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Genethormonal Outlook of Epilepsy: A Case Report Associated with Catamenial Epilepsy

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ABSTRACT

Epilepsy can be considered as unprovoked seizures within 24 hours. From decades, seizures shrouded even when CNS was not studied. With the help of case study, we have tried to point out a hypothetical point correlating genetically acquired epilepsy and catamenial epilepsy. So far, studies have been conducted on the influence of female sex hormones upon differently oriented electrical charges in the brain and related complications. The present article describes genetic variations and hormonal changes as two sides of the disease condition. We have tried to explain the mechanism of QARS gene mutation from previously researched data and an evidence-based study of the same has been done for a better understanding of the reader. The article has aimed discussion upon etiological factors including female sex hormones, thyroid hormones, insulin, prolactin, alteration in bone metabolism, adrenal hormones, and genetic epilepsy for better apprehension of pathological conditions.

Keywords: Catamenial epilepsy, genetic epilepsy, adrenal hormones, unprovoked seizures

INTRODUCTION

Epilepsy is a chronic disorder exhibiting seizures due to increased electrical activity of the brain. The disease affects 70 million people globally.[1] with 7 million people in India. Amongst generalized and partial epilepsy, most of the cases in India are of generalized epilepsy.[2] Epilepsy requires a chronic treatment which is majorly being cured by antiepileptic drugs.[1] Here, we present two different causes or etiological factors of epilepsy which include alterations in hormones and genetic mutations. Endocrine disorder-derived seizures could be due to neuroinflammation, autoimmunity, and metabolic disturbances.[3] The pathophysiology of the female brain during epilepsy can be studied concerning changes in GABA transmission.[4] The altered transmission is observed during certain phases of the menstrual cycle which can be correlated with changes in female sex hormones called Catamenial Epilepsy (CE). It is gender-specific epilepsy.[5] Many women have had an occurrence of seizures during perimenstrual, periovulatory, and luteal phases with most being in the perimenstrual phase. Despite the availability of many antiepileptic drugs, none of them are ideal and shows a spectrum of adverse effects.[2] Genetic epilepsies are characterized by a prompt seizure due to gene variations or mutations causing improper development of certain parts of the brain or loss of neuronal connectivity.[6] Around 70-80% of epilepsy cases are genetically originated and the remaining 20-30% are due to acquired causes.[7]

Risk factors

Epilepsy is a disease that lasts for a longer duration and has prolonged treatment which may interfere with the patient's lifestyle. A

large cross-sectional study has been done to lay an understanding of risk factors associated with epilepsy using National Health And Nutrition Examination Surveys **(**NHANES) data. Data draws attention to criteria including- gender, age, race, marital status, hypertension, smoking, diabetes, general health, Patient health questionnaire-9 (PHQ-9) depression score, and, sleep patterns. It was concluded that people of older age and unmarried showed a high risk of epilepsy and people with good general health and no sleep disorders showed a lesser risk of epilepsy.[8]

Etiological factors for CE include thyroid hormones, insulin, prolactin, alteration in bone metabolism, adrenal hormones, female sex hormones and genetic epilepsy with relevant case study-based understanding for better apprehension of pathological conditions.

Role of hormones in the etiopathology, diagnosis and treatment of CE

Thyroid Hormones:

Based on different studies, we found that thyroid hormones lead to an increase in excitatory neurotransmitters and a decrease in inhibitory neurotransmitters. There are several lines of evidence supporting the notion that oxidative stress, free radicals, and mitochondrial dysfunction play significant roles in the development of seizures and epileptogenesis.[9] There are three pathways to understand direct or indirect molecular mechanisms of thyroid hormones in epilepsy (Fig1). In the first mechanism, T3 directly impacts the mitochondria by the binding of a mitochondrially localized receptor [10] P43, a shortened TRa gene product found inside mitochondria, supplies T3 binding sites in the mitochondrial inner membrane. In the presence of thyroid hormone (TH), P43 binds to many thyroids hormone response element (TRE)-like sequences on the mitochondrial genome and activates transcription in a ligand-dependent manner.[9] T3 binds to nuclear-localized TRs and TREs in the second pathway to regulate the gene expression of nuclear-encoded proteins.[10] In the third pathway, intermediary factors such as the peroxisome proliferator-activated receptor gamma (PPARg), nuclear respiratory factor 1 (NRF-1), NRF-2 transcription factors, as well as the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1a) and peroxisome proliferator-activated receptor gamma, coactivator 1 beta (PGC-1b) may be generated by THs and then these co-activators enter the mitochondrion where they could regulate another group of THs target genes.[11] It has been demonstrated that decreasing TH activity is correlated with reduced mitochondrial function and biogenesis. Thyroid hormone impact on mitochondria has been studied in several brain areas, and it has been shown that mitochondria in the striatum and cerebral cortex are responsive to thyroid hormone activity. Given the significance of THs, particularly T3, in proper mitochondrial functioning and the role of mitochondrial dysfunction in epileptic processes, alterations in THs function may play a role in the etiology of epilepsy.[9]

Case report: As reported by Philip et al., the patient experienced generalized tonic-clonic seizures with no family history of epilepsy. The thyroid function test showed increased levels of T3 and T4 hormones, confirming thyrotoxicosis. A combination of methimazole and carbamazepine was given to the patient. They promote or enhance GABA action in the developing brain but inhibit it in the mature brain. This connection opens up a new line of inquiry into whether the actions of THs on GABAergic systems contribute to the development of epilepsy.[12]

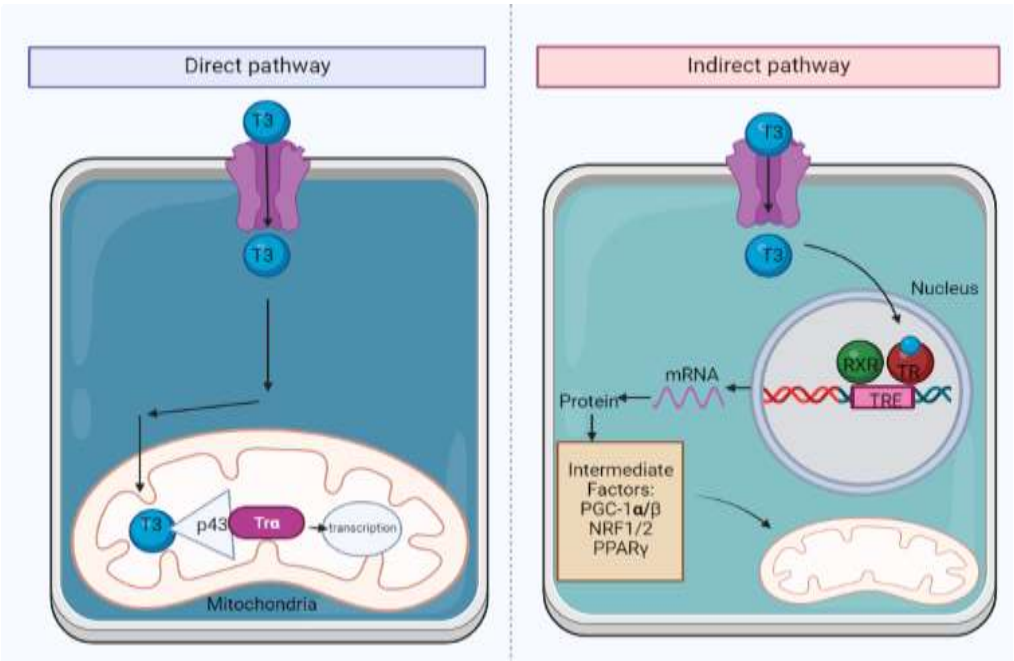


Figure 1: Molecular mechanisms of direct and indirect pathways of TH in the mitochondrial functioning of brain

Insulin

Administration of insulin has been proven to increase neuroprotective mechanisms and decrease seizure frequency.[13] The occurrence of epilepsy in the pediatric diabetic population of the diabetes clinic at the Royal Children's Hospital, Melbourne, Australia, was 0.9%[3] There is a rise in anti-oxidant enzymes such as SOD, GSH-Px, and CAT present in the brain. There has been an observed decrease in enzyme activity of the electron transport chain (ETC) in hippocampi, and increased oxidative stress has been seen in a rat model. Insulin has been shown to target and repair such mitochondrial damage, as well as to reduce the severity of epileptic seizures.[13] In about 80% of patients suffering from type 1 diabetes mellitus, it has been found that they have anti-glutamic acid decarboxylase antibodies (GAD-Ab), which prevent the conversion of glutamic acid (an excitatory neurotransmitter) into GABA (an inhibitory neurotransmitter) through decarboxylation. Studies have also been shown to report that a ketogenic diet prevents seizures by increasing the activity of GAD.[3]

Case report: As reported by Kumar et al., the patient had experienced tonic-clonic seizures in the face and upper body with a frequency of 20–30 times a day. Blood tests showed non-ketogenic hyperglycaemia; she was put on AEDs, but seizures continued. Significant changes in the frequency of seizures were observed after the administration of a hypoglycaemic agent. According to the study, high glucose levels damage the brain and cause epilepsy. However, more studies are required to obtain the relative mechanisms, potency, and efficacy of drugs that are to be used to minimize the disease condition.[14]

Prolactin

Through various studies, it was found that an increase in prolactin level was found among various seizures except for absence seizures. There is no alteration in serum prolactin levels in the patients taking AEDs. However, studies have shown a significant increase in serum prolactin levels after epileptic episodes of generalized complex partial seizures and this criterion may be useful in distinguishing between epileptical seizures and complex syncope. Complex electrical activities in the brain trigger the release of prolactin, which is not observed during psychogenic seizures.[15] Epileptic and non-epileptic conditions may co-exist in some patients, which also causes a rise in

serum prolactin levels. It is still not known if a rise in prolactin occurs during migraines, ischemic heart attacks, cardiac arrhythmias, and other epilepsy-like conditions.[16]

Hormones and alteration in bone metabolism

Epileptic patients have more risk of bone related health problems may be due to fall attacks, change in bone metabolism, due to long term usage of AEDs and ketogenic diet. Decrement in bone mineral density (BMD) has been found in most of the cases. It is understood that leptin is responsible for maintenance of fat metabolism and bone mineralization in the body. When the patients with epilepsy are given ketogenic diet, reduction in leptin level has been found signaling parathyroid hormone secretion leading to reduction in calcium absorption.[17] Data suggests that about 25% of the patients of epilepsy have osteoporosis. There is strong evidence that patients taking carbamazepine and phenobarbital have decreased alkaline phosphatase levels which are in turn responsible for secondary hyperthyroidism.**[18]** Reductions in BMD were observed in the subject's taking carbamazepine or VPA, whereas subjects receiving lamotrigine showed no reductions. N- terminal telopeptide (NTX), a urinary marker for bone resorption, also increased.[19] Vitamin K acts as cofactor for synthesis of osteocalcin which is important for bone formation. This factor is inhibited by phenytoin and phenobarbital.[18] Drugs like phenytoin, phenobarbital and carbamazepine binds to the nuclear receptor Steroid and xenobiotic receptor (SXR) and pregnane X receptor (PXR). PXR translates 25-hydroxyvitamin D3,24-hydroxylase (CYP24) which is responsible for conversion of 25-hydroxyvitamin D to 24,25-dihydroxyvitamin and prevents the formation of active metabolite 1,25-dihydroxyvitamin. These inactive metabolites further suppress the bone formation.[20] At the same time intake of AEDs leads to sedation vertigo or dizziness which corresponds to increase in chances of bone fracture.[18] Treatment of bone diseases associated with AEDs can be relieved with the help of calcium, vitamin D supplements, bisphosphonates (alendronate and risedronate), hormone replacement, selective estrogen modulators (SERMs), and calcitonin. The daily vitamin D dose ranges from 400 to 4,000 IU [21]

Adrenal hormones

Chronic use of valproic acid causes an increase in plasma cortisol levels with no significant changes in ACTH levels. Some studies have also been shown to report symptomatic hyponatremia or SIADH after starting valproic acid.[22] As studied by Galimberti et al., women with more frequent seizures have been shown to have increased cortisol levels and decreased dehydroepiandrosterone sulphate levels. Seizures, also called "stressors," activate the hypothalamus-pituitary-adrenal axis and affect hormone secretion. Adrenaline hormones easily cross the blood-brain barrier and interact with GABA and NMDA receptors, resulting in seizure occurrence. Hence, the association of cortisol with epilepsy is looped. Stress-induced seizures increase the cortisol levels in the blood, which may again lower the seizure threshold. Stress is considered a precipitating factor for epilepsy.[23] Carbamazepine is also prone to increase 24-hour urinary free cortisol, evening plasma cortisol, and cortisol binding globulin by interfering with the negative feedback mechanism in the pituitary.[24] Excessive cortisol levels in the blood from stress lead to neuronal impairment in the hippocampal region that may lead to damage to hippocampal neurons. This chronic stress-induced pathology may trigger temporal lobe epilepsy and related psychogenic disorders.

Management of diverse adrenal hormones in epilepsy: The ultimate goal of antiseizure medications is to modulate the

HPA axis. Synthetic neurosteroids such as ganaxolone, and allopregnanolone, are allosteric modulators of the GABA receptor. Direct Corticotropin releasing factor (CRF) blocking agents can have a positive effect by inhibiting cortisol release, reducing anxiety and depression-like symptoms that are commonly associated with epilepsy and cannot be treated with standard antiepileptic medications. Although these compounds have not successfully yielded results in phase 3 clinical trials.[25]

Role of female sex hormones

The onset or escalation of seizure activity that coincides with a woman's menstrual cycle is known as CE.[26] Defects in various hormones in the body can trigger epilepsy. It includes the sex hormones like progesterone, estrogen, testosterone, and thyroid hormones.[27] Testosterone may show two opposite effects due to its metabolites.[28] Studies have shown that changes in the 24-hour sleep-wake cycle or circadian rhythm may cause alterations in the release of gonadotropin-releasing hormones. Some seasonal affecting disorders have led to a nocturnal forecast of frontal lobe epilepsy and morning, and afternoon occurrence of temporal lobe epilepsy.[29] Patients have consistently reported the occurrence of perimenstrual seizures linked with the associated changes in hormonal levels during menstrual cycles. CE is associated with the neuroactive properties of female sex hormones and the imbalance between them.[30]

Changes in the GABA receptors in the brain alter electrical activity. The two neurosteroids which are primarily associated with the hormonal changes occurring in the female body are pregnenolone which is the precursor of progesterone and allopregnanolone a metabolic product of progesterone.[4] Three types of catamenial seizures have been identified: premenstrual (c1), periovulatory (c2), and luteal (c3).[5] During the luteal phase, the level of progesterone is high which produces a neuroprotective mechanism while in the premenstrual phase, the levels of progesterone are comparatively low, which triggers CE. Some Antiepileptic drugs (AEDs) such as carbamazepine and phenytoin cause cytochrome 450 enzyme induction causing increased metabolism of neurosteroid hormone. Some AEDs also increase the levels of sex hormone-binding globulin and eventually decrease the unbound form of neurosteroid in the blood.[2] Allopregnanolone binds to the GABA A receptors and hyperpolarizes the transmission. During the premenstrual phase, the level of progesterone is low so there is upregulation of the alpha4delta subunit of GABA A receptors. This compensatory mechanism is not capable of balancing the decrement in progesterone level; thus, seizure persists.[5]

kandeepan et al., have reported that the patient experienced epileptical seizures which were not cured with the treatment of antiepileptic drugs like carbamazepine, phenytoin, and topiramate. Further, it was diagnosed that the patient experienced premenstrual seizures and the most of the seizures were generalized with occasional focal seizures. Occurrence of seizure episodes 2 days before menses lasted for 5 days. After intake of medroxyprogesterone, the frequency of seizures decreased from 15-20 attacks per day to 3-4 attacks. Antiepileptic drugs alone cannot treat CE. Non-hormonal treatments include acetazolamide and clonazepam along with hormonal treatments.[31]

Estrogen through various mechanisms (Fig2) has been shown to decrease the seizure threshold. Estrogen is present in two different forms in the female body which are estriol and estradiol. Estradiol along with stress hormone elevates the neuronal activity in the hippocampal region leading to neurodegeneration and over-excitability. Contradictorily, opposite actions of progesterone are observed and can be used in the treatment of CE.

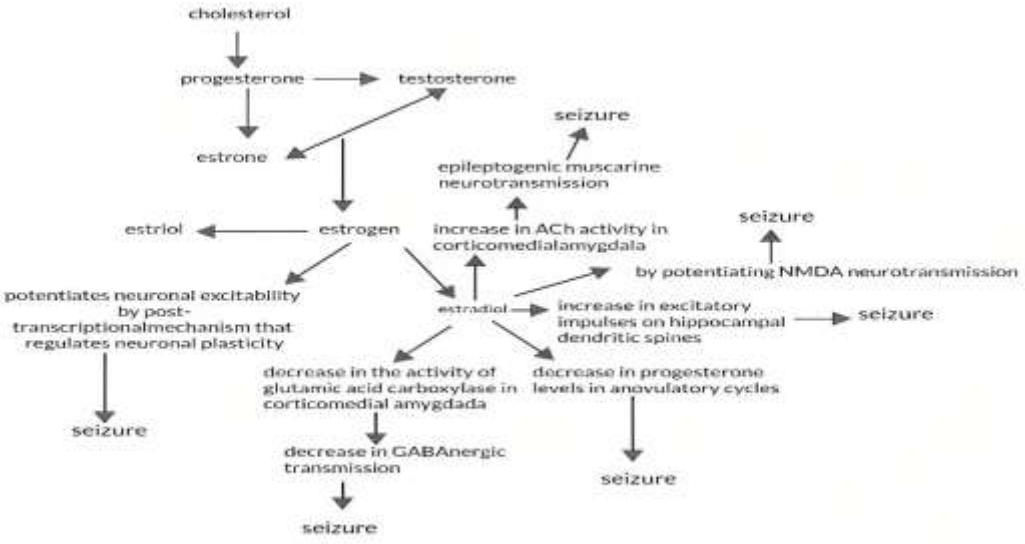


Figure 2: Hormone changes and seizures

Diagnosis of CE:

The patient is asked to keep a track of her menstrual cycles and seizures as part of the CE diagnostic process. To diagnose CE, one must have a certain rise in seizure frequency that is specific to the subtype. In real-world situations, a diagnosis of CE can be made if the patient exhibits a twofold increase in seizure frequency during one of the monthly periods listed as, C1-Perimenstrual (Compared to the follicular and luteal phases, there are more seizures during the menstrual period), C2- Periovulatory phase (Compared to the follicular and luteal phases, there are more seizures on ovulatory days), C3- Inadequate luteal phase (Women with insufficient luteal phase cycles have more seizures on ovulatory, mid-luteal, and menstrual days compared to mid-follicular days) or if the rise simply recurs at comparable intervals during the patient's menstrual cycle.[26]

Studies have shown that natural progesterone and medications that induce amenorrhea, such as medroxyprogesterone acetate and gonadotropin-releasing hormone (GnRH) analogues, are the most promising hormonal therapies for CE.[26] The fact that GnRH analogues lessen the hormonal fluctuations in CE patients suggests that they may be a beneficial therapy. These GnRH agonists act by desensitizing the pituitary with continuous stimulation, which prevents the pituitary from secreting gonadotropins such as follicle-stimulating hormone and luteinizing hormone.[32] In addition, regular exercise and calcium and vitamin D supplements advise women on GnRH agonists.[26]

Complications of CE:

PCOS (Polycystic ovary syndrome) is one of the causes of the occurrence of epileptic seizures in females. Several studies have suggested that HPO axis dysfunction, elevated androgen, obesity, hyperinsulinemia, oxidative stress, and impaired negative feedback regulation of steroidal hormones is together responsible for the syndrome.[1] Studies have found that women undertaking AEDs are more susceptible to having features of PCOS at higher than the expected rate.[33] Minor complications include CSF leak, intra-cranial or extra-cranial infections, aseptic meningitis, deep vein thrombosis, pulmonary embolus, pneumonia, and intracranial hematomas. Neurologic complications include cranial nerve damage, memory disturbances, and hemiparesis.[34] Some AEDs act as psychotropic agents and are involved in changing behavioural patterns. Drugs like valproic acid and carbamazepine cause malaise, mood swings,

and depression conditions. Levetiracetam causes anxiety, depression and irritability mostly in children.[35]

Role of gene swapping in etiopathology, diagnosis and management of genetically based epilepsy

The sole reason for the occurrence of seizures is unpredictable. The hormonal changes that our bodies undergo eventually raise the threshold potential. This paper explores the connectivity between genetic abnormalities and CE that may exist in nature. Genetics provides information about basic processes from birth to death.[36] Epilepsy is a heterogeneous condition involving varied etiological factors. A single defect in the gene sequence can cause severe consequences.[25]

Etiopathology : Genetic causes of epilepsy involve changes in voltage-gated and ligand-gated ion channels, developmental abnormalities, nerve death, single or combined gene modification or alteration, and environmental factors specific to each syndrome.[37] Mostly, cryptogenic epilepsy implies that the origin of genetic epilepsy is undisclosed.[36] Relatives of index cases or trisomies with cryptogenic epilepsy may develop the condition, but it is not associated with brain malfunction or injury-related epilepsy, i.e., seizure disorder. The chances of developing this type of epilepsy are restricted to people under the age of 35.[38] In the absence of that gene in either of the parents, a child's genes may be altered voluntarily. Genetic epilepsy occurs only when a solitary gene or group of genes whose outcome may likely cause epilepsy has taken over.[39] Hildebrand et al., inferred that genetic factors account for about 70% of seizures. Genetic susceptibility together with environmental factors leads to epilepsy.[36]

There are about 977 genes in epilepsy out of which 84 genes are as rated with a major cause of epilepsy or involving epilepsy as a major symptom, 73 genes are associated with neuronal damage or brain developmental abnormalities, and 536 genes involved physical and changes, 284 additional genes are considered as epileptic.[40] Here, we discuss the mutation in the QARS gene [Fig3], which encodes glutaminyl-tRNA synthetase, responsible for linking tRNA with amino acids. It is responsible for the development of structures such as axons and dendrites during the initial stages of brain development. Studies have shown that nonsense and missense variants of this gene are pathogenic.[41]

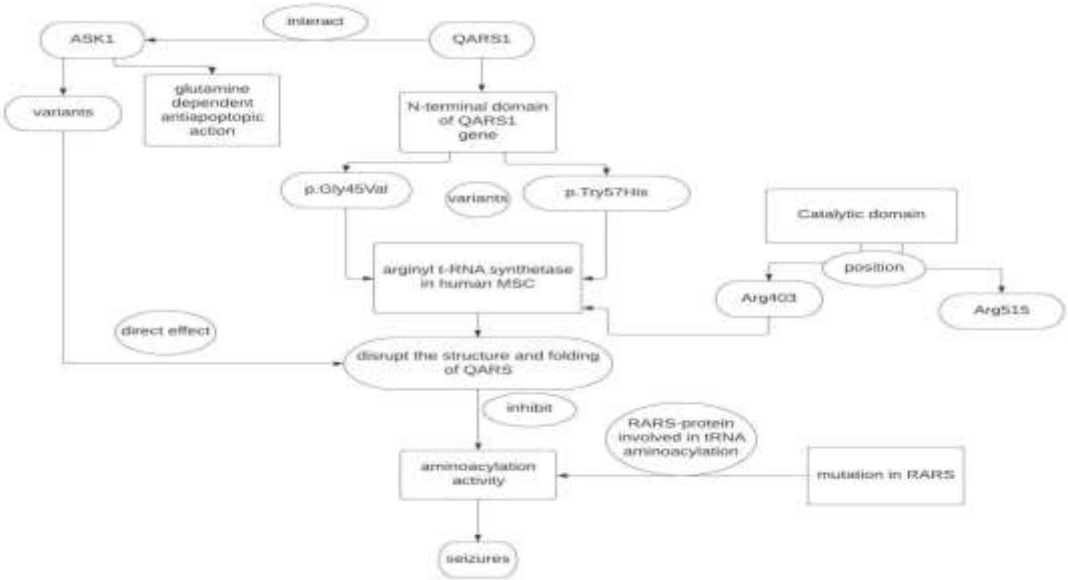


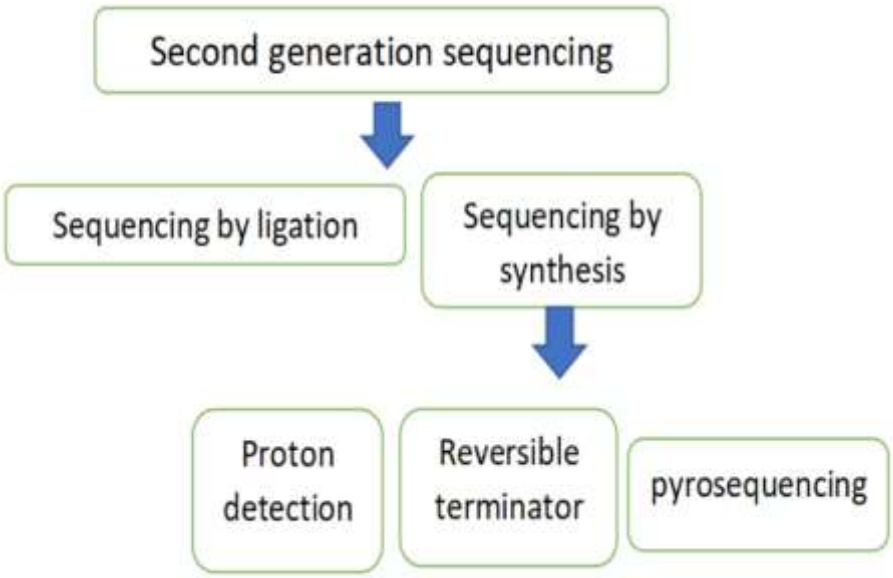
Figure 3: mutation in QARS1 gene

QARS-related mechanisms:[42]

1. This occurs between two unrelated families. The N-terminal domain of QARS has two variants that interact with arginyl tRNA synthetase in human Multi-tRNA Synthetase complex (MSC), disrupt the structure and folding of QARS, and cause seizures. Also, the position of Arg403 in the catalytic domain, close to the tRNA receptor, reacts with variants (p. Arg403Trp) and disrupts QARS; thus, both conditions lead to seizures, mostly focal seizures.
2. QARS reacts with ASK1 (responsible for glutamine-dependent antiapoptotic function), and its variants are responsible for the disruption of QARS and causing seizures.
3. RARS, a protein responsible for tRNA aminoacylation, if mutated, leads to a decrease in aminoacylation activity and causes seizures.

Diagnosis of genetically originated epilepsy:

It has been observed that 70 to 80 percent of cases of epilepsy are genetically derived. The medication used for treatment highly depends on the type of gene-producing seizures. Next-generation sequencing (NGS) is extensively used in parallel or deep sequencing of the entire human genome, including all 22,000 coding genes or small sequences of genes.[43] Second-generation sequencing is well-established for identifying genomic sequences to anticipate genetic abnormalities associated with diseased conditions [45] as shown under: The main steps include.[44]



Management of genetic epilepsy: Treatment includes the use of broad-spectrum anti-seizure medications. More than 20 antiepileptic drugs are available for treatment; however, the triggering of genetic epilepsy cannot be controlled to a greater extent. Basic treatment options available include the ketogenic diet and vagus nerve stimulation, but with very few benefits.[6] Originally, a mutation in SLC2A1 was responsible for the expression of type 1 glucose transporter in the blood-brain barrier, causing hypoglycemia and seizures. This can be cured by providing ketogenic supplements. A diet of vitamin B6 and pyridoxine derivatives can be preferred for patients with biallelic variants of ALDH7A1.[41] Other treatments include gene replacement therapy (GRT) and genetic substrate reduction therapy to reduce the increased expression or increase in the required protein synthesis.[6] People

with focal epilepsy, particularly temporal lobe epilepsy, are better candidates for gene therapy. GRT includes the transport of genetic material directly into the brain, but this might be difficult because of the presence of the blood-brain barrier, so cell transplantation via non-pathogenic viral vectors is feasible.[45] Commonly used adeno-associated viral vectors include AAV-9,[6] the herpes simplex virus, and land viruses. Besides this, increasing GABA receptor expression in epileptogenic areas and the administration of galanin to prevent seizures can be used.[45] Additionally, Drosophila nervy (NVY) expression genes, when introduced in the excitatory neuronal regions, showed a potential decrease in seizures. The transfer of the kv1.1 gene responsible for the expression of the potassium channel at the site of excitability showed a significant anti-seizure effect. Opsins are the proteins present on the membrane that are initially inert but when illuminated produces an inhibitory effect and help reduce neuronal excitability; however, there might be certain opsins responsible for excitatory actions as well that are not taken into use.[41] There are multiple genes responsible for epilepsy as a major disease or symptom, and some do have their targeted therapies. Discussion of all genes and their treatment is beyond the scope of this article. This paper investigates a case study demonstrating similar sex hormone signalling aided by gene mutation background.

Case report 1: Several researchers have reported the role of the above gene in the following study. The patient experienced focal seizures at 7 months of age, which were controlled with carbamazepine. Further, progressive MRI showed mild cortical volume loss without myelination abnormalities. Lastly, based on functional testing, she was found to have a novel compound heterozygous variant, QARS1, which is pathogenic.[46]

Case report 2: One of the live case studies supports the above-discussed mechanism as follows: A Gynaecologist was consulted for a seventeen-year-old female with a complaint of irregular menstrual cycles. The family history suggested that the epilepsy was caused by a mutation in the SCN1A gene. She was diagnosed with menorrhagia and severe hormonal imbalances based on her symptoms. The doctor prescribed her MINESSE (gestodene + estradiol) tablets with multivitamin supplements for 10 months. She had normal menstruation after taking the oral hormonal pill and no episodes of epilepsy were observed. The menstrual cycle remained normal for around 7 months. She again suffered from the same problems, plus delayed periods. This time the doctor suggested her for tests of thyroid hormone levels, haemoglobin, and blood sugar levels. She was diagnosed with severe anaemia, which was overcome by iron supplements before the onset of period irregularities. She had a single episode of myoclonic seizures that might have happened due to high-stress levels. At the age of about 18, she started having frequent single episodes of myoclonic seizures with fall attacks. Although her EEG was normal, she was not able to perform daily activities. Her USG abdomen report done after one month of heavy period revealed 9mm endometrial thickness which is quite higher compared to 1-4 mm thickness in normal situation during the menstrual phase (Fig 4a&4b). Her neurologists prescribed Brivaracetam 50 mg tablets twice a day as per her ongoing treatment. She is normal then after the treatment.

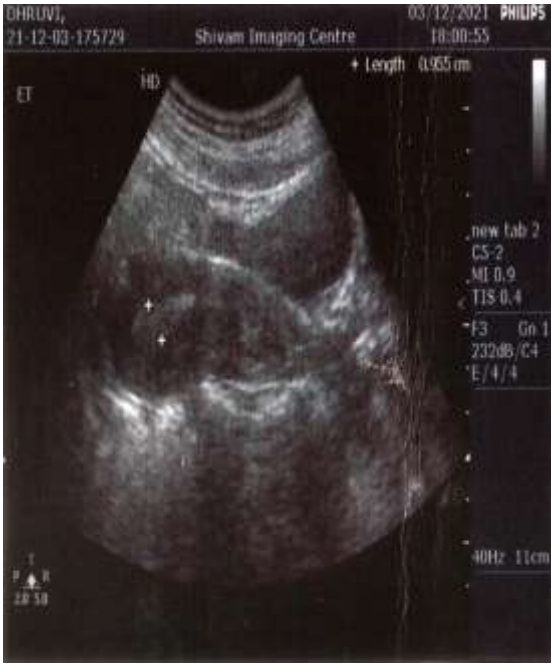


Figure (4a)

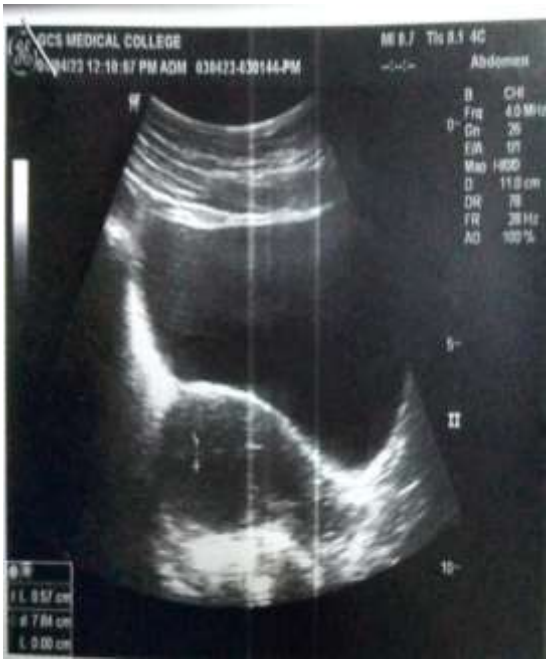


Figure (4b)

(Fig 4a) describes the endometrial thickness of 9mm which was measured before the hormonal treatment. The report was done after one month of heavy bleeding. (Fig 4b) reveals the endometrial thickness of 6mm which was measured in the preovulatory stage after treatment.

In conclusion, there may be some link between genetic mutations and changes in female sex hormones, which may lead to CE. Further pharmacogenetic studies are required to increase the effectiveness of the treatment of CE.

CONCLUSION

Various endogenous factors can trigger the cause of epilepsy, such as female sex hormones leading to CE and hyperthyroidism. Some AEDs and the condition itself also cause alterations in the overall metabolism and body functions. Brief information on genetic epilepsy aided by etiological factors such as infections, surgery, and trauma may lead to undesired mutations in the genes regulating homeostasis. Through this case study, we have tried to recognize the possibility of a correlation between genetic mutations triggering alterations in female sex hormones that might lead to CE. Further pharmacogenetic studies are required to increase the effectiveness of the treatment of CE. Studies on a large number of case reports may yield useful results.

Declaration by Authors

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REFERENCES

1. Li S, Zhang L, Wei N, Tai Z, Yu C, Xu Z. Research Progress on the Effect of Epilepsy and Antiseizure Medications on PCOS Through HPO Axis. Front Endocrinol 2021; 12:787854.
2. Reddy D. Pharmacotherapy of catamenial epilepsy. Indian J pharmacol 2005; 37(5): 288-293.
3. Verrotti A, Scaparrotta A, Olivieri C, & Chiarelli F. Seizures and type 1 diabetes mellitus: Current state of knowledge. Eur J Endocrinol 2012;167(6):749-758.
4. Mtchedlishvili Z, Eh B, Kapur J. Diminished Allopregnanolone Enhancement of GABA A-Receptor Currents in a Rat Model of Chronic Temporal Lobe Epilepsy. The Journal of Physiology 2001; 537(2):453-465.
5. Reddy D. Catamenial epilepsy: Discovery of an extrasynaptic molecular mechanism for targeted therapy. Front Cell Neurosci 2016; 10:101.
6. Goodspeed K, Bailey RM, Prasad S, Sadhu C, Cardenas JA, Holmay M, et al. Gene

Therapy: Novel Approaches to Targeting Monogenic Epilepsies. Front Neurol 2022; 13:805007.
7. Dunn P, Albury CL, Maksemous N, Benton MC, Sutherland HG, Smith RA, et al. Next generation sequencing methods for diagnosis of epilepsy syndromes. Front Genet 2018; 9:20.
8. Yang L, Wang Y, Chen X, Zhan C, Chen J, Cheng H, Zhang L.Risk factors for epilepsy: A national cross-sectional study from national health and nutrition examination survey 2013 to 2018. Int J Gen Med 2021; 14:4405-4411.
9. Tamijani SMS, Karimi B, Amini E, Golpich M, Dargahi L, Ali RA, et al. Thyroid hormones: Possible roles in epilepsy pathology. Seizure 2015; 31:155-164.
10. Weitzel JM, Iwen KAH, Seitz HJ. Regulation of mitochondrial biogenesis by thyroid hormone. Exp Physiol 2003; 88(1):121-128.
11. Cioffi F, Senese R, Lanni A, Goglia F. Thyroid hormones and mitochondria: With a brief look at derivatives and analogues. Mol Cell Endocrinol 2013;379(1, Suppl 2):51-61.
12. Phillip S, Kuan CC2, Mua MC2. Thyroid Hormone-Induced Seizures A Case Report and Review of Literature. Pediatr Ther 2012;2(5)
13. Cheng Y, Zeng X, Mai Q, Bai X, Jiang Y, Li J, et al. Insulin injections inhibits PTZ-induced mitochondrial dysfunction, oxidative stress and neurological deficits via the SIRT1/PGC-1α/SIRT3 pathway. Biochim Biophys Acta Mol Basis Dis 2021;1867(6):166124.
14. Kumar S. Epilepsia partialis continua stopped by insulin. J R Soc Med 2004;97(7):332–333.
15. LušíLuˇLuší IC, Pintarí I, Hozo I, Boí L. Serum prolactin levels after seizure and syncopal attacks. Seizure 1999;8(4):218-22.
16. Chen DK, So YT, Fisher RS. Use of serum prolactin in diagnosing epileptic seizures Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2005;65(5):668-75.
17. Molteberg E, Tauboll E, kverneland M, Iversen PO, Selmer KK, Nakken KO, et al. Substantial early changes in bone and calcium metabolism among adult pharmacoresistant epilepsy patients on a modified Atkins diet. Epilepsia 2022; 63(4):880-891.
18. Manolis N1, Lepetsos P, Tzefronis D, Gketsos A, Christoforidis C, Macheras GA. Metabolic bone disorders in children with epilepsy. Rheumatol Orthop 2017;2(5):1-6.
19. Pack AM, Morrell MJ, Marcus R, Holloway L, Flaster E, Doñe S, et al. Bone mass and turnover in women with epilepsy on antiepileptic drug monotherapy. Ann Neurol 2005;57(2):252-257.
20. Pack A. Bone health in people with epilepsy: is it impaired and what are the risk factors? Seizure 2008;17(2):181-6.
21. Pack AM. current review The Association Between Antiepileptic Drugs and Bone Disease. Epilepsy curr 2003;3(3):91-95.
22. Pitetzis DA, Spilioti MG, Yovos JG, Yavropoulou MP. The effect of VPA on bone: From clinical studies to cell cultures-The molecular mechanisms revisited. Seizure 2017; 48:36-43.
23. Pitetzis DA, Spilioti MG, Yovos JG, Yavropoulou MP. The effect of VPA on bone: From clinical studies to cell cultures-The molecular mechanisms revisited. Seizure 2017; 48:36-43.
24. Galimberti CA, Magri F, Copello F, Arbasino C, Cravello L, Casu M, et al. Seizure frequency and cortisol and dehydroepiandrosterone sulfate (DHEAS) levels in women with epilepsy receiving antiepileptic drug treatment. Epilepsia 2005;46(4):517-523.
25. Maguire J, Salpekar JA. Stress, seizures, and hypothalamic-pituitary-adrenal axis targets for the treatment of epilepsy. Epilepsy Behav 2013;26(3):352-362.
26. Frank S, Tyson NA. A Clinical Approach to CE: A Review. The Perm J 2020; 24:1-3.
27. Pennell PB. Hormonal Aspects of Epilepsy. Neurol Clin 2009;27(4):941-965.
28. Taubøll E, Sveberg L, Svalheim S. Interactions between hormones and epilepsy. Seizure 2015; 28:3-11.
29. Herzog AG. Catamenial epilepsy: Update on prevalence, pathophysiology and treatment from the findings of the NIH Progesterone Treatment Trial. Seizure 2015; 28:18-25.
30. Martínez Ramírez MA, Sanchez Gutiérrez SM, Guzmán Yara YN, Pinzón Jaime KZ, Rueda Cataño SC, Sarmiento Bocanegra L F, et al. Treatment approach to a patient

with Catamenial epilepsy Case report. Case Reports 2022;8(1):105-115.
31. Kandeepan J, Shaaban J. Catamenial epilepsy: A missed cause of refractory seizure in young women. Malays fam Physician 2016;11(2, Suppl 3):24-26.
32. Kumar P, Sharma A. Gonadotropin-releasing hormone analogs: Understanding advantages and limitations. J Hum Reprod Sci 2014;7(3):170-174.
33. Harden CL. Current review in clinical science Polycystic Ovaries and Polycystic Ovary Syndrome in Epilepsy: Evidence for Neurogonadal Disease Definitions and Prevalence in the General Population. In Epilepsy Curr 2005;5(4):142-146.
34. Hader WJ, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, Wiebe S, Kwon CS, et al. Complications of epilepsy surgery - A systematic review of focal surgical resections and invasive EEG monitoring. Epilepsia 2013;54(5):840-847.
35. Nadkarni S, Devinsky O. current review in clinical science Psychotropic Effects of Antiepileptic Drugs. Epilepsy Curr 2005;5(5):176-181.
36. Joshua BO, Benedict OMD, Temitope SS, Olamide BN, Habeeb OT, Abigail AS, et al. Genetics of Epilepsy. J neurol neurophysiol 2019;10(3):1-9.
37. Bhalla D, Godet B, Druet-Cabanac M, Preux PM. Etiologies of epilepsy: A comprehensive review. Expert Rev Neurother 2011;11(6):861-876.
38. Ottman R, Annegers JF, Risch N, Hauser WA, Susser M. Relations of genetic and environmental factors in the etiology of epilepsy. Ann Neurol 1996;39(4):442-449.
39. Wirrell EMD. Genetic causes of epilepsy. Epilepsy foundation. https://www.epilepsy.com/causes/genetic-epilepsy-foundation.
40. Wang J, Lin ZJ, Liu L, Xu HQ, Shi YW, Yi YH, et al. Epilepsy-associated genes. Seizure 2017; 44:11-20.
41. Nicholson E, Kullmann D. Repairs for a runaway brain. Nature 2018; 564:10-11.
42. Zhang X, Ling J, Barcia G, Jing L, Wu J, Barry BJ, et al. Mutations in QARS, encoding glutaminyl-trna synthetase, cause progressive microcephaly, cerebral-cerebellar atrophy, and intractable seizures. Am J Hum Genet 2014; 94(4):547-558.
43. Behjati S, Tarpey PS. What is next generation sequencing? Arch Dis Child Educ Pract Ed 2013;98(6):236-238.
44. Gkazi A. An overview of next generation sequencing. Technology Networks Genomics Research 2021.
45. Riban V, Fitzsimons HL, & During MJ. Gene therapy in epilepsy. Epilepsia 2019;50(1):24-32.
46. Chan DL, Rudinger- Thirion J, Frugier M, Riley LG, Ho G, Kothur K et al. A case of QARS1 associated epileptic encephalopathy and review of epilepsy in aminoacyl-tRNA synthetase disorders. Brain Dev 2022; 44(2):142-147.

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