

CASE REPORT

Central sleep apnea in a patient with Japanese encephalitis

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Abstract

We describe the first case of a patient with Japanese encephalitis suffering from central sleep apnea. The patient was a 58-year-old man who presented with high fever, semicomatose state, nuchal stiffness, and incontinence of feces. The patient had complication of severe pneumonia, and was ventilated with a respirator. After weaning from the respirator, desaturation of oxygen was observed during the night. Simplified polysomnography revealed a pure central apnea pattern. This case illustrates that Japanese encephalitis can result in central sleep apnea.

INTRODUCTION

Central apnea is characterized by a lack of the drive to breathe and defined by a lack of respiratory effort during cessations of airflow.¹ Japanese encephalitis (JE) has a significantly higher frequency of impaired respiratory disturbance when compared to other types of viral encephalitis.² However, to our knowledge, there are no reports of central sleep apnea due to JE as proven by objective examination. In this report, we present a patient with JE who developed episodes of central sleep apnea confirmed by simplified PSG.

CASE REPORT

A 58-year-old man developed malaise one day towards the end of summer. The next day, the patient was febrile with body temperature of 38.7 °C. The third day, incontinence of feces and weakness of left lower limb appeared. On day 4 of the illness, he was brought to our hospital in coma. His body temperature was 39.8 °C, blood pressure was 170/88 mmHg, respiratory rate was 24/min, and pulse was tachycardic (127/min). Stridor was heard. The patient had decorticate rigidity and neck stiffness. Pupil size was 1.5 mm both sides and pupillary light reflex was sluggish. The upper limb deep tendon reflexes were decreased and

lower limb deep tendon reflexes were increased. Pathological reflexes were not seen. Laboratory investigations showed a white cell count of 13,900/ μ l, C reactive protein of 4.87 mg/dl, creatine kinase of 893 U/l, blood urea nitrogen of 29.5 mg/dl, and creatinine of 1.58 mg/dl. Urinary occult blood was 3+ and protein was 100 mg/dl. On lumbar puncture, the cerebrospinal fluid (CSF) opening pressure was 180 mmH₂O. Cell count was 97/mm³ (neutrophils 19, lymphocytes 78). The CSF protein was 124 mg/dl and glucose was 72 mg/dl (serum glucose was 148 mg/dl). Brain MRI showed hyperintense lesions in the right basal ganglia and midbrain, bilateral thalamus, deep white matter and temporal lobe upon T2-weighted and FLAIR imaging (Figure 1). He was treated with IV acyclovir, methylprednisolone, and broad-spectrum antibiotics. Artificial ventilation had to be started on day 8 because of severe pneumonia. On day 21, because of prolonged assisted ventilation, tracheostomy was performed. On day 28, the diagnosis of JE was established based on seroconversion of anti-JE virus IgG by complement fixation methods (titre of <x4 on day 4 to x 256 on day 28). On day 34, the patient could be withdrawn from the respirator and was able to maintain waking respiration with a pH of 7.426, PO₂ of 83.9 mmHg, and PCO₂ of 43.6 mmHg with a bicarbonate level of 27.5 mmol/l.

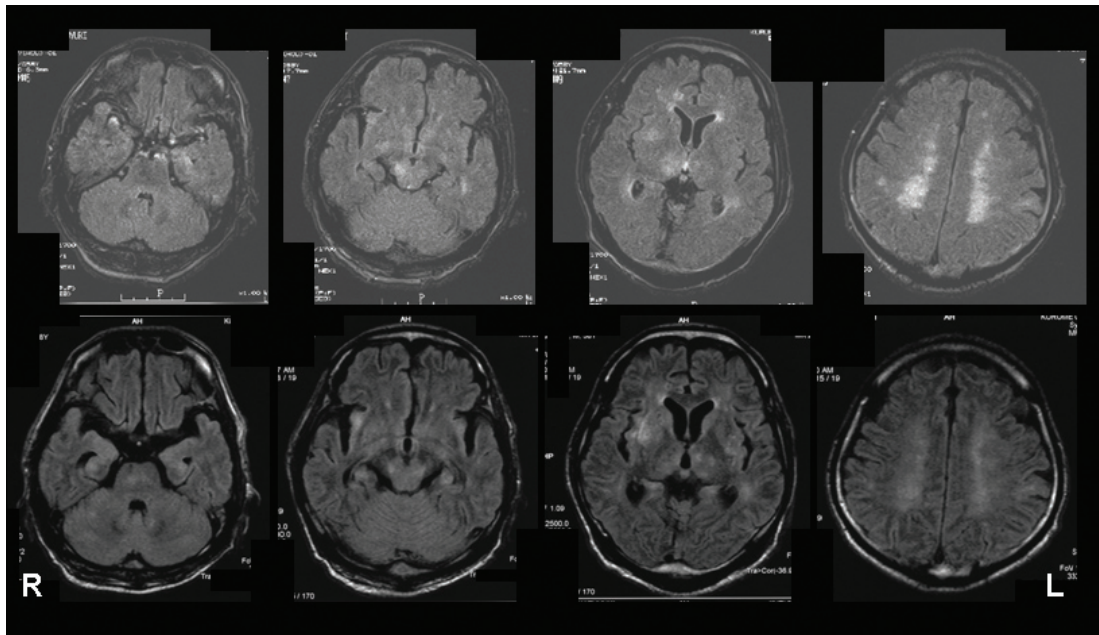


Figure 1. (Top) Brain MRI on day 4 of the illness showed hyperintense lesions in the right basal ganglia and midbrain, as well as bilateral thalamus, deep white matter and temporal lobe upon T2-weighted and FLAIR imaging. (Bottom) On day 34, brain MRI revealed generalized cerebral atrophy without any new abnormal lesion.

However, desaturation of oxygen was frequently observed during the night. Brain MRI revealed generalized cerebral atrophy without any new abnormal lesion (Figure 1). On day 40, simplified polysomnography (PSG) revealed a pure central apnea pattern (Figure 2). The apnea-hypopnea index (AHI) was 17.6, the average duration of apnea was 13 seconds, and the longest duration of apnea was 29 seconds. Oxygen therapy (2 l/min) during the night was able to compensate nocturnal desaturation episodes. On day 53, single photon emission computed tomography (SPECT) demonstrated hypoperfusion in both frontal lobes, right temporal lobe and basal ganglia, and left thalamus (Figure 3). On day 60, simplified PSG showed improvement of the central apnea (Figure 4). The AHI was 4.2, the average duration of apnea was 13 seconds, and the longest duration of apnea was 29 seconds. On day 70, the patient was transferred to another hospital for rehabilitation therapy.

DISCUSSION

JE is caused by the JE virus transmitted by *Culex* mosquitoes. Only a small minority of people exposed to the JE virus develops clinically overt disease. The ratio of symptomatic to asymptomatic infection varies from 0.1 % to 5 %.^{2,3} Currently,

there is no specific treatment available for JE. The mortality rate is about 30%, and around half of the survivors have severe neurological sequelae.³

In this patient, the diagnosis of JE could be established based on serological examination and characteristic changes seen on neuroimaging. Among patients with JE, T2-weighted MR imaging revealed thalamic involvement in about 80 % of patients, and basal ganglia and temporal lobe involvement in about 30%.^{4,6} Diffusion-weighted imaging techniques in MRI shows that all JE patients have bilateral thalamic involvement.⁵ Necropsy studies has shown that thalamus, basal ganglia, and midbrain are the common site of pathology.³ Our patient's T2-weighted and FLAIR imaging showing involvement of right basal ganglia, midbrain, and bilateral thalamus. The changes are thus typical of JE.

SPECT studies 1-12 months after the onset of JE have revealed hypoperfusion of thalami, cerebral cortex, and lentiform nucleus, with thalamic hypoperfusion being particularly common, seen in all patients.⁴ In addition, the improvement of clinical symptoms may correlate with improvement of hypoperfusion in SPECT.⁶ In our patient, the hypoperfused regions in SPECT are consistent with the known findings in JE.

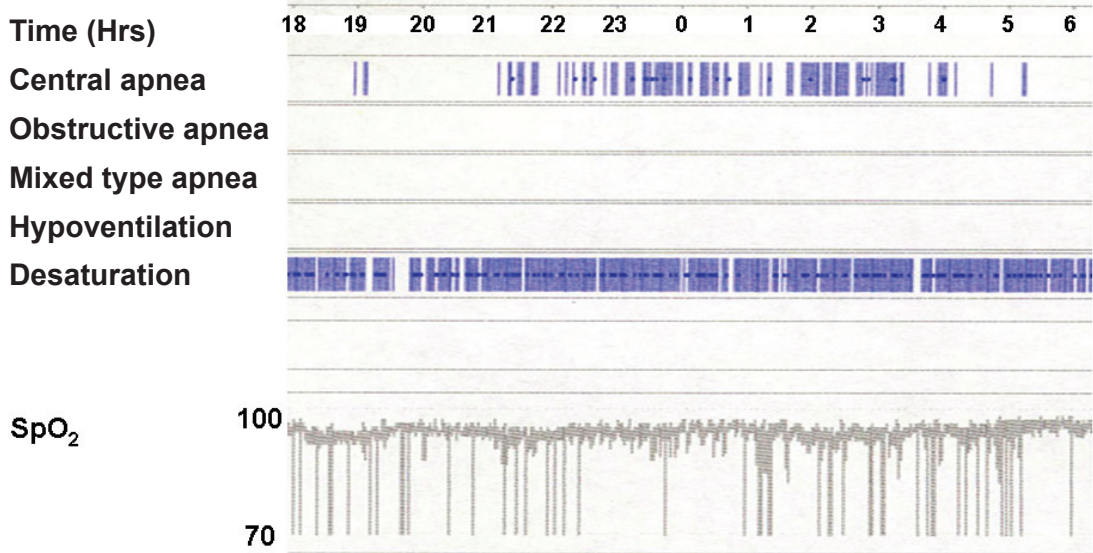


Figure 2. Nocturnal simplified PSG on day 40 revealed a pure central apnea pattern.

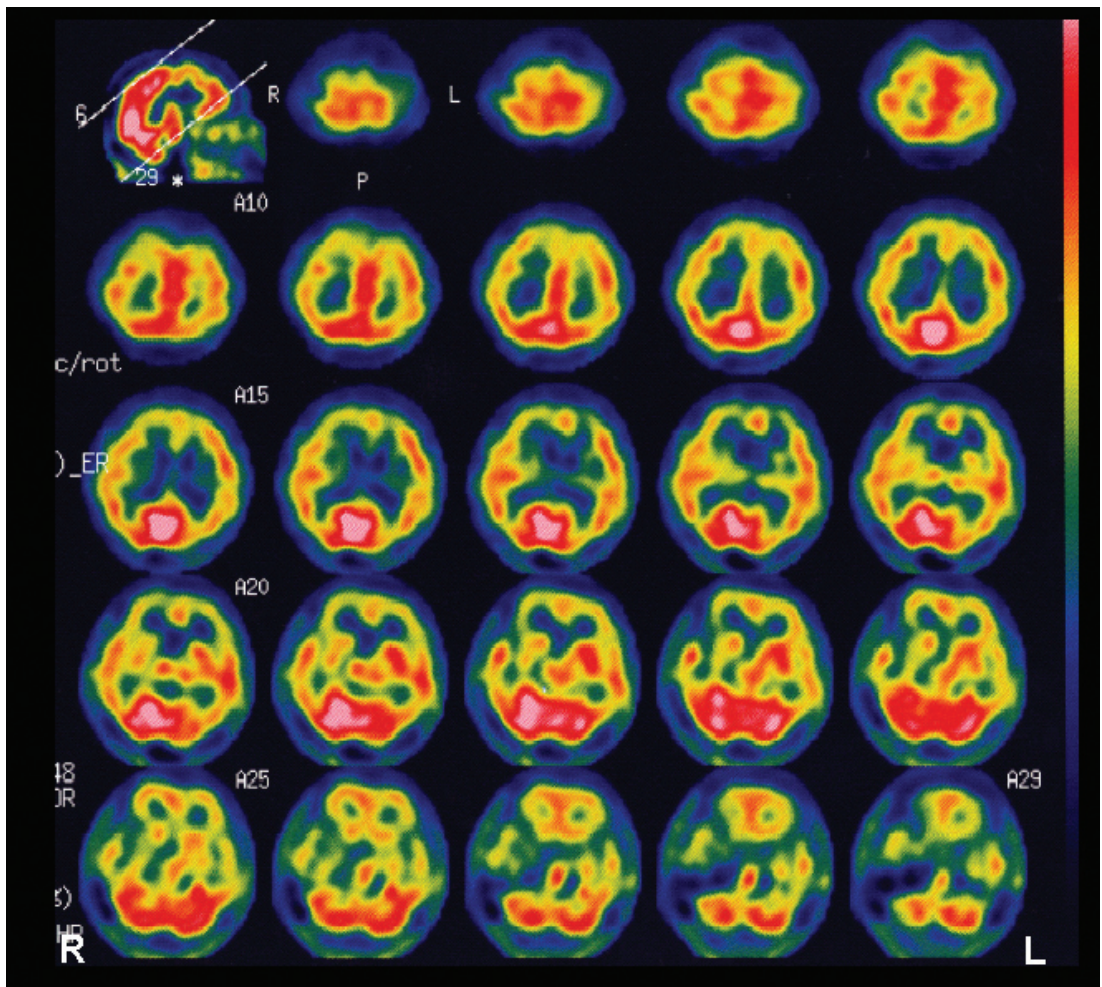


Figure 3. SPECT with ^{99m}Tc-ECD on day 53 demonstrated hypoperfusion in bilateral frontal lobes, the right temporal lobe and basal ganglia, and left thalamus.

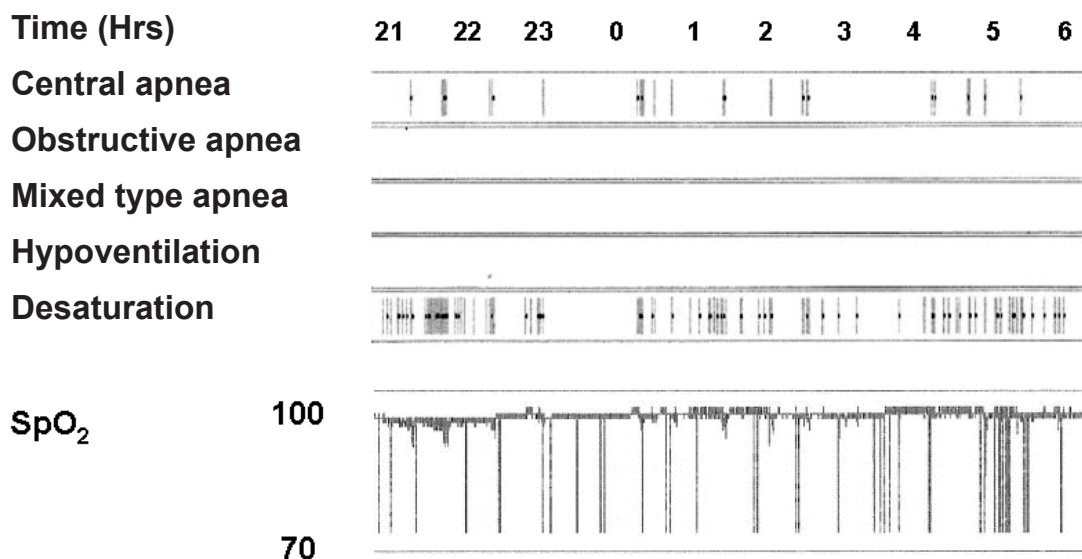


Figure 4. Nocturnal simplified PSG on day 60 revealed remission of central apnea.

Some encephalitis such as bulbar poliomyelitis, Western equine encephalitis, listeria monocytogenes brainstem encephalitis, and paraneoplastic brainstem encephalitis have been reported to cause central apnea. There has also been a case report of transient obstructive sleep apnea in a patient with presumed viral encephalitis, where the apnea disappeared within 10 days.⁷ Up to 51.8 % of patients with JE have been reported to show respiratory disturbance², however, there has not been any previous report of central or obstructive sleep apnea in JE. In our patient, simplified PSG revealed a diagnosis of central sleep apnea, as both thoracic and abdominal movements were not seen during the apnea episodes. Also because this patient had a tracheostomy, obstructive sleep apnea was unlikely. Nevertheless, it was possible that without tracheostomy, the patient could have a mixed central and obstructive apnea.

Automatic breathing depends on the activity of chemoreceptive neurons that respond to changes in oxygen, carbon dioxide, and pH in blood and CSF. These neurons provide inputs to a brainstem network responsible for generation of the respiratory rhythm.⁸ This central respiratory pattern generator includes neurons located in the dorsolateral pons, nucleus of the solitary tract (NTS), and ventrolateral medulla.⁸ In our patient, examination by neuroimaging did not reveal lesions of the pons or medulla. We postulate that there could have been inflammation

in the pons and medulla which was below the resolution of MRI. In addition, recent research has shown that central apneas have wide-ranging abnormal brain circuitry.⁹ The SPECT scan in our patient have demonstrated hypoperfusion in the frontal lobe, temporal lobe, basal ganglia, and thalamus. These could also be associated with the central apnea. Patients with waking hypercapnea due to ventilatory control abnormalities or neuromuscular disease may have central apneas during sleep because these patients have low hypercapnic responsiveness.¹⁰ During sleep, most behavioral influences on breathing are lost and respiration is largely dependent on chemical control mechanisms; therefore, central sleep apnea arises.¹⁰ In our patient, the arterial PCO₂ was of high normal level. Our patient may thus have relatively low hypercapnic responsiveness. On the other hand, hypothalamic lesions have been reported to cause failure of autonomic control of ventilation.¹¹ In our patient, there could also have been inflammation of the hypothalamus as well as thalamus.

In conclusion, physicians should be aware that JE can also be a cause of central sleep apnea.

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