# Case Report

# Kleine-Levin Syndrome: The First Typical Case in Thailand

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*Kleine-Levin syndrome (KLS) is a rare disorder characterized by periodic hypersomnia, cognitive and behavioral disturbances. Other unique symptoms in KLS are megaphagia, hypersexuality and some psychiatric disturbances such as compulsion and depression. Definite diagnosis requires the elimination of other potential etiologies. We reported a typical case of KLS in a young Thai man who suffered from seven episodes of periodic hypersomnia within 1.5 years and eventually he was diagnosed with Kleine-Levin syndrome after excluding known possible neurological conditions and sleep disorders.*

***Keywords:*** *Kleine-Levin syndrome, KLS, Periodic hypersomnia, Megaphagia, Hypersexuality, Thailand*

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**Case Report**

A 27-year-old Thai man, working as a skilled and energetic craftsman, presented with episodes of periodic hypersomnia for 1.5 years. Each hypersomnic episode occurred every 2-3 months and lasted for 3 to 12 days with average duration of 7 days. Because of prolong being sleepy, social communication was less and the daily activities such as having meal, drinking, taking a bath were forced by parents. During each meal he just looked at the plate, scooped the food into his mount without discrimination of the content items. Each scoop was very big and he kept continuing eating scoop by scoop tending to have very big meal prior to returning to bed. He was able to develop his own toilet schedules and he could follow those schedules properly. After each hypersomnic event, he could perform actually daily activities without daytime sleepiness. Communation skill and eating behavior returned to normal baseline. However, he could not remember the events but reported that he might have a long vivid dream. There were no symptoms of hypersexuality, mood instability, hallucination, seizure, or headaches during episode. Pertinent physical examination during event demonstrated drowsiness stage with slow verbal response and apathetic face, bradykinesia and pseudoptosis without other neurological deficit. Repeated physical examination after cessation of each event was unremarkable.

Past history revealed that he developed progressive severe headaches with nausea, vomiting and papilledema in the past five years ago. Computed tomography of the brain showed dilatation of third ventricle and lateral ventricles bilaterally that was consistent with cerebral aqueductal stenosis; there was neither space occupying lesion nor other cerebral anomalies discovered (Fig. 1). All symptoms and signs of intracranial hypertension were markedly alleviated after ventriculo-peritoneal shunt insertion.

Family history was unremarkable for neurological and sleep-disorder.

Actual Sleep pattern (prior to each hypersomic episode) revealed that sleeping time was 10 PM. Sleep duration was 8 hours approximately but could be diminished to 3 hours for busy day without daytime sleepiness on next day. There was no history of sleep attack, sleep paralysis or cataplexy reported.

***Investigations***

- *CBC:* Hematocrit 46.9%, white blood cell count 6,600/cumm, neutrophil 49.3%, lymphocyte

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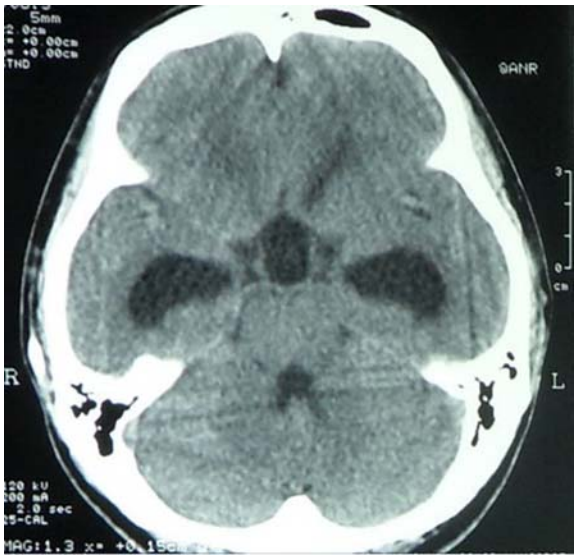

**Fig. 1** CT brain revealed huge lateral ventricles compared to the forth ventricle consistent with obstructive hydrocephalus from cerebral aqueductal stenosis

42.1%, monocyte 7.4%, platelet 267,000/cumm

- BUN 11.4 mg/dL
- Creatinine 0.9 mg/dL
- Electrolytes: sodium 140 mg/dL, potassium 3.7 mg/dL, chloride 99.8 mg/dL, bicarbonate 29.7 mg/dL
- Calcium 9.1 mg/dL, Magnesium 2.4 mg/dL, Phosphorus 3.7 mg/dL
- Thyroid function test: FT3 2.55 pg/mL (2.57-4.43), FT4 1.27 ng/dL (0.932-1.71), TSH 2.69 mIU/L (0.27-4.2)
- Metabolic/toxic screen: negative
- CSF examination: clear, no xanthochromia, WBC 0, red blood cell 25/cumm, protein 39 mg/dL, sugar 76 mg/dL
- MRI brain: as shown in Fig. 2.
- Long term (24 hours) video-Electroencephalography (v-EEG): as shown in Fig. 3.
- Sleep study and multiple sleep latency tests (MSLT) revealed no significant apnea and no evidence of sleep onset REM. Sleep latency was 5 minutes.

Investigations including CBC, electrolytes, calcium, magnesium, phosphorus, BUN, Cr, liver function tests, thyroid function test, metabolic and toxic screening, cerebrospinal fluid analysis were normal. MRI study of the brain (with gadolinium) was normal, without abnormal signal along grey and white matter (Fig. 2). Video-electroencephalography (v-EEG), performed for 24 hours, showed slow background activity with bursts of delta rhythm intermixed with vertex sharp transient and sleep spindles (Fig. 3). Sleep study and multiple sleep latency tests (MSLT) demonstrated sleep latency of 5 minutes without evidence of apnea or sleep onset REM.

**Discussion**

A previously report by Thongtang et al represented a suspicious Thai case of Kleine-Levin syndrome (KLS) who had only one event of hypersomnia without recurrent attack[1]. We reported the first Thai patient that eventually fulfilled diagnosis of KLS after elimination of other potential etiologies that cause hypersomnia such as abnormal metabolic/toxic screening, structural brain anomalies, NCSE, sleep disorders particularly of sleep apnea and narcolepsy.

KLS, firstly reported by Brierre de Boismont in 1862, is a rare and sporadic disorder that comprises recurrent episode of hypersomnia, cognitive and behavioral disturbances[2,3]. KLS is common in male with a ratio of 2:1. Age of onset is between 4 and 82 years (median 15 years of age). More than 80% of cases are diagnosed within the second decade of life and symptoms could persist from 0.5 year to 41 years (average 8 years). The average duration of each episode lasts for 10 days and the free symptoms between the episodes is roughly 3.5 months. Even commonly found in male, the duration of KLS in affected female tends to be longer. The common symptoms of KLS consist of hypersomnia (100%) and cognitive changes (96%). Most patients described specific feeling of derealization or a feeling of unreality as wrong surrounding atmosphere, distorted or unreal, as in a dream. 80% of KLS patient reported eating disturbances such as compulsive eating or megaphagia and they seem not to discriminate the food items. Less than half of patient (43%) experienced hypersexuality. Psychiatric disturbances such as compulsion and depression have been discovered in 30-40% of cases[4]. The differential diagnosis of hypersomnia covered physiologic, organic and non-organic disorders including sleep deprivation, sleep apnea, hypothyroid, CNS lesions, sedative medications, depression, bipolar disorders, narcolepsy, and idiopathic hypersomnia. For an uncommon condition, Kluver-Busy syndrome that caused by bitemporal lobes lesion or resection, patient may present with eating problem. Non-convulsive status epilepticus (NCSE) is another crucial differential diagnosis of prolong and periodic neurological deterioration.

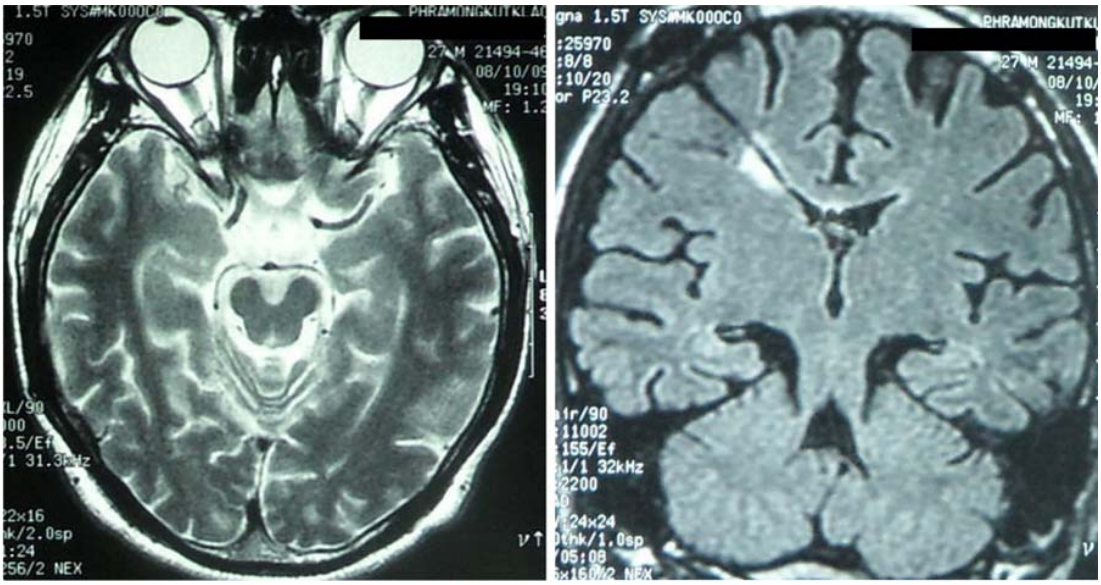

**Fig. 2** MRI brain showed no evidence of hydrocephalus. There was a small hyper-signal intensity lesion around the VP shunt's tube over the right frontal area

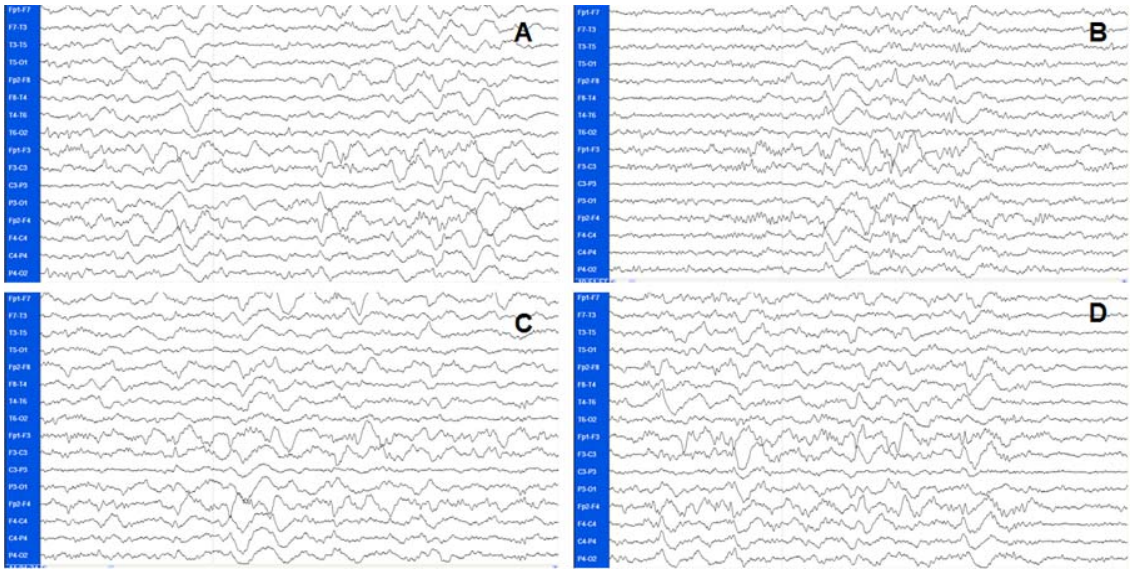


**Fig. 3** Electroencephalographic series during a hypersomnic event illustrated slow backgrounds, bursts of delta rhythm with vertex sharp transient and sleep spindles.

The classification of KLS includes primary and secondary KLS. Primary Kleine-Levin syndrome is used to diagnosed in patient who did not have concurrent neurological abnormalities as well as negative results of all investigations[5-8]. Secondary KLS is found commonly in advanced age and associated with focal neurological signs. Most patients with secondary KLS have frequent attacks with longer symptom duration. The appearance of this condition could be found in patient with post-traumatic brain hematoma, genetic or developmental diseases, multiple sclerosis, hydrocephalus, paraneoplastic syndrome, autoimmune

encephalitis, severe infection and cerebrovascular diseases. For our patient, it is difficult to determine whether primary or secondary KLS he might have because he was underwent VP shunt insertion for cerebral aqueductal stenosis since five years ago. This should suggest secondary KLS by the pre-existing neurological condition. However, because of symptom at young age and no residual neurological signs after operation and prior to onset of hypersomnia, these should be compatible with primary KLS either.

The precipitating factors of KLS are unclear. However, some reports suggested that infection, head trauma and alcoholic consumption might be the precipitating factors. Pathophysiology is likely to be more organic than functional. The possible conditions related with KLS are viral infection, post infectious autoimmune encephalitis with primary impact on the hypothalamus and HLA DQB1*02[9]. Fundamental investigations including including epilepsy (EEG), brain lesion (imaging: CT or MRI brain), meningitis, encephalitis (CSF analysis) and hypothyroid (TSH) should be ascertained to exclude all other hypersomnic conditions. More specific tests *e.g.* sleep study and MSLT are recommended to determine sleep disorders that may mimic KLS.

Regarding treatment, somnolence could be alleviated by some stimulants mainly amphetamine in composition[10]. However, medications would not help in other domains especially behaviors. Lithium is reported a higher response rate but frequent relapsing episodes after discontinuation[11-13]. Carbamazepine is another medication showing a good response in one case report[14]. Other medications such as anticonvulsants, antidepressants and neuroleptics did not show the efficacy to prevent relapses. Electroconvulsive therapy was also unhelpful. It is important to keep in mind that all aforementioned treatments were used in small group of patient. Until recently, there is no sufficient information and physicians need more evidence-base data to conclude the best treatment for KLS. Our patient was treated by sodium valproic acid based on evidences of the right cortico-subcortical lesion, post VP shunt insertion, from MRI study of the brain and occasional sharp transients over the same areas. Six months after treatment, he continued having two episodes of periodic hypersomnia with longer symptom duration. Fluoxetine therefore was added on, and he was in the process of clinical follow-up. Reassure patient himself and his family regarding the natural history and plans of care for patient with KLS was also informed.

**Conclusion**

KLS is a rare and sporadic disorder that comprises recurrent episode of hypersomnia, cognitive and behavioral disturbances. Diagnosis by exclusion of other potential etiologies of hypersomnia is mandatory. Due to unknown pathophysiology and unclear definite treatment, more reports and randomized controlled study is definitely required. .

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## *Kleine-Levin syndrome:* ผู้ป่วยรายแรกในประเทศไทย

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*เป็นกลุ่มอาการที่พบไม่บ่อย ประกอบด้วยอาการสำคัญคือนอนหลับนานผิดปกติโดยเกิดขึ้นเป็นพัก ๆ ร่วมกับพฤติกรรมที่ผิดปกติ เช่น การกินอาหารคำโตๆ ปริมาณมากโดยไม่แยกแยะส่วนประกอบของอาหาร ความรู้สึกทางเพศเพิ่มขึ้น และอารมณ์ผิดปกติ เช่น ฉุนเฉียวหรือซึมเศร้า การวินิจฉัยภาวะนี้ จำเป็นต้องวินิจฉัยแยกโรคทางระบบประสาทหรือโรคความผิดปกติของการนอนหลับอื่นๆ ก่อนโดยอาศัยการตรวจทางห้องปฏิบัติการหลายอย่างร่วมกัน ปัจจัยที่กระตุ้นให้เกิดภาวะ KLS ยังไม่ทราบชัดเจน และข้อมูลปัจจุบันยังไม่เพียงพอที่จะสรุปมาตรฐานการรักษาได้*

*ผู้ประพันธ์นำเสนอรายงานผู้ป่วยชายไทยอายุน้อยหนึ่งรายที่มีอาการนอนหลับนานผิดปกติเกิดซ้ำจำนวนทั้งสิ้น 7 ครั้ง ในช่วงเวลา 1.5 ปี หลังจากการตรวจร่างกายทางระบบประสาทร่วมกับการตรวจทางห้องปฏิบัติการเพื่อหาสาเหตุของอาการดังกล่าว ในที่สุดสามารถให้การวินิจฉัยภาวะ Kleine-Levin syndrome ได้เนื่องจาก ลักษณะอาการทางคลินิกที่เกิดซ้ำหลายครั้ง และผลตรวจทางห้องปฏิบัติการทั้งหมดไม่พบสาเหตุอื่นที่ทำให้เกิดอาการดังกล่าว*