CHRONIC CENTRAL ALVEOLAR HYPOVENTILATION

By Poh Soo Chuan, M.B., B.S., M.R.C.P.E., D.T.C.D.
(Tan Tock Seng Hospital, Singapore)

INTRODUCTION

Alveolar hypoventilation occurring in the presence of normal lung is usually the result of failure of the respiratory neuroregulatory mechanism from overdosage with narcotic drugs and cerebral depressants or from neuromuscular disorders affecting the chest bellows. Occasionally, alveolar hypoventilation is associated with extreme obesity. The syndrome of chronic alveolar hypoventilation occurring in patients with normal lungs and chest bellows is considered a rarity. First described as a clinical entity by Richter *et al* in 1957 (19) the syndrome was reviewed by Seriff in 1965 (22) who added 3 cases to the 12 published ones.

The object of this report is to describe a further case of this syndrome and to review the 27 cases previously reported in the world literature (1-10, 13-26).

CASE REPORT

P.O.Y. a 47 year old Eurasian man was first admitted to another hospital in September 1967 with a history of cough, productive of some yellowish sputum of one month's duration. Clinical examination showed he was 'flushed', blood pressure was 170/100 mm. Hg. and except for some crepitations at the lung bases and a triple rhythm, no other significant abnormality was detected. A chest roentgenogram revealed a slightly enlarged heart. His haemoglobin was 21.9 gm. per cent, the total white and platelet counts were normal. Haematocrit was 78 per cent. Blood urea was 31 mg. per 100 ml. and the serum uric acid 4.8 mg. per 100 ml. The bone marrow examination showed a normoblastic erythropoiesis. An intravenous pyelogram did not reveal any abnormality. He was treated as a case of polycythemia with early cardiac failure.

Since November 1967 he has had regular venesections and has remained well and at work.

In August 1968 he was referred to the Tan Tock Seng Hospital for further investigations. There was no past history of note. He denied any dyspnoea on exertion. He had previously smoked 40 cigarettes/day for the past 25 years but had reduced to 20 a day since his admission to hospital in September 1967. Physical examination revealed a plethoric slightly cyanosed man. His height was 5′ 11½″ and his weight 160 lbs. His blood pressure was 140/90 mm. Hg. No other abnormality was found in the rest of the clinical examination. The chest roentgenogram showed a slightly enlarged heart with normal lung fields (Fig. 1). The electrocardiogram was normal. His haemoglobin was 17.4 gm. per cent and hematocrit 56 per cent. Pulmonary function tests were carried out and the results are presented in Table I. The lung volumes and tests of ventilatory capacity and diffusing capacity are normal. Blood gas analysis revealed hypoxemia, hypercapnoea and respiratory acidosis. The findings suggested chronic alveolar hypoventilation of central origin. Confirmation of the diagnosis was obtained when with voluntary hyperventilation, the arterial oxygen tension (PO_2) and carbon dioxide tension (PCO_2) returned to normal levels. The ventilatory response to carbon dioxide inhalation was

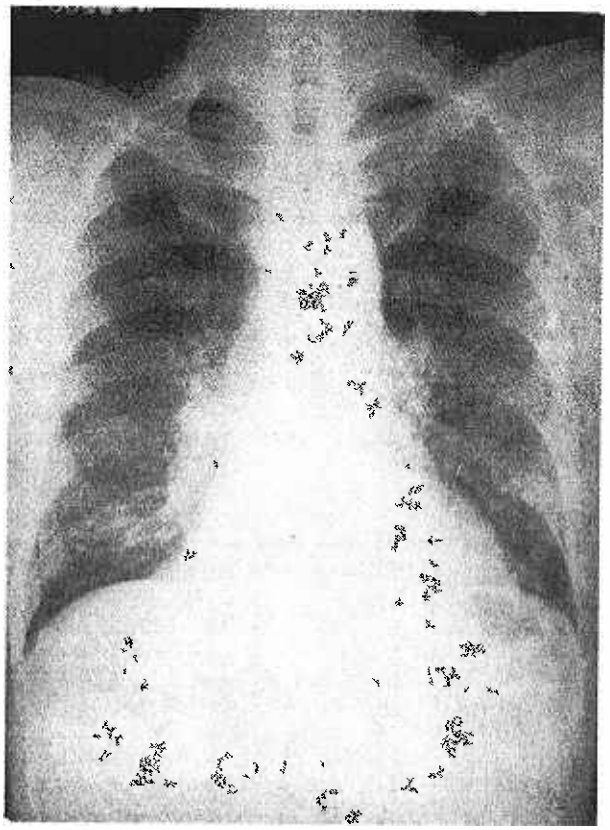

Fig. 1. Chest roentgenogram showing a slightly enlarged heart and normal lung fields.

TABLE I

PULMONARY FUNCTION STUDIES

Function Tests	Observed	Predicted	Percent of Predicted
Vital Capacity (litres)	3.94	4.68	84
Functional Residual Capacity (litres)	3.09	3.99	78
Residual Volume (litres)	2.27	2.32	100
Total Lung Capacity (litres)	6.21	7.00	89
Mixing Efficiency (percentage)	51	55	93
Maximal Mid-Expiratory Flow Rate (litres/sec.)	3.6	3.6	100
Forced Expiratory Volume 0.75 sec. × 40 (litres/min.)	117	114	100
Diffusing Capacity (ml./min./mm.Hg.) for CO	17.2	17.0	100

TABLE II

BLOOD GAS VALUES AND MINUTE VENTILATION

Date		pH	PCO_2 (mm. Hg.)	O_2 Saturation (%)	Ve L/min. (BTPS)
12.8.68					
Room air:	Rest	7.37	56	91	
2.9.68					
Room air:	Rest	7.36	58	89	
	Hyperventilation	7.55	30	98	
16.9.68					
Rest:	100% Oxygen	7.35	58		6.87
	4.1% CO_2 in Oxygen	7.30	66		7.85
Room air:	Rest		56		
	Ethamivan (50 mg. intravenously)		55		
23.11.68					
Room air:	Rest		56		
	Exercise (400 Kg. M/min. for 6 mins.)	7.38	49	93	

studied and showed a minimal increase in ventilation. An intravenous injection of a respiratory stimulant (Ethamivan 50 mg. over 3 mins.) failed to elicit a ventilatory response, whilst exercise (400 kgm./min. for 6 minutes) resulted in a fall of the PCO_2 (Table II). The patient was subsequently given a trial of a long acting progesterone (500 mg. Prolution intramuscularly once a week) for a period of three months, but did not show any improvement of his blood gases.

DISCUSSION

Reports of cases of chronic central alveolar hypoventilation show that these patients usually present with different clinical pictures. The majority of patients are men and the diagnosis is normally made in the third and fourth decades. Chronic cyanosis, episodic somnolence, symptoms of headache and weakness, or oedema is usually the dominant presenting symptom. Although the clinical picture varies, physiologically these patients are quite similar. There is chronic hypoxemia and hypercapnoea with varying degrees of respiratory acidosis. Secondary polycythemia is almost invariably present. The diagnosis is usually first made when following the finding of alveolar hypoventilation normal respiratory function tests are found.

The findings of the cases previously reported are summarised in Table III. The normal response to carbon dioxide inhalation is a marked increase in ventilation. This increase is variable ranging from a 1.8 to 3.7 fold increase in minute ventilation with 5% carbon dioxide (11). Most of the patients with chronic central alveolar hypoventilation, including the present case, have an absent or diminished response to inhaled carbon dioxide, as can be seen in Table III. Voluntary hyperventilation causes a return to normal of the blood gas values and this lends support for the disorder having its origin centrally in a malfunctioning respiratory centre. Control of breathing has been further studied in some of these patients by testing the function of the peripheral chemoreceptors to hypoxia and has been found to be normal in the majority of cases studied. Inhalation of low oxygen mixtures have been shown to cause an increase in ventilation (7, 9, 22), whilst inhalation of oxygen produced a fall in minute ventilation (22, 17, 23, 7, 26, 9, 24). The ventilatory adaptation to muscular exercise has been found to be variable, some cases, as the present one, showing a fall in the PCO_2 (16, 22), whilst others the PCO_2 has remained the same (23, 7, 2, 24) or showed a rise (19, 22, 20). It thus appears that in this syndrome the chemical control of breathing is impaired only by loss or diminution of sensitivity of the central chemoreceptors to carbon dioxide. Furthermore a normal reflex response to a threshold load to inspiration has been demonstrated by Oliva *et al* (15), indicating the presence of normal proprioceptive system for the regulation of tidal volume.

Most of the cases published have a previous history of encephalitis or meningitis, or show clinical evidence of disease of the central nervous system. In about 40 per cent of the cases, including the present case, no neurological disorder was present (19, 17, 18, 23, 13, 1, 6, 14, 5, 26), the chronic central alveolar hypoventilation being an isolated finding.

Necropsy studies have shown a conflicting picture. Seriff's two patients were noted to have an increased number of capillaries with plump endothelial cells in the respiratory centre areas with only a questionable loss of neurons (22). On the other hand, others have reported no recognisable abnormalities (13, 16), non-specific alterations (5) and widespread loss of neurons (14). There appears to be no relationship between the presence of neurological disease and the severity of the physiological defect.

Therapy in this disorder has been disappointing. Central nervous system stimulants, acetozolamide, hypnosis, pacemaker electrodes implanted around the phrenic nerves and mechanical respirators have so far failed to produce satisfactory long term results. Progesterone therapy have been reported to be effective in improving the ventilation of patients with the obesity-hypoventilation syndrome (12). A trial of progesterone therapy in this patient, however, failed to produce a satisfactory ventilatory response. Only one case of this syndrome has been reported of clinical recovery. This occurred despite the continued absence of a ventilatory response to carbon dioxide inhalation. It was not possible to attribute improvement to any specific therapy other than the patient's determination "never to be hospitalised again and to help himself by deep breathing" (15).

SUMMARY

A further case of a patient with chronic central alveolar hypoventilation without any associated evidence of central nervous system disorder is described, together with a brief review of the world literature.

TABLE III

DATA ON CASES OF CHRONIC CENTRAL ALVEOLAR HYPOVENTILATION

Case No.	Ref. No.	Age (yrs.)	Sex	VC % normal	TLC % normal	RV/ TLC %	MBC % normal	Hct. %	Art. O_2 Saturation %			Art. PCO_2 (mm. Hg.)			Ve L/min.	
									Rest	Hyper-ventil-ation	Exer-cise	Rest	Hyper-ventil-ation	Exer-cise	Rest	5% CO_2
1	19	37	M	80	96	35	100	54	68	100	56	64	50	79	4.9	4.8
2	22	27	M	64	60	23		64	90		82	58		incr.	7.7	7.8
3	22	42	F	120	137	32		62	87	91	83	60	29	50	4.7	5.8
4	22	38	F	73	76	22		71	86		74	66			5.6	6.5
5	18	63	M	100	100	32	194L/min.	64	74	99	58	75			8-12	14-21 (7.5%)
6	17	35	M	120	119	22	105	68	86	100		58	34		1.24/M2	2.3/M2
7	23	36	F	63			80	64	77	93	86	54	47	53	6.4	20 (7.5%)
8	3	50	F	102	96		90	54	91	94		72	48			No. inc. with 7% CO_2
9	7	45	M	3.5L	4.8L	27	106L/min.	52	86	99		67	29	65	5.8	5.7 (6%)
10	25	27	F													
11	20	62	M	88	90	42	85	61	73	92	60	70	58	75	5.7	14.8
12	10	38	M	90	100	35		68	68			73				
13	13	35	M	95	91	21	108	66	87	97	76	67			3.3/M2	
14	8															
15	6															
16	1	54	M	79	81		67	51	81	96		81	71		5.7	8.7 (7.5%)
17	14	38	M					52								
18	21	41	M	66	79		103	75	77	97		54			4.0/M2	4.0/M2
19	21	39	M	79	95		70	56	84	94		36			5.0/M2	7.5/M2
20	21	27	M	80			88		96			43			4.0/M2	7.0/M2
21	2	43	M	nil.	nil.	26		53	86	90	89	63	35	65	5.9	7.8
22	5	44	M	63				64	52-60	98	60					
23	4	3½	M													
24	26	42	M	104			105	56	86	97					4.0	10
25	9	49	M	79	75	31	88	62	77	97		61	40			
26	16	42	M	89	85	26	78	61	80		79	86	39	54		No inc. with 15% CO_2
27	24	62	M	76	74	31	62	48	89	96	92	63	43	63		
Present case		47	M	84	89	36	100	56	89	98	93	56	30	49	6.9	7.9

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