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Generalized Epilepsy with Right Hemiparesis Secondary to Herpes Encephalitis

Htay Lwin[1*], Zay Yar Naing[2], Htoo Htoo Kyaw Soe[3], Mila Nu Nu Htay[3], Adinegara Lutfi Abas[3] and Soe Moe[3]

[1]Family Medicine Unit, Department of Community Medicine, Melaka Manipal Medical College, Manipal Higher Academy of Education (MAHE), Malaysia.
[2]Department of Population Medicine, Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman (UTAR), Kuala Lumpur, Malaysia.
[3]Department of Community Medicine, Melaka Manipal Medical College, Manipal Higher Academy of Education (MAHE), Malaysia.

Authors' contributions

This work was carried out in collaboration among all authors. Author HL did substantial contributions to conception and design, acquisition of data, drafting the article, performed the analysis of the study, wrote the protocol, wrote the first draft of the manuscript, revised it critically for important intellectual content, final approval of the version to be published. Authors ZYN, HHKS and MNNH equally managed the analyses of the study and equally contributed the literature searches. Authors ALA and SM equally managed the literature searches. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Herpes simplex encephalitis (HSE) is a medical emergency associated with high mortality and morbidity. Definitive diagnosis is established by history, clinical examination, neuroimaging studies, supportive electroencephalogram (EEG) findings, and cerebrospinal fluid (CSF) analysis.

A 7-year-old Malay girl with known case of right hemiplegia secondary to herpes encephalitis presented to the neuropediatric ward, in General Hospital with refractory seizure. She had a moderate learning disability and diagnosed as right hemiparesis secondary to herpes encephalitis complicated with epilepsy. She was planned for the positron emission tomography (PET) scan and

**Corresponding author: E-mail: drlwin2003@gmail.com;*

to undergo operation if PET scan was feasible (Hemispherectomy). However, the patient refused for operation.
Prompt clinical recognition is important in the HSE to prevent progressive brain tissue damage, haemorrhagic changes, and worsening of the encephalitis. Diagnosis is usually confirmed through an extensive evaluation, including a thorough clinical examination with attention to findings on mental status changes, cerebrospinal fluid (CSF) analysis, electroencephalogram (EEG) testing and findings on neuroimaging.
Once HSE is suspected, high-dose acyclovir should be started immediately before lumbar puncture (LP), and only stopped once a definitive alternate diagnosis has been established.
This case is reported because the patient has generalized epilepsy with right hemiparesis secondary to herpes encephalitis. Herpes encephalitis with right hemiparesis cases are quite rare.

Keywords: Herpes Simplex Encephalitis (HSE); infection; epilepsy; right hemiplegia.

1. INTRODUCTION

Herpes simplex encephalitis (HSE) is an acute or subacute illness that causes both general and focal signs of cerebral dysfunction. Brain infection is thought to occur by means of direct neuronal transmission of the virus from a peripheral site to the brain via the trigeminal or olfactory nerve. The exact pathogenesis is unclear, and factors that precipitate herpes simplex encephalitis are unknown.

Herpes simplex encephalitis is a neurological emergency with high morbidity and mortality. It is most caused by herpes simplex virus-type one (90%), followed by herpes simplex virus-type two (10%). The presentation is usually nonspecific and may include acute febrile illness with headache, progressive altered mental status, hemiparesis, and seizures [1].The virus shows neurotropism with a predilection for medial temporal and inferior frontal lobes. It induces latent or persistent infections via sensory neural pathways. The primary infection involves the mucocutaneous surfaces, which serves as the portal of entry of the viral particles into the nervous system within the same sensory distribution. Under immunocompetent conditions, the infection usually does not spread beyond the anatomic distribution or outside the vicinity of a single dorsal root ganglion. Primary infection commonly presents during the second and third decades of life; however, reactivation can occur at any time by retrograde transmission, resulting in human encephalitis [2].

Prompt clinical recognition is important to prevent progressive brain tissue damage, hemorrhagic changes, and worsening encephalitis. Diagnosis is usually confirmed through an extensive evaluation, including a thorough clinical examination with attention to findings of mental status changes, cerebrospinal fluid (CSF) analysis, electroencephalogram (EEG) testing, and neuroimaging findings. Early brain imaging may reveal changes which may mimic as cerebral ischemic lesions and may mislead the diagnosis. Once HSE is suspected, high-dose acyclovir should be started immediately before lumbar puncture, and only stopped once a definitive alternate diagnosis has been established. Early intervention with high-dose intravenous (IV) acyclovir has been shown to improve neurological outcomes in these patients [3].

2. CASE REPORT

A 7-years-old Malay girl, with birth date of 03/04/2010, had been admitted to paediatric ward for having refractory seizure in February 2017. She had been treated for multiple episodes of seizures with underlying right sided hemiplegia and moderate learning disabilities. Patient was kept in view for epilepsy surgery.

She was full term baby and had no history suggestive of birth asphyxia. In November 2011, when she was 1 year and 7 months old, she was first admitted to the ward with twitching of her right side of mouth, drooling of saliva and right sided body weakness. She was subsequently diagnosed as herpes simplex encephalitis.

She had seizure-free period from November 2011 till April 2013. Since November 2013, she had experienced generalized seizure for daily basic. From January 2014 onwards, she had atonic seizures (drop attacks) every day.

On physical examination, her weight was 16.8 kg (below 3rd centile), and height was 114.5 cm, (between 3rd to 10th centile). Patient was alert

and walking independently with hemiplegic gait. On systemic examination, there was no remarkable finding in respiratory, cardiovascular, and gastrointestinal systems.
Her development was delayed globally mainly impinged by the hemiparesis and poorly controlled epilepsy.

Central nervous system (CNS) examination revealed as follow; (1) gross motor: only be able to walk independently but having frequent drop attacks, (2) fine motor: could scribble only and still dependent for activities of daily living, (3) speech & language: could respond to her own name and could point out 6 body parts, but unable to count or speak meaningfully, (4) social: she was not going to kindergarten yet but able to play with cousins and siblings. For diet history, she usually skipped lunch. She was taking normal adult diet in breakfast, lunch, and dinner time. The details of the CNS examination findings were described in Table 1.

The diagnosis was Symptomatic generalized epilepsy with right hemiparesis secondary to herpes encephalitis.

Important Investigations are as follows:

2.1 MRI Studies

MRI Brain (March 2014) – left parietal lobe encephalomalacia due to the previous insult.
MRI Brain (November 2016) – acute disseminated encephalomyelitis (ADEM).
EEG Studies:
EEG (Nov 2011) – Normal sleep pattern.
EEG (May 2013) – Suggestive of symptomatic focal epilepsy (abnormal background with frequent focal epileptiform discharges and focal slowing noted at left Centro temporal and mid temporal region)
EEG (July 2015) – Suggestive of symptomatic epilepsy
EEG (Dec 2016) – Epileptic encephalopathy with lots of atypical absences.

2.2 Treatment

The patient had been treated with intravenous methylprednisolone, 160 mg 8 hourly for 5 days, and was discharged with oral prednisolone, that was tapered off in December 2016. She seemed to be more active after starting methylprednisolone. She was on sodium valproate (Epilim syrup) 300 mg BD, clobazam 5 mg BD. However, the patient still had atonic seizures (drop attack) and generalised tonic seizures 1-4 times per day.

She was planned for PET scan, two to three months from last EEG. She was also planned to undergo operation if the PET scan feasible (Hemispherectomy).However, the patient refused for operation.

2.3 Outcome and Follow-up

She was discharged in August 2017, and was given phenytoin 30 mg TDS, clobazam 5 mg BD. However, she still had atonic seizure 2-3 times a day for daily. The patient was reviewed in September 2017 and antiepileptic medication (AED) was modified from single therapy to dual therapy. Syrup Epilim was switched to Syrup Topiramate 25 mg BD, oral Phenytoin 30 mg TDS, oral clobazam 5 mg BD. Since then she was under regular follow-up in Paediatric Neuro Medical Clinic.

The diagnosis was right hemiparesis secondary to encephalitis complicated with epilepsy.

The patient was following up regularly with the same treatment together with physiotherapy, occupational therapy, early childhood intervention. The patient was also registered under OKU (Orang Kurang Upaya), a disabled person.

3. DISCUSSION

The clinical presentation of HSE is non-specific, especially in young children. Early symptoms may include malaise, mild irritability, or lethargy with no fever as the only manifestation. There is no characteristic finding in routine laboratory studies among children with HSE. CSF findings are abnormal in most cases of HSE, typically with lymphocytosis and, at times, a high red cell count indicating a haemorrhagic process.

Herpes simplex encephalitis is the most frequent cause of sporadic fatal encephalitis in the Western world, with an incidence of one case per million per year [1]. Nevertheless, the condition is rare and presents with non-specific symptoms; it has a varied nature of presentation making a diagnosis of HSE challenging in both adults and children. The virus infects the sensory branch of the lingual nerve, then ascends to the trigeminal ganglion and remains latent. Reactivation can result in fulminant hemorrhagic necrotizing encephalitis. The clinical manifestation typically presents with fever, headache, confusion, and focal or generalized seizures [2]. Around 90% of the patients have a fever and abnormal mental status as the primary signs and symptoms of

Table 1. Central nervous system examination findings

	RUL[a]	LUL[b]	RLL[c]	LLL[d]
Power	3/5	5/5	4/5	5/5
Tone	Increase	Normal	Increase	Normal
Clonus	-	-	No clonus	No clonus
Reflex	Brisk	Brisk	Brisk	Brisk
Plantar			Upgoing	Downgoing

[a] RUL- Right Upper Limb, [b] LUL- Left Upper Limb, [c] RLL- Right Lower Limb, [d] LLL- Left Lower Limb

Table 2. The 20-year risk of unprovoked seizures [5]

	20-year risk of unprovoked seizures	
Type of infection	With acute-context seizures	Without acute-context seizures
Viral encephalitis	22%	10%
Bacterial meningitis	13%	2.4%

HSE. Vomiting, nausea, pseudomeningitis, and seizures occur in about 50% - 60% of patients, and focal neurological deficits appear in 30 - 50% [1].

Abdul Jabbar and colleagues reported the case of a 17-year-old girl who presented with headache and acute onset hemiparesis preceded by classical HSE presentation, including fever, altered mental status, and seizures. Similar to our patient, her diagnosis was based on MRI and positive titers of antibodies against herpes simplex type one in CSF analysis. This puts it in the differential diagnosis of acute stroke in young patients, even in the absence of encephalitic features, and emphasizes that early MRI examination could be of great help in delineating the pathology at presentation [4].

The 20- years risk of developing unprovoked seizure in survivors of encephalitis or meningitis was 6.8%. (Conducted as retrospective study between 1935 and 1981). It is highest among first 5 years after CNS infection, but risk is still increased over next 15 years during follow-up [5] (Table 2).

Retrospective analysis for risk of seizures from infection is challenging as it depends on multisystem and other unrecognized factors implicated during or after the course of illness [6]. There are limited data highlighting breakthrough seizures in clinical practice in the paediatric field especially post-encephalitic complication [7,8].

Based on various clinical presentations and different underlying diagnosis, it is important to stratify prognosis-based outcomes. Therefore, indications of surgical management for refractory seizures or epilepsy would be clearly discussed [9]. To prevent breakthrough seizure, adherence, minimal handling of dose changes and modification of lifestyles play important roles [10].

The 'time is brain' is applicable for children with epilepsy. Cognitive functions are obviously affected by seizures induced white matter impact, deranged brain network topology, and chronic use of AEDs in developing children [11].

Timing for epileptic surgery is an indicator of post-surgery risk of seizures, neurodevelopmental potential, developmental quotient, and intelligent quotient. Early discontinuation of AEDs is also associated with postoperative intelligence outcomes. The shorter the duration of seizure prior to epilepsy surgery, the better post-surgical outcome and lesser risk of recurrent seizures [12].

4. CONCLUSION

It is crucial to consider the diagnosis of HSE as early as possible and to start treatment even before obtaining the laboratory data that confirm or exclude the diagnosis.

Despite the major advantages in diagnosis and treatment of HSE, this disease is still associated with significant mortality and morbidity. Therefore, it is important to consider HSE as possible diagnosis if children presented with an encephalitis process, and should provide early treatment to suspected cases.

This case is reported because the patient had generalized epilepsy with right hemiparesis

secondary to herpes encephalitis. Herpes encephalitis with right hemiparesis and post-encephalitic epilepsy cases are quite uncommon.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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