

Chronic Mountain Sickness—Phobrang Type

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Abstract. Clinical features of 27 cases of Chronic Mountain Sickness (CMS) from the Himalayas are reported. They are compared with 75 native highlanders (NH). All CMS patients were immigrants to high altitude. Mean duration of stay at high altitude was seven years. Mean values for haematocrit and haemoglobin were 80% and 23 G% respectively for the CMS group and 40% and 17.9 G% respectively for the native highlanders group. Mean QRS axis in the former was $+110^\circ$ and in the latter $+76^\circ$. Incidence and quantum of proteinuria were significantly higher in the CMS group. Cardiac catheterisation studies done in eight CMS cases showed elevated Pulmonary Artery (PA) pressures even after a mean of 14.2 days at sea level. The disease which has four diagnostic elements—hypoxemia and polycythemia, pulmonary hypertension, right ventricular enlargement and nephropathy with dense proteinuria—is a variant of 'Monge's Disease' and a name CMS Phobrang Type is suggested, along with a new approach to clinical classification which may help in diagnosis before cor pulmonale sets in. Limited therapeutic trials conducted at high altitude seem to indicate that yogic deep breathing exercises, low-dose aspirin and diamox may be beneficial in the prevention and therapy of CMS Phobrang Type at high altitude.

1. Introduction

Chronic Mountain Sickness (CMS) is not uncommon among both the natives and immigrants of the Peruvian Andes^{1,2}. However the disease was considered to be non-existent in the Himalayas^{3,4} till the first series of 13 cases were reported⁵ in February 1982. Subsequently we identified a total of 27 cases of CMS in the Western Himalayas,

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at altitudes of 11,500 to 16,730 feet above mean sea level⁶. In this article we present our findings in detail.

CMS has been defined as a variety of hypoxic chronic cor pulmonale⁴. Prolonged exposure to high altitude causes desensitisation of the chemosensitive respiratory mechanisms to hypoxia and/or hypercapnoea^{4,7}. This leads to alveolar hypoventilation, hypoxemia, polycythemia, hyperviscosity states, hypoxic hypertensive pulmonary vascular disease and finally to hypoxic chronic cor pulmonale and nephropathy with gross proteinuria. Sleep hypoxemia due to breathing dysrhythmias may be a major triggering factor⁸. According to Heath⁴, CMS may be the clinical manifestation of ageing at high altitude being the result of excessive polycythemia secondary to age related fall in ventilatory rate.

2. Material and Methods

Twenty seven cases of CMS were studied. All were male immigrants, in robust health prior to the onset of the disease, without any history of respiratory diseases or of exposure to occupational hazards conducive to the development of cor pulmonale. None had current evidence or past history of cardiac or renal disease. Mean age of the cases studied was 36.1 years (range 25 to 48 years). At the time of diagnosis, 26 were living at altitudes beyond 13,000 feet and one was at 11,500 feet. Mean duration of stay at high altitude (HA) was seven years (range 1.2 to 15.3 years). They were compared with 75 native highlanders (NH), for generations inhabitants of the Western Himalayas at altitudes of 13,430-14,100 feet above mean sea level (AMSL). Parameters studied were clinical examination which included a cardiorespiratory and neurological questionnaire, conventional ECG, skiagram chest, haematological examination (haemoglobin-Hb-, haematocrit-VPFC-, total and differential leucocyte cell counts) and urinalysis. Cardiac catheterisation and right heart studies were conducted in eight cases after evacuation to Army Hospital, Delhi Cantt. This involved unavoidable delays of 4 to 24 days, mean 14.6 days.

Diagnosis of CMS was made on the basis of clinical features (the classical facies, RV heave, accentuated P₂) VPFC above or equal to 70%, ECG evidence of RV enlargement (RVE)/RV haemodynamic overload⁹, prominent main pulmonary artery segment (MPA) and proteinuria-cloud or precipitate on the boiling test¹⁰.

3. Results

The data are presented in Tables 1 to 7.

4. Discussion

Since CMS was not known to exist in the Himalayas, Lahiri thought that factors other than HA hypoxia may be playing a vital role in the genesis of the disease³.

Table 1. Symptomatology

Symptoms	No. with the symptom	%
Malaise, lethargy, easy fatiguability	19	70.4
Exertional dyspnoea	16	59.3
Impairment of memory	16	59.3
Lack of concentration	16	59.3
Bleeding Diathesis	9	33.3
Exertional Angina	7	25.9
Exertional Palpitation	7	25.9
Mild GIT symptoms	5	18.5

Table 2. Clinical signs

Signs	No. with the signs	%
Facies of hypoxemia and polycythemia	27	100
Palpable and/or accentuated P ₂	21	77.8
RV Heave	12	44.4
Koilonychia/platynychia	18	66.7
Splenomegaly	1	3.7
Phlebothrombosis	1	3.7
Clubbing (Reported as a common finding in the Andean CMS ^{1,2,4})	0	0

Table 3. Haematological and urinalysis data

The Parameters	CMS Phobrang Type	Native highlanders	Lamas (Banchero)	Lamas (Reynafarje)
Altitude (feet AMSL)	14181.5	13765	11220	13779.4
Number	27	75	3	12
Haematocrit (%)	80.2	47.6	26.83	38
Haemoglobin (G%)	23.0	17.9	11.8	15.1
MCHC	28.7	37.6	44.13	39.6
% with Resting Proteinuria				
No Proteinuria	33.3	82.8		
'Haziness'	0	17.3		
'Cloud'	14.8	0		
'Precipitate'	51.9	0		

Table 4. ECG data

The Parameters	CMS Group	NH Group
QRS Axis	+118.5°	+76°
Amplitude of P in Lead II in mm	1.8	0.9
RVE/RV Overload seen in	55.6%	28.0%
LVE by voltage criterion seen in	50.0%	64.0%
Data on Skiagram Chest		
C:T Ratio	0.44	0.41
MPA Prominence seen in	91.7%	17.7%

Table 5. Haemodynamic data (8 cases)

Site	Pressures		Mean
	Systolic	Diastolic	
Rt Atrium	—	—	4.5 (3-5)
Rt Ventricle	39.5 (30-45)	4.5 (3-5)	—
Pulmonary Artery	37.3 (30-44)	14.4 (12-18)	20.5 (18-22)
Pulmonary Wedge	—	—	11.3 (5-18)

Note : 1. Figures in parenthesis indicate the range of pressures.

2. The time-lag between HA to Cath lab = 14.6 days (4-24 days).

Table 6. CMS—Phobrang type versus Monge's disease : a comparison

Features	CMS Phobrang Type	Monge's disease (Penalzoza Monge)
Altitude	Majority were above 14000 feet	Above 9840 feet
Cor pulmonale	Seen in only 55.6%	Sine que non for diagnosis
Neuropsychiatric features	Not disabling	Dominant (Coma, convulsions, sudden death)
Cardiorespiratory symptoms	Disabling	Not common
Clubbing	Not seen	Common
Semnlence	Not seen	Common
Insomnia	Common	Rare
Koilonychia/Platynychia	Common (66.7%)	Not reported

Table 7. CMS—Phobrang type—the three grades of the disease

Features	Grade I Disease	Grade II Disease	Grade III Disease
No of cases	(414.8%)	8(29.6%)	15(55.6%)
Mean altitude in feet AMSL	14181.5 (13430-14432)	14172.0 (11500-14645)	14885.3 (13430-16730)
Mean Haematocrit %	83.5 (74-94)	81.0 (67-94)	77.1 (62-91)
Mean Haemoglobin G%	22.5 (20.24)	24.0 (20.5-29.2)	22.56 (20-26.5)
Mean MCHC	26.9	29.6	29.6
Incidence of Proteinuria %			
No proteinuria	75.0	25.0	26.7
'Haziness'	0	0	0
'Cloud'	25.0	25.0	20.0
'Precipitate'	0	50.0	53.3

This study was undertaken to find out whether CMS exists in the Himalayas or not, if it does what are its characteristics and how does it compare with Monge's disease (eponym for CMS) as seen in the Peruvian Andes.

In the twenty seven cases of CMS identified in this study, the mean age was 36.1 years (range 25 to 48 years). This is in agreement with the findings of Penalzoza^{11,12} and Hurtado¹³. Mean total HA tenure (THAT) was seven years (range 1.2 to 15.3 years). Mean time lag between last sojourn to plains (LSTP) and diagnosis was only 8.9 months (range 1 to 24 months) LSTP was below 1 year in 16 patients and below 6 months in 6 patients. The duration of LSTP in all of them extended between 10 to 18 weeks, periods adequate to achieve resolution of the pathophysiological changes of HA⁴. In the 6 cases with LSTP below 6 months, the VPRC values were 74, 71, 72, 67, 78, and 70%; two of them had proteinuria 'cloud' and 4 had proteinuria 'precipitate'. These findings indicate that prolonged exposure to HA hypoxia, even in different spells has cumulative effects in hampering cardiac, haematological and renal functions leading on to CMS.

Presenting complaints varied widely, true to the observation of Monge and Monge^{1,2} that the disease is polysymptomatic in its expression effecting any organ system (Table 1 and 2). However, we noted that cardiorespiratory symptoms were the more distressing ones. We did not come across major neurological problems like cerebral crises, coma and convulsions^{1,2}. In spite of the wealth of subjective and objective data, all patients were ambulatory. These observations lead us to believe that the disease expresses itself in a milder form in the Himalayas in comparison to the Andean CMS.

The typical facies of CMS is unmistakable-plethoric florid face with suffused conjunctiva showing injected vessels, cyanosis of lips and buccal mucosa, intensely red palms with cyanosed digital tips, koilonychia/platynychia^{5,6}. The last two features do not seem to have been reported from the Andes.

CMS group had very high VPRC in comparison to the NH (Table 3). Mean corpuscular Hb concentration (MCHC) on the contrary was significantly higher in the NH group. This, we believe, is a reflection on the two different approaches adopted by the two groups in combating HA hypoxia. This has to be viewed in concert with our observation that not a single case of CMS was seen in the NH of the Himalayas and the observation of Banchero¹⁴ and Reynafarje¹⁵, who found the VPRC of the Lamas of Peru somewhat identical to the values noted by us in the NH group. We believe that the NH of the Himalayas, over many centuries have adapted to the HA hypoxia, whereas their Andean counterparts have only acclimatized to HA hypoxia, because that race has been in the Andean mountains for a shorter span of time. This would also explain why earlier workers like Lahiri³ failed to identify CMS in the Himalayas, as the search was made only among the NH of the Himalayas. Our study was the first systematic attempt made to identify CMS among the immigrants to the Himalayas.

The lower incidence and quantum of proteinuria, as also the normal QRS axis on ECG, and normal skiagram chest of the NH group support the hypothesis mentioned above (Table 4).

Cardiac catheterisation and right heart studies were done in eight cases. The mean time-lag between arrival at sea level and these studies was 14.6 days (range 4 to 24 days). The mean pulmonary artery pressure was 20.5 mm Hg (Table 5).

Our CMS group is compared with Monge's disease as described by Monge and Monge^{17,2} and by Penalzoa^{11,12}, in Table 6. The differences are subtle yet significant, and so we believe that what we see in the Himalayas is a variant of Monge's disease^{5,6}. Therefore, we had suggested the name CMS Phobrang Type for this entity⁵ in 1982 (Phobrang is the name of the place from where the first 5 cases of our series came).

In all 27 cases, resolution was spontaneous on evacuation to plains with some of them claiming dramatic relief on arrival at sea level². Relapse on re-induction to the mountains was established in case No 27, albeit inadvertently^{19,20}.

Based on clinical, haematological, radiological, and electrocardiographic data we could classify the disease into 3 grades of severity (Table 7).

- Grade I Disease :- They had exaggerated accentuation of HA erythrocytosis only (EAHAE); no pulmonary arterial hypertension (PAH) or RVE.
- Grade II Disease :- ~~They had EAHAE plus PAH, no RVE.~~
- Grade III Disease :- They had EAHAE plus PAH plus RVE. Only Grade III disease has hypoxic chronic cor pulmonale, other 2 grades do not have cor pulmonale.

Therefore, we believe that CMS Phobrang type can be diagnosed before cor pulmonale sets in, and we are reluctant to define the disease as a variety of hypoxic chronic cor pulmonale. We would define CMS Phobrang type as a syndrome caused by HA hypoxia and characterised by hypoxemia, polycythemia, PAH and RVE/RV overload and nephropathy with gross proteinuria, each of which appear at different stages in the evolution of the disease and each of which resolve spontaneously on evacuation to plains only to relapse on re-induction to the mountains.

When we compared the 3 Grades of the disease, it was found that Grade III disease occurred at higher altitudes (Table 7). VPRC was lower in Grade III than in Grades I and II. This raises another possibility; that differing individual reactions to HA hypoxia may be decisive in a given individual contracting Grade I or Grade III disease. Those who respond primarily through an overproduction of erythrocytes ("erythropoetin secretors") develop Grade I disease, whereas those who respond primarily through pulmonary arteriolar constriction ("vasoreactors") develop Grade III disease. The same phenomenon causing renal vasoconstriction and

renal parenchymal hypoxia¹⁷ may explain the significantly higher frequency and quantum of proteinuria in Grade III disease.

Various forms of therapy have been advocated in literature—evacuation to plains, phlebotomy and administration of steroids and of medroxy progesterone acetate — a ventilatory stimulant^{12,218}. None of them are acceptable in our circumstances at HA. Therefore, we evolved a therapeutic regime which we call by the mnemonic 'DAY'—D for diamox (ventilatory stimulant), A for aspirin (anti prostaglandin agent) and Y for yogic deep breathing exercises, which formed the central pillar. Cheap, almost non toxic in the doses administered, and available in the remotest of mountains, this regime, we feel may help man in developing 'long-term friendship' with the mountains, as naturally as possible. Limited therapeutic trials were conducted at an altitude of 14,432 feet AMSL in 4 cases over a period of 7 days. Results were gratifying^{19,20} Mean fall in haematocrit was 3.8%, mean fall in amplitude of P waves in lead II was 11.8% over pre-treatment values, mean left-ward shift of QRS axis was 10.1% over pre-treatment values, LV : RV ratio improved by 51% over pre-treatment values. At different altitudes above 11,500 feet AMSL we tried out this regime of 'DAY' in eight more cases of CMS, all with gratifying and some with dramatic results^{16,19,20}.

5. Conclusion

~~Chronic Mountain Sickness in the Himalayas is a distinct entity and we call it CMS~~ Phobrang type after the place from where the first five cases came. HA hypoxia is the sole incriminating factor in the genesis. Prolonged exposure to HA hypoxia, even in different spells has a cumulative effect in hampering cardiac, haematological and renal functions leading on to CMS. Role of 'DAY' in therapy and prevention of CMS at HA needs to be further elucidated.

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