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A case of central neurogenic hyperventilation without tachypnoea

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Abstract

Central neurogenic hyperventilation (CNH) is a rare condition, with 37 cases reported in the literature to date. The underlying mechanisms remain unclear. Primary central nervous system lymphoma (PCNSL) is the most common cause of CNH, with 17 cases reported so far. Among these, CNH was usually accompanied by tachypnoea. Only two cases, including the present case, showed CNH with normal respiratory rate. Here, we present a case of PCNSL-induced CNH in a 60-year-old man. Magnetic resonance imaging of the brain demonstrated hyperintensity of the left cerebral cortex, basal ganglia, corona radiata, midbrain, and ventral pons on fluid-attenuated inversion recovery. The patient complained of dyspnoea and showed hyperventilation without tachypnoea on admission or during hospitalization. Examining CNH cases without tachypnoea and comparing those cases to cases of CNH with tachypnoea might provide new insights into the mechanisms of CNH. Moreover, it should be remembered that CNH can occur without tachypnoea.

Introduction

Central neurogenic hyperventilation (CNH) is defined as hyperventilation caused by a central nervous disorder [1]. This pathology usually consists of deep, rapid breathing at a rate of at least 25 breaths/min. Only 37 cases of this rare condition have been reported since the first description was given by Plum and Sweanson in 1959 [1]. Most reported cases were associated with infiltrative lymphoma of the brainstem, but the mechanisms underlying CNH remain unclear. Seventeen cases of primary central nervous system lymphoma (PCNSL)-induced CNH have been reported to date, and cases showing a normal respiratory rate have been extremely rare among these. Here, we describe a case of PCNSL-induced CNH without tachypnoea. Comparing CNH cases without tachypnoea to CNH with tachypnoea might yield new insights into the mechanisms of CNH.

Case Report

A 60-year-old human immunodeficiency virus-negative man was admitted to our hospital with a 4-day history of dyspnoea, appetite loss, and night sweats. He reported a history of blurred vision in both eyes for over 2 months before admission. He did not have any relevant medical history. Although his Glasgow Coma Scale score was 15, his conversation was slow and slightly constrained. Vital signs were normal, including regular breathing at a rate of 20 breaths/min. Respiratory sounds on auscultation were normal. Arterial blood gas (ABG) analysis in room air showed marked respiratory alkalosis (pH 7.62, $PaCO_2$ 10.3 mmHg, PaO_2 130.8 mmHg, bicarbonate 10.4 mEq/L). Computed tomography (CT) of the chest showed patchy, upper lobe-predominant, ground-glass opacities in the periphery of both lungs and excluded pulmonary embolism (Fig. 1A). Blood tests showed inflammation and liver dysfunction: white blood cell count, 10,300/μL; aspartate aminotransferase (AST), 164 IU/L; alanine aminotransferase (ALT), 291 IU/L; lactate dehydrogenase (LDH), 381 IU/L; alkaline phosphatase (ALP), 681 IU/L; gamma glutamyl transferase (γ-GTP), 489 IU/L; C-reactive protein (CRP), 17.2 mg/dL; and soluble interleukin-2 receptor 430 U/mL. Results for

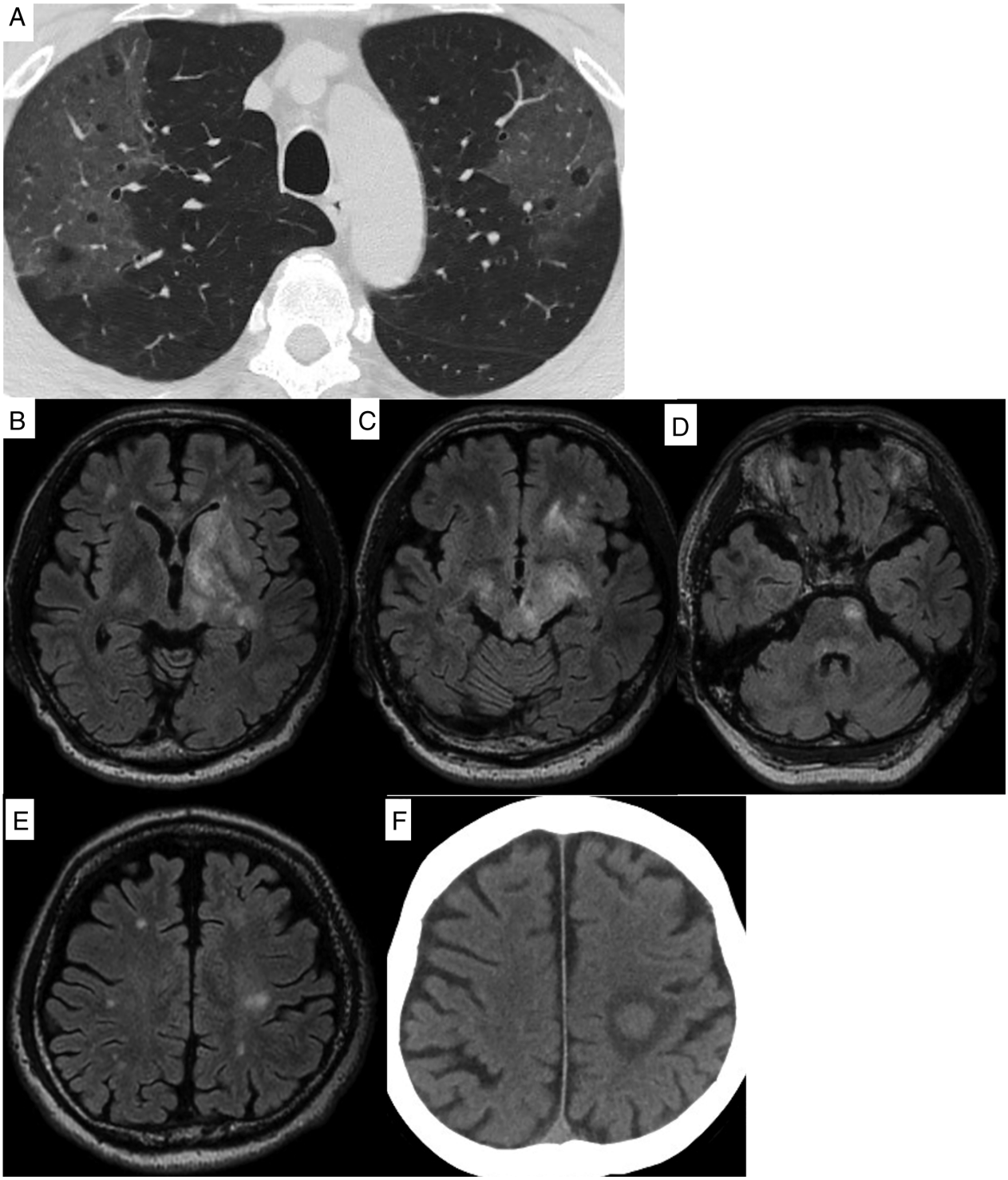

Figure 1. (A) Patchy, upper lobe-predominant, ground-glass opacities in the periphery of both lungs from thoracic computed tomography on admission. (B–D) Brain magnetic resonance imaging in hospital day 3 shows hyperintensity of the left cerebral cortex, basal ganglia, corona radiata, midbrain, and ventral pons on fluid-attenuated inversion recovery. (E) Tumour-like lesion in the left frontal lobe on the brain MRI of day 3 (F) and day 31.

markers of renal and thyroid function from blood tests were normal. Levels of serum prolactin, lactate, and ammonia were within the normal ranges. Urine ketone testing yielded negative results. The results of electro- and echocardiograms were also normal. The provisional diagnosis was atypical pneumonia, and intravenous levofloxacin was started at 500 mg/day. Pneumonia improved day by day, but dyspnoea and respiratory alkalosis without tachypnoea persisted (day 3: pH 7.59, $PaCO_2$ 14.8 mmHg, PaO_2 136.7 mmHg, bicarbonate 13.9 mEq/L). The patient underwent brain magnetic resonance imaging (MRI) on hospital day 3 for further investigation, demonstrating hyperintensity of the left cerebral cortex, basal ganglia, corona radiata, midbrain, and ventral pons on fluid-attenuated inversion recovery (FLAIR) images (Fig. 1B–D). We therefore diagnosed CNH. The results of cerebrospinal fluid cytology (CSF) collected on day 4 were as follows: opening pressure 9 cm H_2O, glucose 65 mg/dL (plasma glucose 102 mg/dL), protein 57 mg/dL, and 1 mononuclear cell/μL. CSF cytology was negative. As the mycoplasma antibody titre was positive at 1:160 according to a particle agglutination assay, we made a presumptive diagnosis of acute disseminated encephalomyelitis associated with mycoplasma pneumonia. Intravenous methylprednisolone pulse therapy (1000 mg/day for 3 days) was administered from day 6, 12, and 24, but this

Table 1. Cases of central neurogenic hyperventilation caused by primary central nervous system lymphoma.

Author	Sex/age	Respiratory rate	pH	$PaCO_2$ mmHg	HCO_3^- mmHg	Area of involvement
Lange and Laszlo [6]	Male/51	32	7.58	12	19	Midbrain, pons (diffuse), meninges, occipital lobes
Tinaztepe et al. [7]	Male/7	42–62	7.52	8.62	8.6	Pons, nucleus caudatus, thalamus, cerebral peducles
Sunderrajan and Passamonte [8]	Male/41	26	7.62	7	12	Cerebral hemispheres
Bateman et al. [9]	Male/62	26	7.61	12	12	Temporal lobes, right frontal lobe, right internal capsule
Pauzner et al. [10]	Female/61	36–50	7.66	8	NS	Copus callosum, parietal regions
Sugama et al. [11]	Female/58	25–30	7.603	10.5	10.4	Brain stem (diffuse), cerebral cortex, cerebellum, thalamus, basal ganglia
Krendel et al. [12]	Female/52	30	7.63	9	NS	Leptomeninges, frontal lobes, left cortex, left striatum
Karp and Nahum [13]	Male/57	40	7.53	15	12.1	Meninges
Shibata et al. [14]	Female/72	Fast, deep	7.613	17.4	NS	Pons (diffuse), paraventricular hypothalamic nucleus, corpus callosum
Chang [4]	Female/40	35	7.65	9.7	11.1	Leptomeninges, left temporal lobe
Sakamoto et al. [15]	Male/72	30	7.58	16.7	15.3	Pons (diffuse), medulla
Shams et al. [16]	Male/54	23	7.58	16.8	16	Pons (dorsal), thalamus, internal capsule, corona radiata
Tarulli et al. [17]	Male/87	>25	7.6	14	NS	Midbrain (dorsal), right frontal lobe, left cerebellar hemisphere and penduncle
Adachi [3]	Female/51	16–20	7.64	6.7	NS	Leptomeninges
Enam and Ali [18]	Male/47	47	7.54	30.2	16	Midbrain (diffuse), medulla, left cerebellar peduncle
Yasunami et al. [19]	Male/68	28–32	7.564	11.4	10.4	Midbrain, pons (diffuse), right cerebellar peduncle, cerebellar hemisphere, thalamus, hypothalamus
Pantelyat [5]	Male/69	25–35	7.63	9	9.5	Midbrain, pons (dorsal), bilateral cerebral hemispheres, thalami
Present case (2019)	Male/60	20	7.62	10.3	10.4	Midbrain, pons (ventral), left cerebral cortex, basal ganglia, corona radiata

therapy was only partially effective. At the same time, a tumour-like lesion in the left frontal lobe became larger during therapy and appeared quite obvious on his MRI of day 31 (Fig. 1E,F); he underwent stereotactic brain biopsy on day 35, which demonstrated diffuse large B-cell lymphoma. CT of the trunk showed no evidence of systemic spread, and PCNSL was finally diagnosed.

Discussion

Hyperventilation is defined as increased airflow into the lung alveoli, eliminating more carbon dioxide than is produced, and is usually accompanied by tachypnoea. Several conditions stimulate the inspiratory centre (dorsal respiratory group (DRG)) and cause hyperventilation, such as hypoxia, metabolic acidosis, increased metabolic demands (fever, hyperthyroidism), salicylic acid use, pregnancy, or hyperventilation syndrome triggered by emotional upset [2]. We ruled out each of those conditions. Because a series of his ABG analysis showed extreme respiratory alkalosis, we examined brain MRI and diagnosed CNH. To date, 37 cases of CNH have been reported in the literature. PCNSL is the most common cause of CNH, and 17 cases of PCNSL-induced CNH have been reported so far (Table 1). However, only the present case and one other case presented by Adachi showed a normal respiratory rate [3]. In the case related by Adachi, brain MRI did not show any lesions suggesting infiltration of lymphoma, but CSF showed positive results. Our case showed negative CSF cytology but lymphomatous lesions in the ventral pons and midbrain on MRI, whereas most other cases of CNH with tachypnoea also show lymphoma in the dorsal pons, medulla, or meningeal space. We presume that lymphomatous meningitis and diffuse infiltration of lymphoma including the dorsal pons are possible causative factors for CNH with tachypnoea. Administration of morphine at 10–20 mg/day has been reported to reduce tachypnoea in several cases of CNH, except for cases of lymphomatous meningitis [4]. The underlying pathophysiological mechanisms of CNH have been suggested to involve direct infiltration of the respiratory control centres of the brainstem or stimulation of these centres by inflammatory cytokines secreted from neighbouring tumour tissues but are not yet fully understood [5]. Additional work to gain more understanding and insights into the mechanisms of CNH is needed by studying more cases of CNH with or without tachypnoea and by comparing those MRI images, CSF results, and possibly biopsy of the brain tissues. First and foremost, clinicians should keep in mind that some cases of CNH do not show tachypnoea.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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