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Case Report

Acute coronary syndrome in young males after a prolonged stay at high altitude

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ARTICLE INFO

Article history:
Received 4 February 2020
Accepted 22 September 2020
Available online 26 November 2020

Keywords:
Myocardial infarction
Smoking
Hypoxia
Polycythemia
Coronary artery disease

ABSTRACT

The Indian population is predisposed to acute coronary syndrome at a younger age, but very few cases are reported at high altitude. Acute coronary syndrome is frequently associated with multiple cardiovascular risk factors. During management of seven young patients with acute coronary syndrome, it was found that none of them had conventional cardiovascular risk factors including recent physical exertion. It is a known fact that the risk of vascular thrombosis increases by 30 times in Indian soldiers after a long stay at high altitude. Therefore, it is necessary to carry out the tests for procoagulant markers to know whether the acute coronary syndrome was because of the prothrombotic state, and if yes, was high altitude responsible for the procoagulant state or whether the person per se had a procoagulant syndrome. With the absence of these tests at hospitals at high-altitude areas, it becomes difficult to ascertain the exact cause of acute coronary syndrome. This study highlights the importance of aggressively testing for procoagulant markers in young patients presenting with chest pain at high altitude, even in the absence of traditional risk factors.

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, with coronary artery disease (CAD) and acute coronary syndrome (ACS) together accounting for 32% of total deaths due to CVD.[1] ACS is a lethal manifestation of CAD and can result in sudden death. ACS was earlier typically seen in older patients (age >45 years), but in recent times, younger patients (age<45 years) are experiencing ACS.[2] ACS in Indians develops 5–10 years earlier than people in the Western world, and its occurrence in patients younger than 40 years is 5- to 10-fold higher.[3] In India, of the total incidence of ACS, 25% occur in those younger than 40 years and 50% occur in those younger than 50 years.[4] Commonest risk factors for ACS in the young include

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https://doi.org/10.1016/j.mjafi.2020.09.007

Table 1 – The characteristics of the patients and their altitude with duration of stay.

Patient number	Age (years)	Sex (M/F)	BMI (kg/m^2)	Traditional risk factors	Significant past history	Altitude (feet)	Duration in that altitude (days)
01	28	M	24.9	No	Nil	10,500	365
02	23	M	22.3	Tobacco	Nil	12,000	365
03	40	M	23.87	No	Nil	15,000	75
04	35	M	23.17	No	Nil	12,300	180
05	42	M	23.38	Tobacco	Nil	10,500	67
06	42	M	25.3	No	Nil	13,500	45
07	37	M	24.5	No	Nil	12,000	366

BMI, body mass index; M, male; F, female; kg, kilogram; m^2, meter square.

Table 2 – Clinical characteristics of the patients.

Patient number	Presenting symptoms	Symptom duration	Vital signs at presentation			Electrocardiographic changes at presentations
			HR (beats/min)	NIBP (mmHg)	SpO_2 (%)	
01	Precordial/retrosternal pain radiating to the left shoulder	>12 h	64	118/76	90	ST elevation in LII, LIII, aVF
02	Precordial pain radiating to the left arm	02 h	124	118/76	88	ST elevation L1, aVL, V1–V3, ST depression in inferior leads
03	Retrosternal pain radiating to both shoulders, nausea, diaphoresis, and breathlessness	24 h	90	136/92	91	ST elevation in L1, aVL, V2–V5
04	Retrosternal pain radiating to both upper limbs, nausea, breathlessness, diaphoresis	4 h	86	132/90	90	ST elevation in V1–V4
05	Retrosternal pain radiating to both shoulders, nausea, diaphoresis, breathlessness	12 h	86	114/72	89	ST elevation in L1, aVL, V2–V5
06	Right-sided chest pain, breathlessness, and orthopnea	36 h	94	118/76	92	ST elevation and inverted T waves in L-II, III/aVF, and right ventricular leads V3–V4
07	Precordial pain and heaviness	4 days	76	130/78	90	WNL

HR, heart rate; NIBP, noninvasive blood pressure; SpO_2, oxygen saturation by pulse oximetry; V1, chest lead 1; V2, chest lead 2; V3, chest lead 3; V4, chest lead 4; V5, chest lead 5; V6, chest lead 6; L1, limb lead 1; LII, limb lead II; LIII, limb lead III; aVL, lead augmented vector left; aVF, lead augmented vector foot; aVR, lead augmented vector right; WNL, within normal limits.

smoking, diabetes mellitus, dyslipidemia, hypertension, family history of coronary heart disease (CHD) or premature CHD, low physical activity, alcohol consumption, high waist–hip ratio, unhealthy diet, physical exertion in athletes, and psychosocial stress.[4] Myocardial ischemia at high altitude (HA) is uncommon in young individuals, but it can occur with exertion.[5] We present seven cases of ACS in the young presenting at HA with the absence of common risk factors.

Table 3 – Laboratory investigation reports of the patients.

Patient number	Hb (g/dl)	Hct (%)	TLC (per mm^3)	Platelet (per mm^3)	Lipid profile (mg/dl)	Blood sugar random (mg/dl)	Cardiac biomarkers			Renal function test	Liver function test
							CKMB, IU/L		cTnl		
01	18.3	54.6	17,100	1.91	Normal	76	59	Positive	Positive	Normal	Normal
02	17.6	52.5	19,100	4.6	Normal	106	59	Positive	Positive	Normal	Normal
03	19.8	58.4	9600	2.7	Normal	86	83	Positive	Positive	Normal	Normal
04	15.8	55.7	14,700	1.8	Normal	94	93	Positive	Positive	Normal	Normal
05	16.6	53.8	12,800	3.2	Normal	96	96	Positive	Positive	Normal	Normal
06	18.2	54.9	12,700	2.6	Normal	82	265	Positive	Positive	Normal	Normal
07	16.2	49.9	8500	1.8	Normal	88	54	Positive	Positive	Normal	Normal

Hb, hemoglobin; Hct, hematocrit; TLC, total leukocyte count; cTnl, cardiac troponin I; CKMB, creatine kinase muscle bone isoenzyme; IU/L, international units/liter; g/dl, gram/deciliter; mg/dl, milligram/deciliter; mm^3, cubic millimeter.

Table 4 – Echocardiography and cardiac catheterization findings of the patients.

Patient number	Diagnosis	Thrombolysis	Echocardiography	Cardiac catheterization	Angiographic findings
01	ST elevation MI inferior wall	Yes	No RWMA, LVEF normal	Yes	LMCA, LCX: normal, LAD: slow flow, RCA: recanalized
02	ST elevation MI anteroseptal wall	Yes	Hypokinesia of the apex, anterior wall, and apical septum	Yes	LMCA, LCX, RCA: normal, LAD: mid LAD plaque
03	ST elevation MI anterolateral wall	Yes	Dilated and globular LV, hypokinesia of the apical and anterior wall of the LV, hypokinesia of the anterior septum and apex	Yes	LMCA, LCX, RCA: normal, LAD: proximal thrombus, no flow after mid LAD
04	ST elevation MI anterolateral wall	Yes	Dilated and globular LV, LVEF 30%, hypokinesia of the apical and anterior wall of the LV, hypokinesia of the apical septum	Yes	LMCA, LCX, RCA: normal, LAD 30% proximal plaque
05	ST elevation MI anterolateral wall	Yes	Dilated and globular LV, LVEF 30%, hypokinesia of the apical and anterior wall of the LV, hypokinesia of the anterior septum and apex	Yes	LMCA, LCX, RCA: normal, LAD <30% stenosis
06	ST elevation MI inferior wall and RV MI	No	Mild inferior wall hypokinesia, LVEF: 60%	Yes	LMCA, LAD, LCX: normal, RCA: post ostial cutoff
07	ACS	No	Normal	Yes	Normal coronaries

LMCA, left main coronary artery; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery; LV, left ventricle; RWMA, regional wall motion abnormality; LVEF, left ventricle ejection fraction; ACS, acute coronary syndrome; RV, right ventricle; MI, myocardial infarction.

Case reports

We present seven cases of ACS in young patients at HA who reported to our peripheral government hospital. The study was approved by our institutional review board. Data of all the 31 patients admitted for pain chest in our hospital from January 2019 to December 2019 were collected and analyzed, of which seven suffered ACS. None of the patients had any history of prior myocardial infarction (MI), hypertension, diabetes mellitus, cardiac surgery, valvular heart disease, and any physical exertion. The characteristics of the patients and their altitude with duration of the stay are described in Table 1. Their mean age was 35.2 years (range = 23–42 years). The clinical characteristics are given in Tables 2 and 3. Six patients (85.2%) had ST elevation MI, with anterolateral ST elevation MI being the commonest followed by inferior wall MI. The seventh patient had non obstructive left anterior descending (LAD). All patients had polycythemia with normal platelet count, prothrombin time, and activated partial thromboplastin time. Tests for fibrinogen, D-dimer, protein C, protein S, antithrombin III, platelet activation factors, i.e., platelet factor 4 and β-thromboglobulin, plasminogen activator inhibitor-1, lupus anticoagulants, anticardiolipin antibodies, and homocysteinemia were not performed, neither in our hospital (as the facility was not available) nor in the referred tertiary government hospitals. Six patients had obstructive CAD on cardiac catheterization, as shown in Table 4. All the seven patients recovered completely.

Discussion

The majority of young patients suffering ACS are reported to have at least one identifiable common cardiovascular risk factor. Yusuf et al. identified smoking as the most important risk factor associated with ACS in the young, whereas Oliveira et al. observed increased incidence of ACS in those smoking more than 15 cigarettes per day.[4] The smoking rate among young patients with ACS are between 51% and 89%, whereas in our study, it was only 28.5%, that too with smoking less than five cigarettes per day.[4] Rest of the patients did not have any known common risk factors but still suffered ACS. Thus, identification of a risk factor in our patients was required. After thorough analysis, the only common factor identified among all of them was staying at HA. All the patients had history of first-onset angina leading to MI, unlike typical cases involving worsening of angina progressing to MI. This indicates that pathophysiological factors other than atherosclerosis such as coronary arterial vasospasm and prothrombotic state might be the primary cause wherein there is less time for ischemic preconditioning, leading to rapid progression to AC. Anand et al.[6] had reported a 30-fold higher risk of spontaneous vascular thrombosis in Indian soldiers during long duration of stay at high and extreme HA. The prothrombotic state could be due to sequelae of hypoxia at HA, or the patients per se might be suffering from a procoagulant disorder. At HA, the coronary oxygen extraction ratio is already high, which results in decreased coronary oxygen reservoir and any impairment of blood flow can

precipitate ACS.[5] Effect of HA on coronary circulation is multimodal. First, hypoxia and acclimatization leads to hyperventilation and alkalosis, resulting in coronary arterial spasm; second, increased catecholamine secretions cause arterial vasospasm and platelet aggregation; and third, hypoxia induces various hematological changes, leading to a procoagulant state.[5]

Studies reveal that 30% of fatalities among avid mountaineers are due to sudden cardiac deaths, which include a non-significant number of ACS cases.[7] Cardiac deaths due to ACS are reported exclusively from extreme HA such as Mount Everest (8840 m) or Mount Kilimanjaro.[7] The same was substantiated by Malconian et al.,[8] who did not witness a single case of ACS during his simulated study involving ascent of young males to Mount Everest over 40 days. However, in our study, all patients were deployed at a lower altitude (3200 m–4572 m). Hypoxia associated with HA causes various physiological and pathological changes in the cardiovascular system on short- and long-term basis. During short-term adaptations, there is increase in sympathetic activity, resulting in increase in systemic vascular resistance, heart rate, blood pressure, cardiac output, and resting myocardial blood flow, which helps in maintenance of cardiac function.[9] Long-term adaptation is associated with increase in parasympathetic and sympathetic activities. The heart rate and arterial blood pressure return to normal with decrease in stroke volume and maximal heart (the heart rate at maximal exercise), with preserved contractility. Right ventricle hypertrophy occurs, which helps in counteracting the increased afterload caused by persistent pulmonary hypertension.[9] These adaptations help in preserving exercise-induced coronary blood flow and act as preventive mechanisms against myocardial ischemia during exercise.[9] Therefore, the main suspicion of ACS in our patients was thought to be due to the presence of the procoagulant state, but in the absence of the test reports for procoagulant markers, it is difficult to comment on the exact cause of ACS.

The limitation of our study is the absence of a large sample size, over a large period of time with testing for procoagulant markers, which would have helped us to ascertain whether procoagulant condition is responsible for causing ACS in the young at HA.

Conclusion

This study highlights the importance of conducting tests for procoagulant markers especially in the young who are deployed at HA for long durations and present with ACS in the absence of any known risk factors. The test facility for procoagulant markers should be made available in all hospitals at HA, and these tests should form an integral part of the standard operating procedure for management of patients with ACS.

Disclosure of competing interest

The authors have none to declare.

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