetal and maternal mortality rate secondary to chorea gravidarum has been decreased from 50% and 13% to 3% and 2%, respectively.[1] The average age of patients that may acquire this condition is marked at 22 years old.[6] Attacks of chorea gravidarum tend to be most severe in women who have their first episode during pregnancy.[1] The estimated relapse rate among those previously affected by chorea gravidarum is between 4% and 25%, but this should not be an absolute contraindication for future pregnancies.[1] Chorea gravidarum is commonly caused by rheumatic fever and other autoimmune diseases such as lupus and antiphospholipid antibody syndrome.[1] Wilson's disease and Huntington's disease can also be considered in patients with new onset chorea.[1]

In this patient's case, chorea gravidarum is traced to rheumatic fever. Chorea gravidarum linked to rheumatic fever normally manifests in the first trimester and resolves during the second or third trimester.[1] Among patients who had previous attacks, the striatum had sustained damage.[1] Hormonal changes during pregnancy sensitise dopamine receptors of the caudate nucleus and putamen which progresses to hypermetabolic state.[1] This damage in the striatum and the hypermetabolic state induced by pregnancy promotes the manifestation of chorea among affected women. This patient had no previous history of any attacks. The only pertinent information that strongly points to a possible previous streptococcal infection is the patient's history of recurrent sore throat from her childhood to adolescence. The most probable explanation for her case could be drawn to a possible reinfection with beta-haemolytic streptococcus. This notion is supported by the patient's elevated ASO titre which proves recent streptococcal infection. The constellation of signs and

symptoms presented by this patient is explained by the concept of molecular mimicry. Acute rheumatic fever is a common sequelae of group A beta-haemolytic streptococci infection, most commonly by *Streptococcus pyogenes*.[7] Group A streptococcus has an antigenic M-protein and N-acetylglucosamine which appear similar in structure to tissues in the heart, brain, skin and joints.[7] This theory postulates that the cross-reactive antibodies bind to the cells of tissues in the heart, brain, skin and joints which are similar in structure to the M-protein and N-acetylglucosamine in GAS.[7] In Syndenham's chorea, it is usually triggered by the cross-reactivity of human monoclonal antibodies with group A streptococcal carbohydrate epitope N-acetyl-betaD-glucosamine, lysoganglioside and tubulin in the brain via molecular mimicry.[8] This cross-reactivity activates increased dopamine release hence, promoting hyperkinetic motions.[8] The patient may also have inherent predisposition to suffer from rheumatic fever because she already had a history of suffering from inflammatory bowel disease which is also an autoimmune condition.

After an extensive investigation, the patient was only able to fulfil one major and one minor criteria based on the revised Jones criteria in diagnosing acute rheumatic fever. Although, it has been reported that rheumatic chorea is one of the three circumstances where diagnosis of rheumatic fever can be made without strict adherence to the Jones criteria.[7] The patient was noted to have no carditis despite non-specific findings in 2-D echocardiogram. However, she was still given prophylaxis for rheumatic heart disease of two doses of benzathine penicillin G (1.2 million units per dose) intramuscular. The patient was discharged after 3 days of no attacks. She currently has an unremarkable pregnancy and is due for a congenital anomaly scan at 20 weeks age of gestation to rule out any physical congenital malformations of the fetus.

Patient's perspective

I was baffled the first time my attending physician and doctors explained to me my condition. I have no idea how I got it and what it was. I do not know how a rare condition such as this could affect me. I had to ask myself, why do I have to suffer? The more days I stay in the hospital, the better I know about my disease, and it frightens me. What if my involuntary movements become permanent? This thought scares me because it might prevent me from doing my passion for the arts. Being unable to coordinated my fine movements would restrict me from creating sculptures. And if I still could, it won't be the same way as I did before. I fear, too, that this condition might terminate my pregnancy. Even my doctors were puzzled identifying whether my movements were seizures or not. During my attacks, I would try to suppress my movements and relax so they won't inject me with painful medications that might harm or trigger complications to my baby. I got helpless when my body starts moving on its own and I cannot control it. I cannot control my movements and my speech during an attack. I often lose my balance when walking.

Sometimes, I feel so small since I had to depend on my family to help me do simple tasks like handling a glass of water or even going to the toilet. After my hospitalization, I would still have occasional attacks and I am gradually getting used to it. Coping with it is a challenge but being optimistic and believing that 1 day this condition would heal on its own makes me feel better.

Learning points

- Chorea gravidarum is a rare condition referring to choreic movements during pregnancy regardless of cause.
- It is a syndrome that is strongly linked to rheumatic fever and other autoimmune diseases such as systemic lupus erythematosus and antiphospholipid antibody syndrome.
- Choreic attacks tend to be more severe the first time it occurred during the first trimester of pregnancy.
- Immediate investigation on the aetiology of chorea gravidarum is important because it decreases fetal and maternal mortality and morbidity rates.
- The use of benzathine penicillin G as prophylaxis against the development of rheumatic heart disease (RHD) even without the presence of inflammation can lessen the odds of developing RHD in the future.

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