Syphilis, caused by a spirochete, *Treponema pallidum*, is a complex systemic disease with protean manifestations where virtually any organ in the body can be involved. It has been described as “the great imitator” or “the great impostor” in view of its multiple clinical manifestations, many of which are severe [1].

The term “neurosyphilis” describes a spectrum of manifestations of central nervous system (CNS) involvement in individuals with *T. pallidum* infection [2]. The CNS may be invaded during the septicemic phase, and neurologic manifestations can occur during any stage of the disease [3]. Seizures (partial or partial with secondary generalization), focal neurologic deficits (e.g., hemiplegia or aphasia), and delirium are classified as complications in neurosyphilic syndrome.

The incidence of seizure in neurosyphilis ranges from 14% to 60%, but status epilepticus as a presenting picture of neurosyphilis is rare [4]. Also less common in these described cases were focal abnormalities, such as hemiplegia, aphasia, or mental status changes [2].

We report a patient with neurosyphilis, presenting with status epilepticus, and review the literature.

**CASE PRESENTATION**

A 41-year-old unmarried man, with a traceable history of sexual exposure in the last 2 years, was brought to the emergency room (ER) of Kaohsiung Medical University Hospital at 2:30 AM on March 28, 2003 because of generalized tonic-clonic (GTC) convolution, and mental confusion.

According to his sister’s statement, the patient experienced a dull headache over the left temporal area in the first 3 days, until difficulty in verbalization and poor concentration was noted on March 26, 2003. He was brought to the ER of another medical center on the evening of March 27, where cerebral vascular disease (CVD) with expressive dysphasia and mild hyperglycemia were diagnosed by a neurologist,
although emergency brain computed tomography (CT) without contrast enhancement showed no intracranial lesions. The patient refused admission for further management.

Subsequently, he had GTC convulsion at 1:50 AM on March 28. On his way to our ER, the GTC convolution occurred twice again, which drove him into disturbed consciousness. On arrival to the ER at 2:30 AM, another episode of GTC convolution was noted on site. The ER physician instantly gave diazepam 10 mg and lorazepam 4 mg intravenously (IV), along with a diphenylhydantoin 1 g IV drip to control seizure, but the convulsions recurred soon after until an additional midazolam 7.5 mg IV with 2.25 mg/hour IV drip was administered, after which the convulsions ceased.

In the ER, physical examination and laboratory data showed fever (37.9°C), tachycardia (159/minute), elevated blood pressure (179/95 mmHg), leukocytosis (23,740/µL), and nonketoacidotic hyperglycemia (370 mg/dL). Arterial-blood gas showed severe metabolic acidosis (pH, 6.856; PCO₂, 40.5 mmHg; HCO₃⁻, 7.3 mM/L). Other metabolic disorders included hyperkalemia (5.7 mmol/L), hypercalcemia (5.8 mg/dL, free form), hypercreatinemia (BUN/Cr = 18/2.0 mg/dL), hyperammoniemia (331 µg/dL), and hyperlacticemia (13.2 mmol/L). Emergency brain CT without contrast enhancement still revealed no intracranial lesions. He was then admitted to the neurologic intensive care unit (NICU) with a midazolam IV drip under the diagnosis of status epilepticus.

In the NICU, monitoring electroencephalogram (EEG) revealed diffuse background-slowing activities without active epileptiform discharges under the sedation of midazolam.

Under the impression of suspicious CNS infection, a lumbar puncture was performed thereafter, which revealed mild pleocytosis (WBC, 25/µm³; PMN/Mono = 5/95%), high protein level (120 mg/dL), but normal glucose ratio (cerebrospinal fluid, CSF/serum = 84/120) in the CSF profile.

The patient was then treated as a case of suspected herpes simplex virus (HSV) encephalitis, status epilepticus and diabetes mellitus (DM) with impending nonketoacidotic hyperglycemic syndrome in the first 3 days, until the 4th admission day when laboratory data showed positive serum and CSF VDRL reaction. The T. pallidum hemagglutination (TPHA) test titer in serum was 1:640. Other serum and CSF surveys including HSV, human immunodeficiency virus (HIV), tuberculosis, and fungal infections were all negative.

The therapeutic regimen was then switched to penicillin-G (PCN-G 24 MU per day) IV over the following 2 weeks. Three days later, the patient regained consciousness after PCN-G use and was seizure-free with DM under control.

Brain magnetic resonance imaging (MRI) on the 8th day of hospitalization revealed patch areas of relatively high signal intensity on fluid-attenuated inversion recovery and apparent diffusion coefficient (ADC) image, and slightly low signal intensity on exponential ADC map in the left cingulate gyrus (Figure 1), left temporal lobe and peri-Rolandic area (Figure 2). The edematous change in the above-mentioned areas was thought to be an inflammatory process.

Follow-up CSF study on April 14 (2 weeks after PCN-G therapy) revealed a normal profile except for positive CSF VDRL reaction.

After 20 days of hospitalization, the patient was discharged with only mild neurologic sequela of retrograde amnesia.

**DISCUSSION**

Neurosyphilis can be divided into several clinical syndromes that tend to occur at different points in the natural history of untreated syphilis. Clinical classification may be further subdivided into five categories: (1) asymptomatic CNS involvement; (2) syphilitic meningitis; (3) meningovascular syphilis; (4) parenchymatous neurosyphilis (general paresis and tabes dorsalis); and (5) gummatous neurosyphilis [2].

Syphilitic meningitis is thought to be the consequence of direct meningeal inflammation, most likely due to a small-vessel arteritis and most often occurring within 2 years of acquisition of syphilis. It is one of the least common neurosyphilis syndromes and has been estimated to occur in only 0.3–2.4% of syphilis cases [5]. Some authors further subdivide the syndrome into three variants, based on the area of CNS predominantly affected.

1. Acute syphilitic hydrocephalus: the predominant findings are nonfocal and include headache, nausea, and vomiting.
2. Acute vertical syphilitic meningitis: there are additional abnormalities such as seizures, focal
Figure 1. Magnetic resonance imaging. The fluid-attenuated inversion recovery image shows (A) hyperintensity in the left cingulate gyrus (arrow). (B) The same area reveals hyperintensity on apparent diffusion coefficient (ADC) map and (C) hypointensity on exponential ADC map, suggesting vasogenic edema. (D) Minimal enhancement of the lesion is noted on postgadolinium T1-weighted imaging.

Figure 2. Magnetic resonance imaging. The axial fluid-attenuated inversion recovery image shows (A) hyperintensity in the left cingulate gyrus and the left temporal lobe (arrows). (B) The level more cranial to (A) shows hyperintensity in the left cingulate gyrus and the left peri-Rolandic area (arrowheads).
neurologic deficits (e.g., hemiplegia or aphasia), and delirium or confusion, chiefly resulting from inflammation that predominates on the vertex of the brain.

3. Acute basilar syphilitic meningitis: characterized primarily by the presence of cranial nerve involvement [2].

Our case had expressive dysphasia, mental confusion, and seizures (partial with generalization and status epilepticus), which might be classified as “acute vertical syphilitic meningitis”. This diagnosis was confirmed by the positive CSF profile, and was further supported by the MRI findings, which revealed focal edematous changes over the left cingulate gyrus, left temporal, and peri-Rolandic area.

However, other than neurosyphilis, many other factors contribute to status epilepticus, including hyperglycemia [6–8] and severe metabolic acidosis. As the clinical pictures such as headache and fever could not be well explained by a high blood glucose level and abnormal acid-base data, we considered, therefore, that “syphilitic meningitis” chiefly and directly induced GTC seizures, and deteriorated to status epilepticus [4,9–13], which disturbed the systemic metabolism and acid-base equilibrium [14]. The hyperglycemia and ongoing disturbance of systemic metabolism further worsened this vicious cycle. The MRI focal lesions in this case also supported our consideration, because the sole systemic metabolic disorders did not usually make up the inflammatory lesions over the focal cortex [15,16].

“Neurosyphilis” is described as the great imitator or the great imposter in view of its multiple possible clinical manifestations, mimicking most commonly CVD, and less commonly HSV encephalitis [17], and may be as benign as asymptomatic CNS involvement or as malignant as status epilepticus. In the post-antibiotics era, the clinical presentation of neurosyphilis seems to have changed; chronic, progressive, dementing illness (or paretic neurosyphilis) and tabes dorsalis are rarely diagnosed. Instead, seizures, neuro-ophthalmologic manifestations, and meningeo-vascular presentations turn out to be more common [3].

Despite the emergence of syphilis with the acquired immunodeficiency syndrome epidemic, neurosyphilis is often ignored in the differential diagnosis of patients with aseptic meningitis and mental status changes who are negative for HIV. The high mortality rate associated with the delay in recognition, diagnosis, and treatment of neurosyphilis obligates its inclusion in the differential diagnosis among young patients with cognitive decline and seizure [18].

In conclusion, we underscore again the importance of considering neurosyphilis among the possible causes of status epilepticus and CNS diseases.

REFERENCES

C.H. Li, C.L. Su, W.C. Lin, and R.T. Lin


神經性梅毒以癲癇重積狀態為表現 —— 病案報告

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癲癇發作和局部神經功能缺損可能是神經性梅毒的併發症。但是以癲癇重積狀態為初始症狀表現仍是相當罕見的。我們提出一位四十歲男性個案，起始表現有急性表現性語言困難，伴隨著持續性癲癇狀態以及嚴重的系統性內科併發症。經由廣泛的實驗室評估，確定神經性梅毒及糖尿病的診斷。腦部磁共振影像顯現出非特異性炎症反應的變化。由於神經性梅毒的多樣化臨床表現。我們再次強調面對任何中樞神經系統疾病，特別是癲癇重積狀態，神經性梅毒應列入鑑別診斷。

關鍵詞：中樞神經系統疾病，神經性梅毒，癲癇重積狀態
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