Eur J Pediatr (1987) 146:81–83

Congenital central alveolar hypoventilation (Ondine's curse): a case report and review of the literature

F. Yasuma, H. Nomura, I. Sotobata, H. Ishihara, H. Saito, K. Yasuura, H. Okamoto, S. Hirose, T. Abe, and A. Seki

First Department of Internal Medicine and Department of Thoracic Surgery, Nagoya University School of Medicine, Tsurumai-cho 65, Showa-ku, Nagoya, 466, Japan

Abstract. Congenital central alveolar hypoventilation (C-CAH), so called Ondine's curse, is known to be quite a rare neuropathology that has been reported in only 23 cases to date. C-CAH was diagnosed in a 2-year-5-month-old infant. In the treatment of C-CAH, we implanted a right unilateral diaphragm pacemaker in the infant and his respiratory status was remarkably improved after diaphragm pacing. Twenty-three reported cases of this disorder are reviewed in the literature.

Key words: Congenital central alveolar hypoventilation – Ondine's curse – Diaphragm pacing

Introduction

Congenital central alveolar hypoventilation (C-CAH), so called Ondine's curse [15], is known to be quite a rare neuropathology caused presumably by congenital failure of the central automatic respiratory system. To the best of our knowledge, only 23 cases have been reported to date. We encountered this syndrome in a 2-year-5-month-old infant. Diagnosis, treatment, complication and prognosis of C-CAH are discussed.

Case report

The patient was a male infant born by a 25-year-old healthy mother after a normal course of pregnancy in the 38th week of gestation. Intermittent cyanosis was observed during his early weeks of life. On the 7th day after birth, he showed the first convulsive attack due to hypoventilation, which was managed by endotracheal intubation and intermittent positive pressure ventilation (IPPV).

At the 5th month of age, he was able to breathe without ventilatory assistance when awake. He was, therefore, maintained under IPPV only during sleep. Drug treatment with Methylphenidate, Dimefline and Hopantate was attempted to stimulate his ventilation, but they were all ineffective. The results of a series of electroencephalograms, chest X-ray films and CT-scans of the brain were normal. The existence of congenital cardiac and metabolic diseases was ruled out. On polygraphic recording and simultaneous arterial blood gas analysis during his sleep state, apnoea over 40 s, progressive respiratory acidosis and hypercapnoea were recognized (Fig. 1). However, these respiratory abnormalities were normalized immediately after the initiation of IPPV. Ventilatory responses to hypercapnoea during non-REM sleep were assessed by the steady state method [3], and there was obviously no increase in ventilation. C-CAH was diagnosed on the basis of the criteria proposed by Deonna et al. [4], and diaphragm pacing (DP) was indicated for the infant.

At the 29th month of age, a right unilateral diaphragm pacemaker implantation was performed (Avery Labo. Inc., Farmingdale, NY 11735, USA) [6]. A pacing electrode was attached to the intrathoracic part of the right phrenic nerve through the third intercostal space. A receiver was implanted in the subcutaneous pocket made on the wall of his abdomen. After the installation of over-night DP therapy, upper airway obstruction was manifested, therefore, tracheostomy was performed [7]. Paradoxical movement of the left hemidiaphragm under pacing was not observed on the fluoroscopy. The initial pacing parameters of the pacemaker were as follows. The tidal volume was set at 120 ml/breath, the frequency at 14/min, and the threshold at 2.2 mA. DP was effective in keeping the arterial blood gas within the normal range during his sleep state, and IPPV was no longer required.

After a 2-year follow-up, his respiratory status was satisfactory with over-night DP at home.

Discussion

The 23 cases of previously reported C-CAH are summarized in Table 1, which includes sex, complication, DP therapy and outcome.

The 19 sex-identified cases in the literature consist of 13 boys and 6 girls.

As for the complications of C-CAH, the occurrence of Hirschsprung's disease or ganglioneuroblastoma in 6 of the 19 C-CAH cases (31.5%) suggests the possibility that these three disease entities represent common primary defects of brain stem cells and ganglion cells in the gastro-intestinal plexus, both of which have a common embryologic origin [8, 17].

The prognosis of C-CAH is usually poor. Eleven of the 23 cases died of cor pulmonale due to chronic hypoxia, heart failure or secondary infection to C-CAH. The age of death in ten specified cases was 9.9 ± 6.4 months (mean ± standard deviation).

Since pharmacological treatment is known usually to be ineffective, artificial ventilation is required, which is generally achieved by IPPV using a mechanical ventilator or by DP. DP is a method that affords artificial negative pressure ventilation induced by the regular contraction of the diaphragm with electrical stimulation to the phrenic nerve. The greatest advantage of DP, as demonstrated in our case, is that, under optimal functioning of DP, a mechanical ventilator for respiratory control can be released, substantially contributing to improvement of the quality of life and return to social activities.

With the advancement of neonatal respiratory therapy, it is predicted that C-CAH cases will increase in number and it is thought that DP will gain more therapeutic significance.

Offprint requests to: F. Yasuma

Abbreviations: C-CAH = congenital central alveolar hypoventilation; IPPV = intermittent positive pressure ventilation; DP = diaphragm pacing

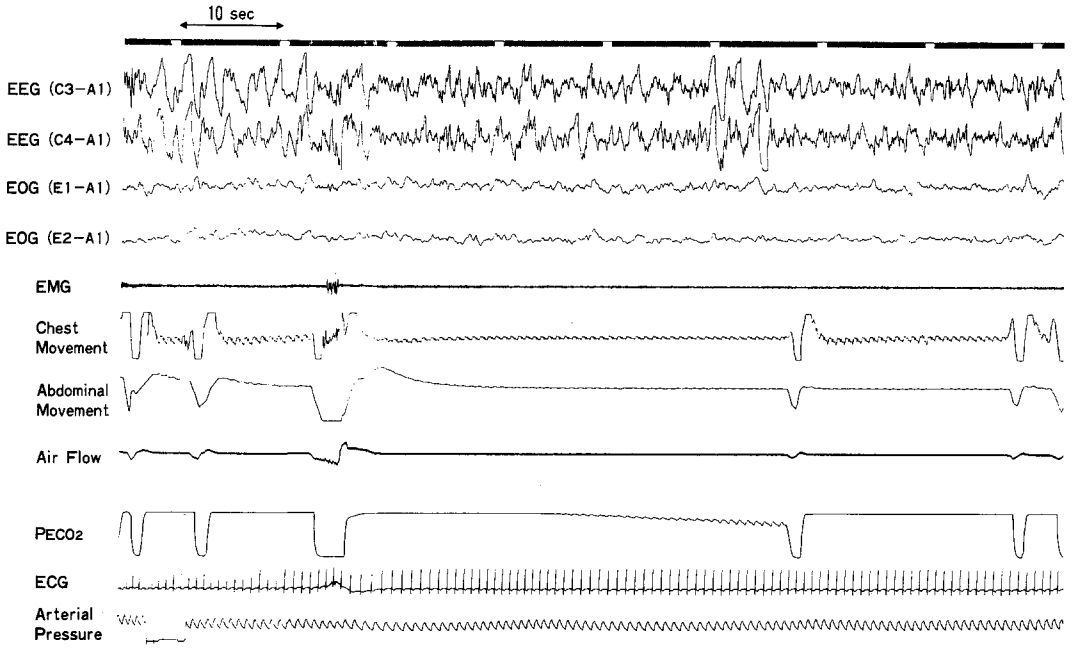

Fig. 1. Polygraphic records during non-REM sleep. *EEG,* electroencephalogram; *EOG,* electrooculogram; *EMG,* electromyogram of mentalis muscle; *Air Flow,* airflow from the endotracheal tube; *$PECO_2$,* PCO_2 of expiratory gas; *ECG,* electrocardiogram

Table 1. Outlines of congenital central alveolar hypoventilation in 23 cases

No.	Author	Sex	Complication	Diaphragm pacing (DP)	Outcome	Literature
1.	Mellins RB	M	None	DP (11 mo.)	Died, Cor pulmonale at 14 mo.	[14]
2.	Lonsdale D	M	None		Alive, Spontaneous recovery at 12 mo.	[12]
3.	Deonna T	M	LD[a]		Alive, Spontaneous recovery at 21 mo.	[4]
4.	Shannon DC	F	None		Alive, IPPV when asleep	[16]
5.	Shannon DC	M	None		Died, Septicemia at 6 mo.	[16]
6.	Haddad GG	F	HD[b]		Died at 2 mo. (cause unknown)	[8]
7.	Haddad GG	F	HD		Died, Pneumonia at 5 mo.	[8]
8.	Haddad GG	F	HD and GNB[c]		Died at 2 mo. (cause unknown)	[8]
9.	Liu HM	M	None	DP (5 mo.)	Died, Respiratory failure at 8 mo.	[11]
10.	Hunt CE	F	GNB	DP (7 mo.)	Died, Cor pulmonale and pneumonia at 17 mo.	[9]
11.	Hunt CE	M	None	DP (9 mo.)	Alive, DP when asleep	[9]
12.	Bower RJ	M	HD and GNB		Died, Heart failure at 9 mo.	[1]
13.	Stern M	M	HD		Died, Heart failure and dehydration at 15 mo.	[17]
14.	Flemming PJ	F	None		Alive, IPPV when asleep	[5]
15.	Wells HH	M	None		Alive, IPPV when asleep	[18]
16.	Ilbawi MN	M	Unknown	DP (unknown)	Died, *E. coli* meningitis (age unknown)	[10]
17.	Ilbawi MN	M	Unknown	DP (unknown)	Alive, DP when awake, IPPV when asleep	[10]
18.	Ilbawi MN	?	Unknown	DP (unknown)	Alive, DP when asleep	[10]
19.	Meisner H	M	None	DP (6 mo.)	Alive, DP when asleep	[13]
20.	Brouillette RT	?	Congenital lubella	DP (9 mo.)	Died, DP failure at 21 mo.	[2]
21.	Brouillette RT	?	None	DP (9 mo.)	Alive, DP when asleep	[2]
22.	Brouillette RT	?	None	DP (15 mo.)	Alive, DP when awake, IPPV when asleep	[2]
23.	Yasuma F	M	None	DP (29 mo.)	Alive, DP when asleep	Present case

[a] Leigh disease
[b] Hirschsprung's disease
[c] Ganglioneuroblastoma

Conclusion

C-CAH was diagnosed in a 2-year-5-month-old infant. DP was performed with success. Twenty-three previously reported cases are reviewed.

References

1. Bower RJ, Adkins JC (1980) Ondine's curse and neurocristopathy. Clin Pediatr 19:665–668
2. Brouillette RT, Ilbawi MN, Hunt CE (1983) Phrenic nerve pacing in infants and children: a review of experience and report on the usefulness of phrenic nerve stimulation studies. J Pediatr 102:32–39
3. Cherniack NS, Dempsey J, Fencl V, Fitzgerald RS, Lourenso RV, Rebuck AS, Rigg J, Severinghaus JW, Weil JW, Whitelaw WA, Zwilich CW (1977) Work-

shop on assessment of respiratory control in humans. 1. Methods of measurement of ventilatory responses to hypoxia and hypercapnia. Am Rev Respir Dis 115: 177–181
4. Deonna T, Arczynska W, Torrado A (1974) Congenital failure of automatic ventilation (Ondine's curse). J Pediatr 84:710–714
5. Flemming PJ, Cade D, Bryan MH, Bryan AC (1980) Congenital central hypoventilation and sleep state. Pediatrics 66:425–431
6. Glenn WWL (1978) Diaphragm pacing: present status. PACE 1:357–370
7. Glenn WWL, Gee JBL, Cole DR, Farmer WC, Shaw RK, Beckman CB (1978) Combined central alveolar hypoventilation and upper airway obstruction: treatment by tracheostomy and diaphragm pacing. Am J Med 64:50–60
8. Haddad GG, Mazza NM, Defendini R, Blanc WA, Driscoll JM, Epstein MAF, Epstein RA, Mellins RB (1978) Congenital failure of automatic control of ventilation: gastrointestinal motility and heart rate. Medicine 57:517–526
9. Hunt CE, Matalon SV, Thompson TR, Demuth S, Loew JM, Liu HM, Mastri A, Burke B (1978) Central hypoventilation syndrome – experience with bilateral phrenic nerve pacing in 3 neonates. Am Rev Respir Dis 118:23–28
10. Ilbawi MN, Hunt CE, Deleon SY, Idriss FS (1981) Diaphragm pacing in infants and children: report of a simplified technique and review of experience. Ann Thorac Surg 31:61–65
11. Liu HM, Loew JM, Hunt CE (1978) Congenital central hypoventilation syndrome: a pathologic study of the neuromuscular system. Neurology 28:1013–1019
12. Lonsdale D, Merger RD (1972) Primary hypoventilation syndrome. Lancet 1:487
13. Meisner H, Schober JG, Struck E, Lipowski B, Mayser P, Sebening F (1983) Phrenic nerve pacing for the treatment of central hypoventilation syndrome – state of the art and case report. Thorac Cardiovasc Surg 31:21–25
14. Mellins RB, Balfour HH, Turino GM, Winters RW (1970) Failure of automatic control of ventilation (Ondine's curse). Medicine 49:487–504
15. Severinghaus JW, Mitchell RA (1962) Ondine's curse: failure of respiratory center automaticity while awake. Clin Res 10:122
16. Shannon DC, Marsland DW, Gould JB, Callahan B, Tordes ID, Dennis J (1976) Central hypoventilation during quiet sleep in two infants. Pediatrics 57:342–346
17. Stern M, Erttmann R, Hellwege HH, Kuhn N (1980) Total aganglionosis of the colon and Ondine's curse. Lancet 1:877–878
18. Wells HH, Kattwinkel J, Morrow JD (1980) Control of ventilation in Ondine's curse. J Pediatr 96:865–867

Received September 13, 1984 / Accepted May 12, 1986

Eur J Pediatr (1987) 146:83–85

Haemorrhagic shock-encephalopathy syndrome: plasmapheresis as a therapeutic approach

B. Roth[1], A. Younossi-Hartenstein[1], R. Schröder[2], H. Hörnchen[3], and L. Heymans[2]

[1]Children's Hospital, University of Cologne, [2]Department of Pathology, University of Cologne, and [3]Department of Pediatrics, Medical Faculty, RWTH Aachen, Federal Republic of Germany

Abstract. We present the case of a 4.5-week-old boy with acute encephalopathy, shock, intestinal bleeding and disseminated intravascular coagulation. The clinical course and typical laboratory parameters were compatible with a diagnosis of haemorrhagic shock-encephalopathy syndrome (HSE). Immediate shock treatment, repeated haemodialysis and plasmapheresis did not prevent a fatal outcome 4 days after the onset of clinical symptoms.

Key words: Shock – Encephalopathy – Diffuse intravascular coagulation – Renal failure – Hepatic failure

Offprint requests to: B. Roth, Universitätskinderklinik, D-5000 Köln 41, Federal Republic of Germany

Abbreviations: HSE = haemorrhagic shock-encephalopathy syndrome; HUS = haemolytic uraemic syndrome

Introduction

Since 1983 patients with a hitherto unknown combination of haemorrhagic shock and encephalopathy have been described (HSE; [8]). The encephalopathy manifests itself acutely with an altered state of consciousness, convulsions, hyperthermia, haemorrhagia, intravascular coagulation, renal failure and hepatic failure. The disorder affects predominantly children between 3 and 8 months old [1, 4, 6, 8, 12]. The clinical course was fatal in the large majority of cases; survivors always suffered from severe neurological damage.

The aetiology and pathogenesis are unknown, but hyperthermia following overwrapping [1], septicaemia caused by a yet undetected viral agent [8], and bacterial endotoxin shock [11] have been incriminated as causal factors.

Only unspecific and supportive therapeutic measures are available.

We present the case of a 5-week-old German boy with HSE and we discuss a diagnostic and therapeutic approach which included plasmapheresis with fresh frozen plasma.

Case report

This boy (KK-1411-83) was the first child born to unrelated healthy parents. After an uneventful gestation the infant was delivered by forceps 10 days after term after imminent intra-uterine asphyxia with a birth weight of 2960 g, a length of 50 cm, and an Apgar score of 7/9/10. Development throughout the first 4 weeks was normal until at 4.5 weeks watery, non-bloody stools occurred. One day later the child became unresponsive, refused fluids and breathed irregularly. There was no vomiting. The patient's body temperature was not measured prior to hospitalisation. On admission to hospital he weighed 4.1 kg and was in a severe cardiovascular shock. His blood pressure was 60/30 mm Hg, his heart rate 140/min, the body temperature 36.8°C. Massive haemorrhagic stools occurred. Investigations showed a metabolic acidosis (pH 7.24, pCO_2 37 mm Hg, base deficit 14.4 mval/l), hyperkaliaemia (6.3 mval/l), and a leukocytosis (27900/