Case Report: Ondine’s Curse Syndrome Secondary Brainstem Infarction

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Abstract

Objective: To investigate the clinical and imaging characteristics of Ondine's curse syndrome secondary brainstem infarction.

Methods: Analysis based on the clinical and imaging data of 3 patients with Ondine's curse syndrome secondary brainstem infarctions in last four years.

Case Report: All the 3 patients were found in with brainstem lacunar infarction and had further afflicted with Ondine's curse syndrome. Among these 3 patients, 2 patients died and the other one survived by mechanical ventilation.

Conclusion: Sleep-apnoea should be closely monitored to prevent from the occurrence of Ondine's curse syndrome with brainstem infarctions. Timely treatment by mechanical ventilation can reduce the occurrence of fatal Ondine's curse.

Keywords: Brainstem infarction; Ondine's curse syndrome; Sleep apnoea; Central; Magnetic resonance image (MRI)

Introduction

Ondine’s curse Syndrome is an extremely rare condition characterized by failure of breathing mechanisms during sleep, it is also a particular type of Central Sleep Apnoea Syndrome (CSAS). The name of Ondine's curse is derived from an ancient legend in Germany, where goddess Ondine's punishment is said to befall those people who made mistakes at night [1]. This syndrome is rarely occurred and it have poor prognosis. We analysed and summarized the clinical data of 3 Ondine's curse patients secondary with brainstem lacunar infarction.

Cases Report

Case 1: Male, 67 years old, who was admitted in the clinic due to "dysphagia with unstable walking for one day", at 15:12, on June 26, 2016. Physical examination showed his BP was 250/140 mmHg, his mind was clear. He was afflicted with vague speech and dysarthria. His right nasolabial sulcus was shallower. When being stretched out, his tongue turned to the right uncontrollably and his gag reflex abated. His right limb's strength was graded V-. The National Institute of Health stroke scale (NIHSS) was 3 points.

The patient has been afflicted with high blood pressure, and has a long history of smoking and drinking, as well as sleep apnoea.

After admission, head CT showed he suffered from multiple lacunar infarction and myelomalacia on bilateral cerebellum, basal ganglia and centrum ovale. After the brain MRI and MRA were performed, it appeared that the patient was afflicted with acute cerebral infarction on medulla and right cerebellum lobe, and basilar artery severe stenosis. The patient's breath suddenly stopped in the morning on the second day after received treatment and his consciousness was lost immediately. We performed timely cardiopulmonary resuscitation (CPR), endotracheal intubation and breathing machine at the same time. Unfortunately, he died after two hours’ continuous rescuing (Figure 1).

Case 2: Male, 66 years old, he was admitted to the hospital at 17:23 of August 26th, 2015, after being found "consciousness loss for an hour". Physical examination showed his BP was 175/94 mmHg. His mind was light coma, with snoring breathing and unable to speak. His left nasolabial sulcus was shallower than right. His right limb was...
hypotonic, his right upper limb strength was graded II and lower limb was graded III, and his left limb was normal. The patient was afflicted with hypertension, diabetes and had a long history of smoking and alcohol. His breath always pauses while asleep. On the admission day, head CT revealed multiple lacunar infarction on the left side of the cerebellum and bilateral basal ganglia, with myelomalacia. His blood sugar was 7.7 mol/L. After relevant treatment in the hospital, he was conscious and able to have a little verbal communication. At half past zero a.m. on 27, his breath was suddenly stopped, with purpled face. At that time physical examination showed: his pulses was 96 times/minute, BP was 130/87 mmHg, SPO2 was 39%, and his consciousness was severe comatose, bilateral mydriasis of pupil aperture was 4.0 mm and light reflex was disappeared. We immediately gave cardiopulmonary resuscitation: airway open and respiration improvement by aiding balloon machine. However, the patient not having spontaneous breath and heartbeat, clinical death was announced after a rescue of 100 min (Figure 2).

**Head CT**

![Image](http://example.com/image.jpg)

**Figure 2:** B1: infarction on the right side of cerebellum; B2: old cerebral infarction on the left side of cerebellum; B3: old lacunar infarction on the right side of pontine.

**Case 3:** Male, 65 years old, he was admitted to the hospital for "left limbs weakness and dizziness for four hours", at 5:05 a.m., on September 23, 2013. Physical examination showed that his BP was 180/100 mmHg, his mind was lethargy and he was unable to speak clearly. His left eyeball outreach was limited with left horizontal nystagmus. He had left Horner syndrome (ptosis of lidless eyelid, less impressive hyperemia of pupil aperture was 4.0 mm and light reflex was disappeared. His left frontal lines was disappeared and his left nasolabial sulcus was shallower than right side. His tongue turned to the left uncontrollably when being stretched out, and his gag reflex abated. His left upper limb strength was graded IV and his left lower limb was graded III and His left pathological sign was positive. The NIHSS was 12 points. The patient was afflicted with high blood pressure, diabetes, long-term smoking and alcohol and usually had apnoea while asleep. On the admission day, the patient's head CT showed multiple lacunar infarction on bilateral basal ganglia and Centrum Ovale with myelomalacia. His blood sugar was 11.2 mol/L. After admission for 4 h (at 10:00 a.m. the next day), he suddenly suffered left limb weakness and myobradia. At that moment, his BP was 150/100 mmHg and SPO2 was 82%. His left upper limb was graded II, and the left lower limb was graded III. His left pathological sign was positive. Head CT was immediately performed. Oxygen was immediately offered with respiratory tract being kept unobstructed. Rescue by injection of Los Behring, Nikethamide, etc. was given, and the patient was turned to Intensive Care Unit (ICU), provided with breath assistant by ventilator. Three days after the positive airway pressure ventilation, the patient became stable gradually, and turned out of ICU. At 5:13 a.m. on the sixth day, he was afflicted with shallow breathing again, with Blood Oxygen Saturation Falling (SPO2 79%) and loss of consciousness. Physical examination showed his BP was 180/100 mmHg, mild coma and his bilateral pupils were equal round and small which diameter 1.0 mm with light reflex. Intubation and ventilator were immediately offered, he was transferred to ICU again. One week after positive airway pressure ventilation, he turned stable gradually. The patient still had left hemiplegia and lost self-care ability after 2 months'-rehabilitation therapy (Table 1). Head MRI showed multiple lacunar infarction on bridge, pons, bilateral basal ganglia and Centrum Ovale which was examined in 30 days (Figure 3).

**Head MRI**

![Image](http://example.com/image2.jpg)

**Figure 3:** C1 and C2: lacunar infarction on the right lateral medulla oblongata (T2/T2 flair); C3 and C4: lacunar infarction on the right lateral medulla oblongata (T1/T1 flair); C5: lacunar infarction on the right lateral medulla oblongata (T1).

| Hypertension | Diabetes | Alcohol | Gender | Age | Sleep apnoea | Past physical | Habit | Infarction location | Apopstasis | Therapy method | Prognosis |
|-------------|----------|---------|--------|-----|-------------|--------------|-------|-------------------|-----------|---------------|----------|
| +, 250/110 mmHg | + | + | male | 67 | + | well | sloppy | Medulla/cerebellum/pons | once | No ventilator | death |
| +, 180/100 mmHg | + | + | male | 67 | + | well | sloppy | Cerebellum/pons | once | No ventilator | death |
| +, 180/90 mmHg | + | + | male | 67 | + | well | sloppy | Right lateral medulla oblongata | twice | ventilator/ICU | aggravation |

| Case 1 | Case 2 | Case 3 |
|--------|--------|--------|
| Age | 67 | 67 | 67 |
| BMI | 25.0 | 26.0 | 27.0 |
| Blood pressure | 180/100 mmHg | 180/90 mmHg | 180/90 mmHg |
| Diabetes | + | + | + |
| Alcohol | + | + | + |
| Gender | male | male | male |
| Hypertension | + | + | + |
| Sleep apnoea | + | + | + |
| Past physical | well | well | well |
| Habit | sloppy | sloppy | sloppy |
| Infarction location | Medulla/cerebellum/pons | Cerebellum/pons | Right lateral medulla oblongata |
| Apopstasis | once | once | twice |
| Therapy method | No ventilator | No ventilator | ventilator/ICU |
| Prognosis | death | death | aggravation |

**Table 1:** Clinical characteristics of the three patients.

**Discussion**

Ondine's curse (OC) syndrome is a very particular disorder of the regulating mechanism of respiratory center. At the same time, the chemical sensor in respiratory center becomes less sensitive to CO2, which leads to obstacles of alveolar gas exchange and hypercapnia and hypoxemia. There is no respiratory failure caused by primary diseases about heart, lung, respiratory muscles and so on [2]. OC syndrome, also known as congenital central hypoventilation cause of genetic, is more likely to occur to babies [3,4].

Acquired OC syndrome is often secondary to some sorts of brainstem diseases (infection, trauma, tumour, stroke, surgery, and...
During hospitalization, their Blood Oxygen Saturation had gone down sharply while sleeping, and their breath and heart slowed down or even stopped, without any clinical aura before aggravated. All the three patients have no basic respiratory diseases, their respiratory and/or cardiac arrest cannot explain by the theory of central or peripheral breathing/circulatory failure. Respiratory center is in the medulla oblongata, which consists of three groups of neurons (dorsal group of solitary nucleus, ventral group of nucleus ambiguus and medial parabrachial nucleus) (Figure 1) [1,9]. Automatic respiration is not obstructed unless the medulla and pons are severely damaged. Only very few patients suffered from CO₂ retention. All the three patients were suffered with sudden slow-downed breath and heart with sleeping, there is enough reason to support secondary OC with brainstem infarction. The main part of the automatic central res which leads to inhibition of respiratory center and stop in spontaneous breathing, during the occurrence of hypoxemia. Only this rare central respiratory inhibition was defined as the OC syndrome (Figure 4) [6,10].

All the patients were suffered from lacunar infarction on unilateral medulla oblongata/pons, however, central respiratory inhibition was still occurred. Why the apnoea occurred is due to automatic breath system (medulla oblongata/pons respiratory center) was impaired, while spontaneous breath can't effectively respond to carbon dioxide retention when patients in sleeping.

The importance of brainstem infarction area to OC syndrome is not unclear for the extremely low occurrence. Some researchers believe that both pons/medulla and oblongata infarction are more likely to cause OC otherwise only few literatures about of OC with merger bilateral infarction were reported. Head MRI/DWI was not performed with case 2, it is not sure whether the patient had a new cerebellum infarction, the other patients were suffered from bilateral cerebellar infarction, this suggests that the cerebellum may be affected breath. Most OC occur at night during sleeping, especially for acute infarction, but some OC occur at sub-acute or stabilization of infarction [11].

Two patients occurred in 24 h after admission, another occurred respectively in 4 h and 6 days after admission. It suggested OC may occur at any phase of infarction. Sugawara E [11] reported a patient occurred in the sub-acute phase. This will undoubtedly increases the treatment difficulties. Sugawara E [11] reported a patient occurred in the sub-acute phase. This will undoubtedly increases the treatment difficulties. The OC syndrome occurs without any warning, and always results in disastrous/fatal consequences; many clinical staff may know little about the disease, which leads the difficulties to prompt treatment; moreover, the disease progresses rapidly. Due to the above reasons, most patients got poor prognosis. Summary and analysis the clinical features as follows: People like male, approximately 65 years old, slovenly life, divorcement, long history of heavy smoking and alcohol, sleep apnoea, having hypertension and/or diabetes suffering from cute pons/medullary lacunar infarction, they would be more likely to suffer from OC syndrome [12,13].

It was recently recognized that pharmacological treatment seems to be invalid for OC syndrome [14]. Only few individual spontaneous recoveries have been documented [15]. Most of them need breathing machine treatment of mechanical ventilation varying in timePart of these patients who are not able to get off the machine after a long time, would be taken diaphragm pacemaker [16]. The involved parts of brainstem and the pathological performance have important impact on OC prognosis, most of them have no time to be rescued and decease in sleep [17].

The clinical data of the three patients showed that only one patient was given breathing machine for auxiliary breath in time and then restored normal breathing rhythm, which saved his life; which demonstrated breathing machine for auxiliary breathing is the preferred and necessary treatment for OC syndrome.

How can we take an effective treatment to rescue patients with OC syndrome? We thought such measures should be taken as follows: 1. To raise awareness and discuss diagnosis of OC syndrome 2. The doubted OC syndrome patients should be given continuous monitoring on sleep - breathing and blood oxygen saturation 3. If decrease of breathing or heart rate occurs, “wake up” should be timely given and mechanical ventilation for auxiliary breathing should be taken immediately 4. When breathing rhythm gets normal, mechanical ventilation should be gradually weaned [18]. For patients who are highly susceptible to OC syndrome, the highest alert should be emphasized and breathing machine should be performed immediately [19].

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