PRINZMETAL'S ANGINA IN SINGAPORE

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SYNOPSIS

The syndrome Prinzmetal's angina due to coronary spasm has previously not been documented in Singapore. We describe 4 patients presenting with classical features of Prinzmetal's angina collected over a period of 1 year. Coronary angiography done in 2 patients revealed normal coronary arteries in one and severe 3 vessel disease in the other.

Nifedipine a new calcium antagonist drug was given to all 4 patients resulting in marked improvement in symptoms and abolition of anginal attacks.

We conclude that Prinzmetal's angina is not uncommon in Singapore. It is important to recognise this entity because drug therapy is completely different from the usual case of "Heberden's" angina pectoris.

INTRODUCTION

The syndrome of Prinzmetal's angina was first described in 1959 (1). It is characterized by angina at rest associated with transient ST segment elevation during attacks with normalization of the electrocardiogram in between. It occurs in both patients with fixed obstructive coronary artery disease as well as in those with normal coronary arteries (2). Coronary artery spasm has been shown in several reports to be the cause (2, 3, 4).

The treatment of Prinzmetal's angina has been difficult. Many drugs have been tried, including nitroglycerin, atropine, vasodilators and propranolol but the results have been disappointing. Recently, Hosoda et al reported the effectiveness of nifedipine, a calcium antagonist, in the treatment of Prinzmetal's angina (5).

We describe in this paper 4 cases of Prinzmetal's angina seen in the University Department of Medicine over a one-year period, highlighting the important therapeutic role of nifedipine. This is the first report of Prinzmetal's angina in Singapore.

Case 1

H.M.C., a 45-year old Chinese male, was previously well until the evening of 6th January 1979 when he suddenly experienced severe chest pain associated with sweating whilst resting. The pain persisted throughout the night and he was admitted to hospital the next morning. He was a non smoker and had no previous history of hypertension. Clinical examination on admission was normal and the blood pressure was 100/60 mmHg. The twelve lead electrocardiogram done showed marked elevation of the ST segment in leads V1 to V3, with reciprocal ST segment depression in the inferior limb leads (Fig. 1). The serum CPK was within normal limits. A few hours after admission, he developed ventricular fibrillation, but was immediately cardioverted with success. He was then maintained on Lidocaine infusion. A 12 lead ECG repeated several hours later was normal (Fig. 2). He was diagnosed as suffering from Prinzmetal's angina and was treated with oral Disopyramide. The patient was well in the subsequent days, but was found to develop progressive jaundice. Biochemical tests showed obstructive jaundice and percutaneous cholangiography confirmed a large stone at the common bile duct. Ten days after hospitalization, he developed his second spontaneous attack of chest pain, again whilst at rest. The 12 lead ECG recorded was identical to that seen on admission, showing raised ST segment from leads V1 to V3. The chest pain subsided with sublingual nitroglycerin and the ECG recorded several hours later was normal. He was then started on oral Nifedipine (40 mg daily) and had no further episodes of chest pain. He was discharged from hospital one month after admission.

Three months later he underwent a successful operation for removal of his gall stone.

It is now 20 months since his first attack of chest pain and he has been asymptomatic. Currently, he is still maintained on oral Nifedipine. His present 12 lead ECG is normal. He was advised to undergo coronary angiography, but he refused because he was well.

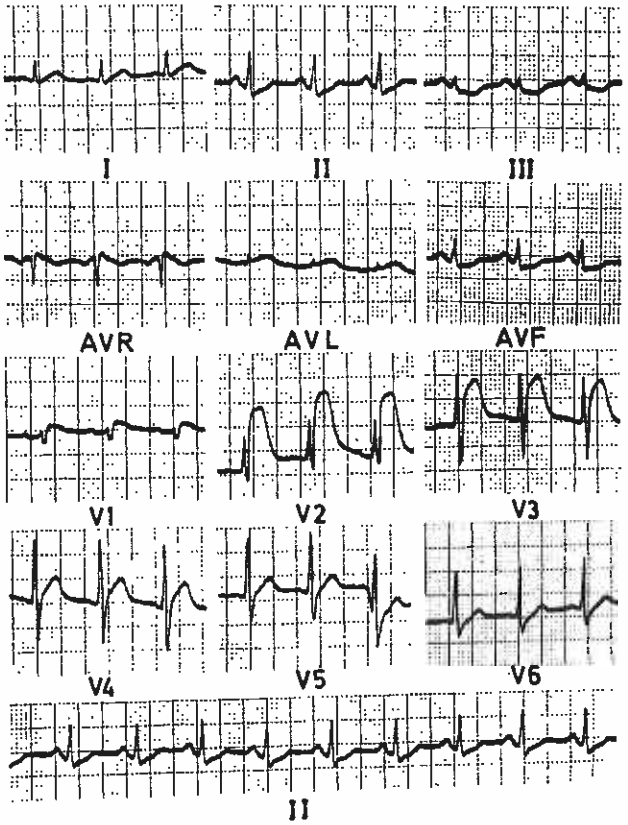

Fig. 1 Twelve lead ECG of Case 1 showing marked ST segment elevation in leads V1 to V3 with reciprocal ST segment depression in the limb leads.

Case 2

W.Y.W., a 48-year old Chinese male presented with a 10-year history of classical angina pectoris. He experienced chest pain each time he walked quickly or climbed up flights of stairs. The frequency and severity of chest pain was stable until 10 days before hospitalization, when he experienced chest pain at rest, occurring 2 or 3 times a day, mostly in the early hours of the morning, awakening him from his sleep.

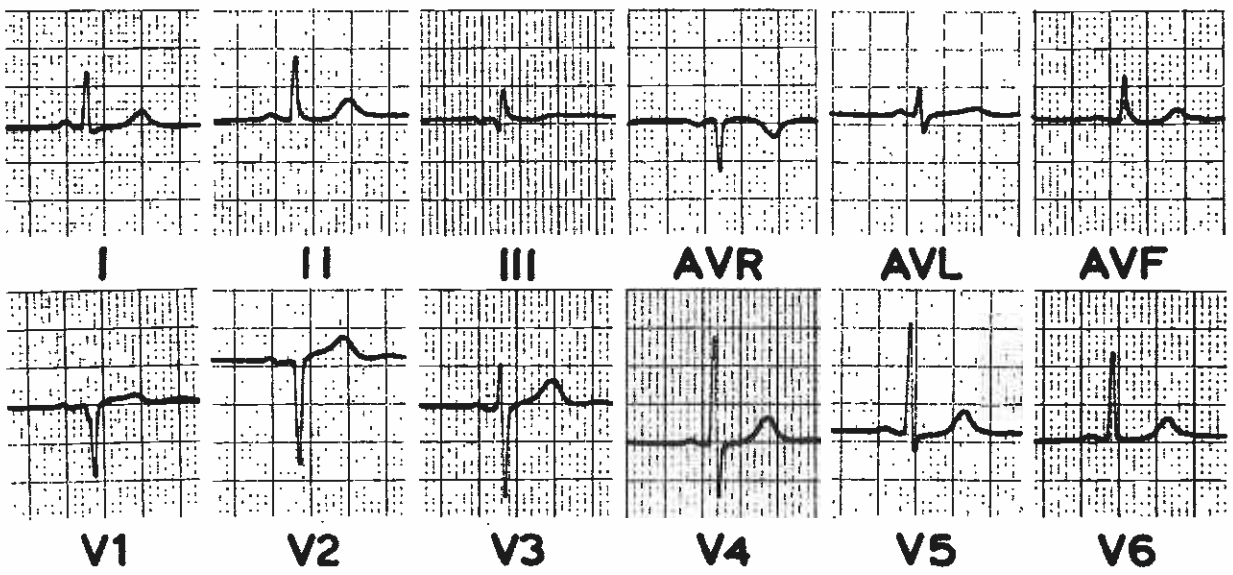

Fig. 2 Twelve lead ECG of Case 1 repeated several hours after Fig. 1 showing normal pattern.

Whilst being monitored in the coronary care unit for the next 3 days, he was found to have 15 spontaneous attacks of chest pain at rest, occurring usually at around 2.00 a.m. Each episode was associated with raised ST segments in leads I, II & AVL, reciprocal ST segment depression in leads III, AVF and V1 to V6, and frequent ventricular premature beats. Sublingual nitroglycerin promptly relieved the chest pain during each ischaemic episode. Serial ECG after nitroglycerin administration showed ST segment returning to isoelectric line, followed later by ST segment depression and still later (usually about 20 minutes) complete normalization of the ECG (Figs. 3-6). Prinzmetal's angina was diagnosed and oral Nifedipine 10 mg QID was started. No chest pain was seen after this. A treadmill exercise stress test done subsequently showed a markedly positive response. At stage 1, the patient experienced chest pain and the ECG showed 2 mm horizontal ST segment depression (Fig. 7). On the basis of this test, he was diagnosed as having severe coronary artery disease.

Cardiac catheterization was then performed. The right and left heart pressures and the left ventricular angiogram was normal. Selective left coronary angiography using the Judkin's technique showed total occlusion of the left anterior descending artery at its origin (Fig. 8). There was a 99% stenosis of the proximal portion of a large first obtuse marginal branch of the circumflex artery. Selective angiography of the right coronary artery showed marked irregularity and ectasia of the artery with proximal subtotal stenosis of the posterior descending branch. The left anterior descending artery was seen to be filled retrogradely via collateral branches from the right coronary artery. (Fig. 9, 10).

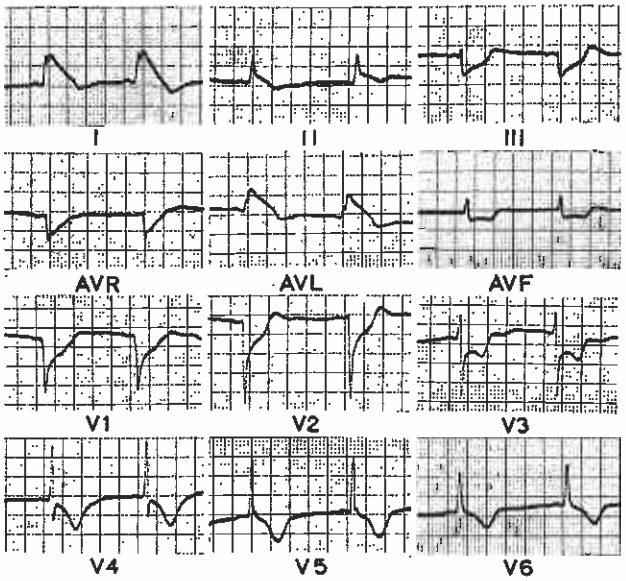

Fig. 4 Twelve lead ECG of Case 2 during chest pain showing ST segment elevation in leads I, II and AVL.

Saphenous vein bypass grafts were inserted to the left anterior descending artery, the first obtuse marginal branch of the circumflex artery and the posterior descending branch of the right coronary artery.

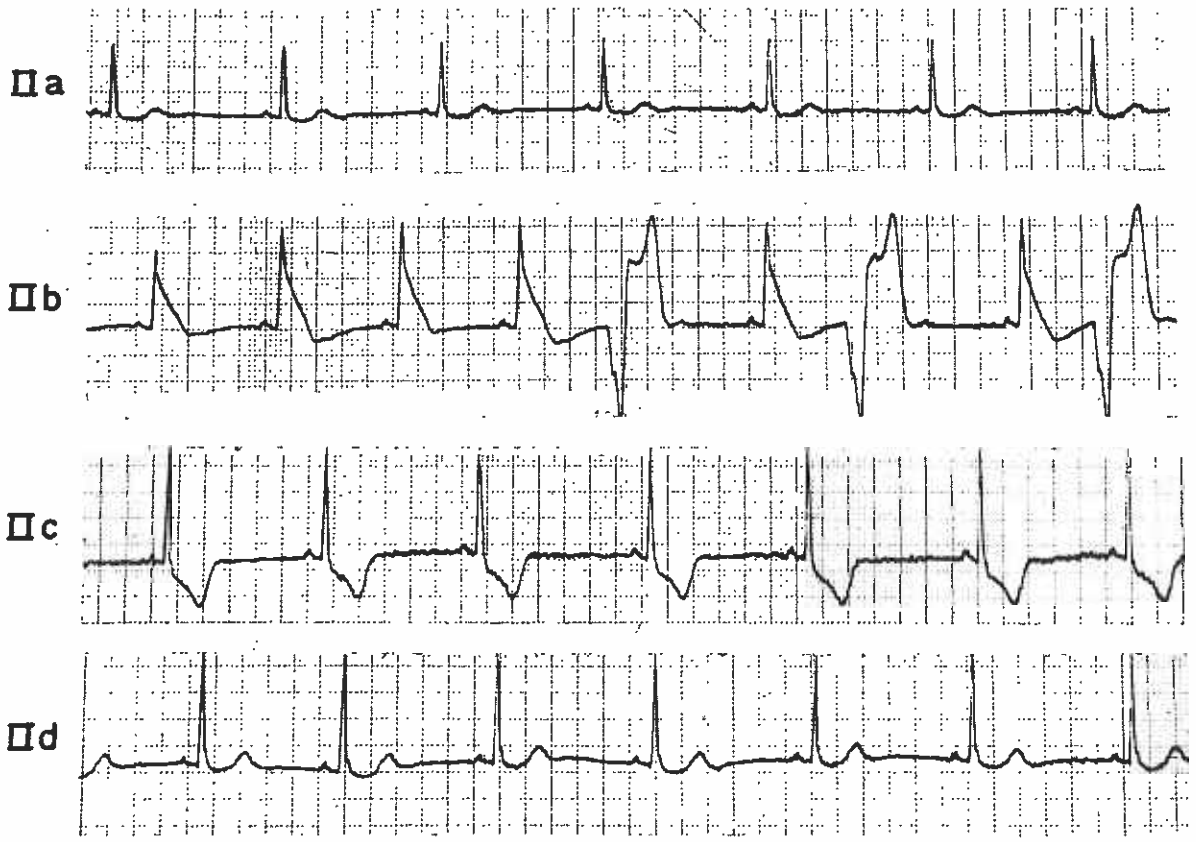

Fig. 3 Monitoring strips (lead II) recorded from Case 2. IIa recorded when patient was pain free was normal. IIb recorded when patient experienced chest pain showed ST segment elevation accompanied by ventricular bigeminy. IIc recorded after sublingual nitroglycerin showed ST segment depression. IId recorded about 20 minutes later showed normalization of ECG.

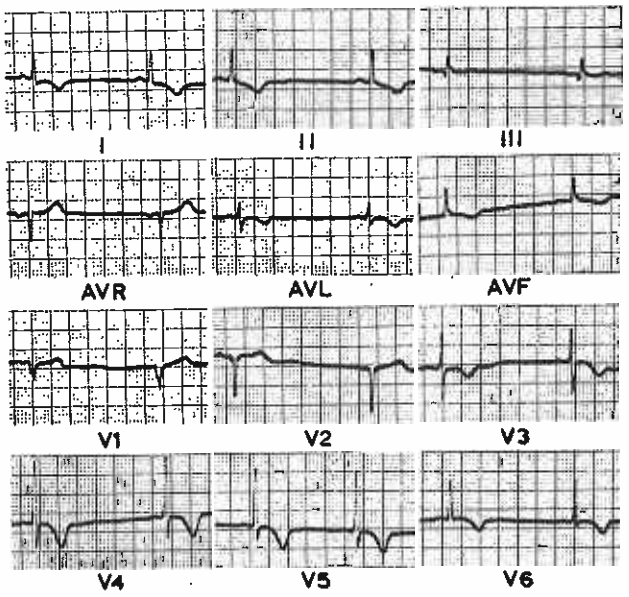

Fig. 5 Twelve lead ECG of Case 2 soon after sublingual nitroglycerin showing widespread T wave inversion.

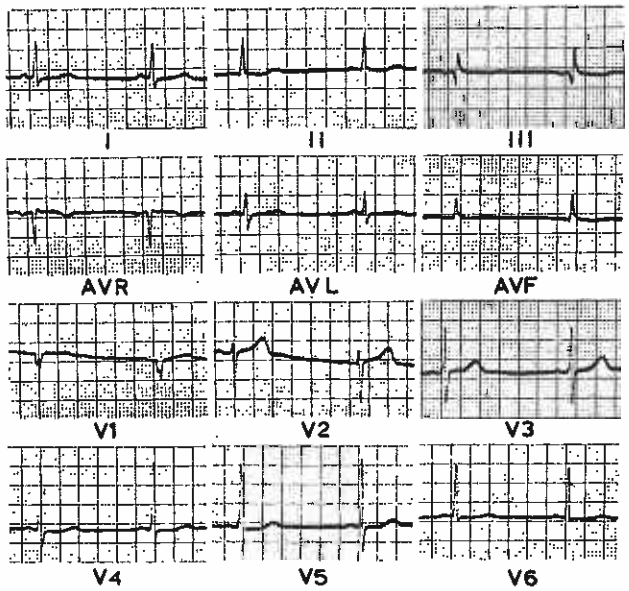

Fig. 6 Twelve lead ECG of Case 2 about 20 minutes later showing normal ECG.

The patient has now been followed up 6 months post-operatively. He is asymptomatic, his 12 lead ECG is normal and he is still on oral Nifedipine.

Case 3

L.Y.H., a 73-year old Chinese woman who was previously well until 2 weeks before admission when she began to experience spontaneous attacks of chest pain of 5 minutes duration unrelated to physical exertion. The frequency of these attacks had increased to 5-7 times daily at the time of hospitalization. She was a heavy cigarette smoker for the past 50 years. Clinical examination and 12 lead ECG on admission were both normal.

During observation in the coronary care unit for the first 14 hours, she developed 6 spontaneous attacks of chest pain which were relieved on each occasion by sublingual nitroglycerin. Each anginal episode was associated with raised ST segments in leads II, III & AVF. After relief of the chest pain by sublingual nitroglycerin, the ST segments returned to the isoelectric line and this was followed several minutes later by inverted T waves and still later by complete normalization of the ECG (Fig. 11). During one such attack, complete heart block followed by hypotension was seen. With IV Atropine, the conduction defect reverted to 2:1 second degree heart block. However with sublingual GTN, the chest pain subsided immediately followed by normalization of the ECG and cardiac rhythm (Fig. 12). She was diagnosed as having Prinzmetal's angina and started on further oral Nifedipine 10 mg QID. During the next 24 hours, 8 spontaneous episodes of chest pain occurred, each time accompanied by raised ST segment. All these attacks responded promptly to sublingual GTN. At this juncture the 12 lead ECG showed recent transmural inferior myocardial infarction. Oral Nitro-bid 6.5 mg tds was added to the Nifedipine and no further episodes of chest pain was observed. She was subsequently discharged from hospital and has remained well over a one year follow-up period with Nifedipine and nitroglycerin.

Case 4

O.L.K., a 45-year old Chinese male, presented with sudden severe retrosternal pain which woke him from his sleep at 3 a.m. on 28th August 1979. Clinical examination was normal and his blood pressure was 120/80 mmHg. While his electrocardiogram was being recorded, he suddenly developed ventricular fibrillation (Fig. 13). He was successfully cardioverted, and maintained on a Lidocaine infusion. His electrocardiogram shortly after showed atrial fibrillation and marked ST segment elevation in leads AVL, and V3 to V6, with reciprocal ST segment depression in the inferior leads (Fig. 14). He was then given 2-hourly sublingual nitroglycerin. An electrocardiogram done 5 hours later showed sinus rhythm, an incomplete right bundle branch block and normal ST segments (Fig. 15). Prinzmetal's angina was diagnosed and he was treated with Nifedipine 10 mg QID and Isosorbide 10 mg QID. No further episodes of chest pain occurred thereafter, and he was discharged from hospital three weeks later.

Coronary angiography revealed normal coronary arteries (Fig. 16 and 17). Three months later, he developed thyrotoxicosis which was confirmed biochemically. He was treated with carbimazole and is now euthyroid. He has now been followed up one year and is well on Carbimazole and Nifedipine with no further episodes of chest pain.

DISCUSSION

Our 4 patients have exhibited the characteristic features of Prinzmetal's angina with chest pain at rest associated with transient ST segment elevation during the attacks. The three male patients' were in their forties which is the average age for Prinzmetal's angina (6).

The first three cases who experienced multiple attacks of Prinzmetal's angina had the characteristic ST segment elevation in the same leads in each

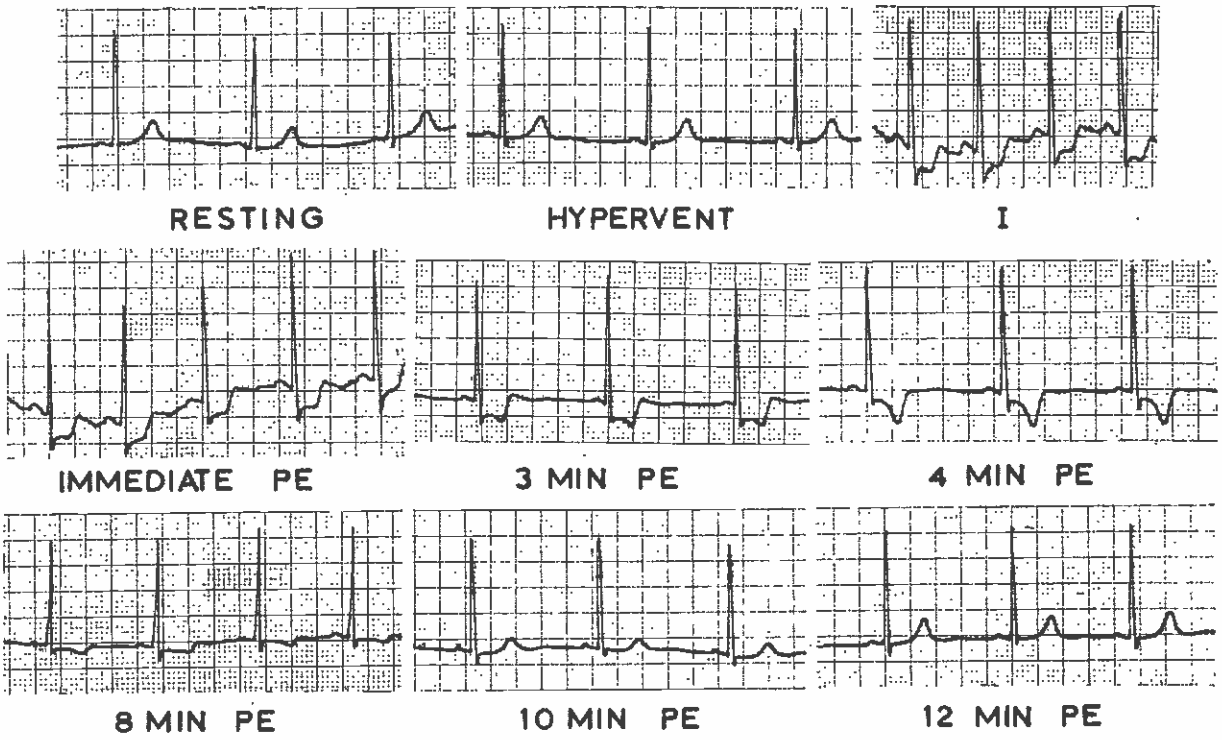

Fig. 7 Treadmill exercise stress test of Case 2 showing a markedly positive response. I = stage 1 PE = post exercise.

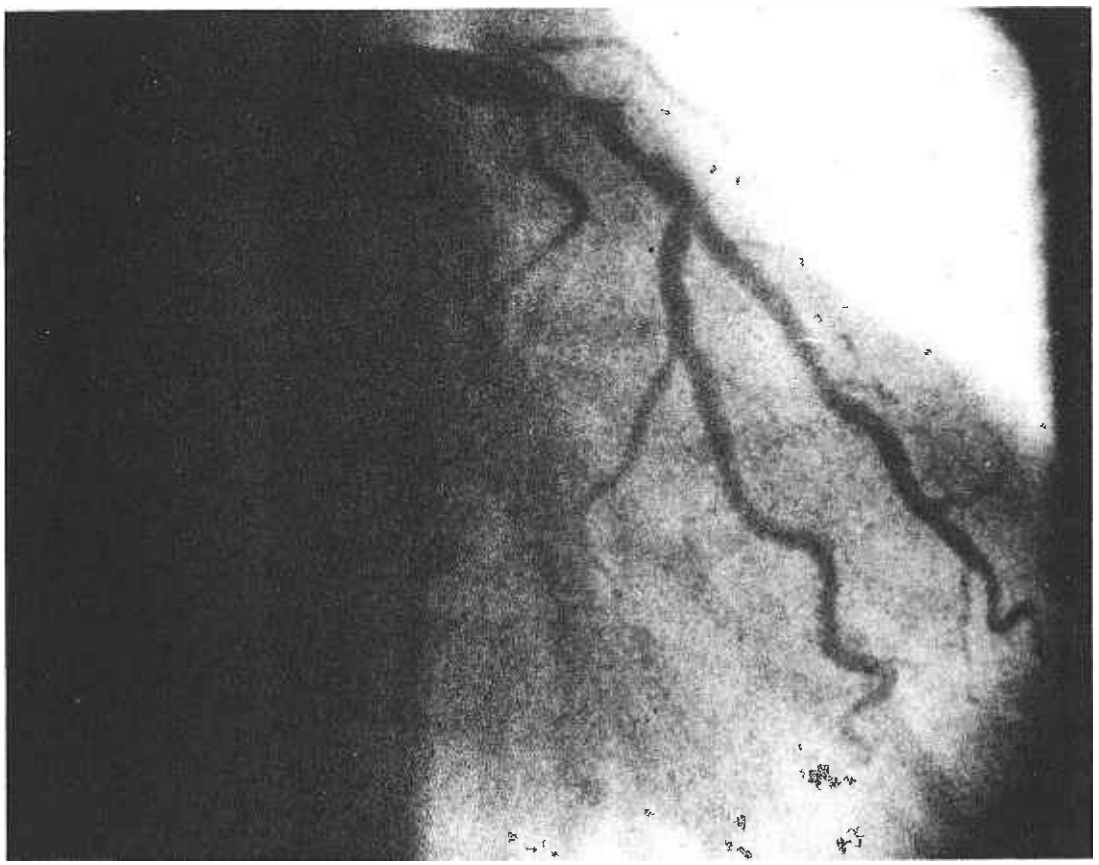

Fig. 8 Right anterior oblique view of left coronary angiogram showing complete occlusion of left anterior descending artery and 99% stenosis of the proximal portion of the first obtuse marginal branch of the circumflex artery.

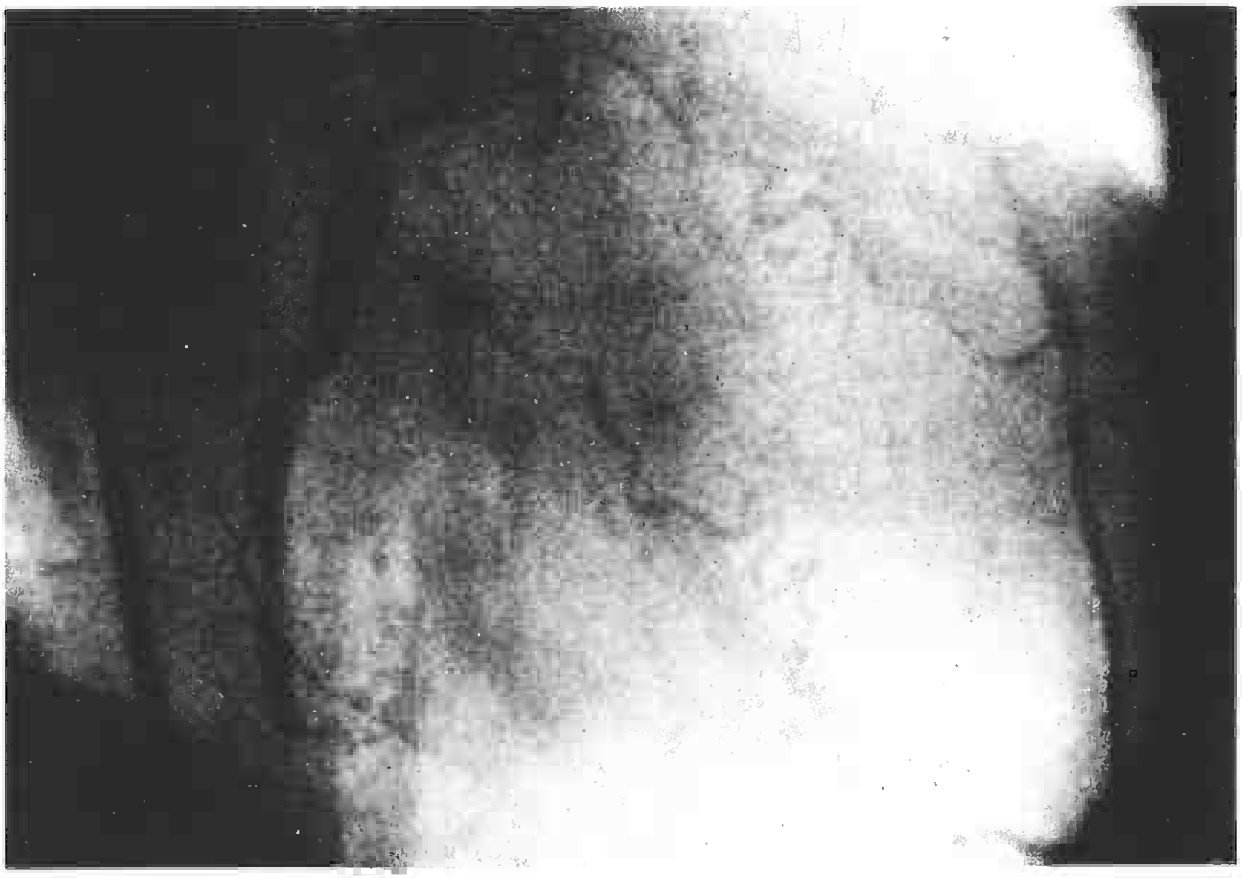

Fig. 9 Right anterior oblique view of right coronary angiogram showing marked irregularity and ectasia of the right coronary artery with proximal subtotal stenosis of the posterior descending branch. The distal left anterior descending artery is filled retrogradely by collaterals.

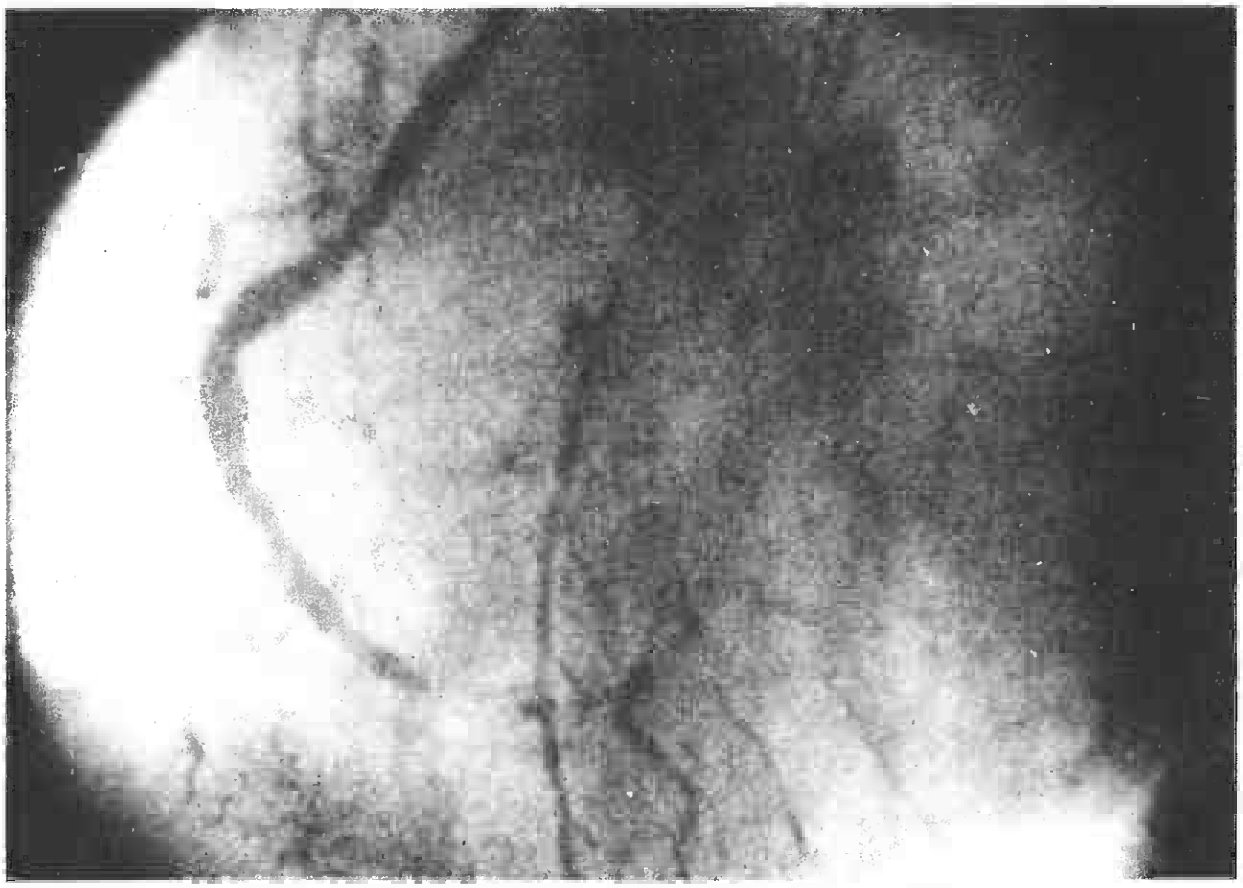

Fig. 10 Left anterior oblique view of right coronary angiogram showing similar changes as Fig. 9.

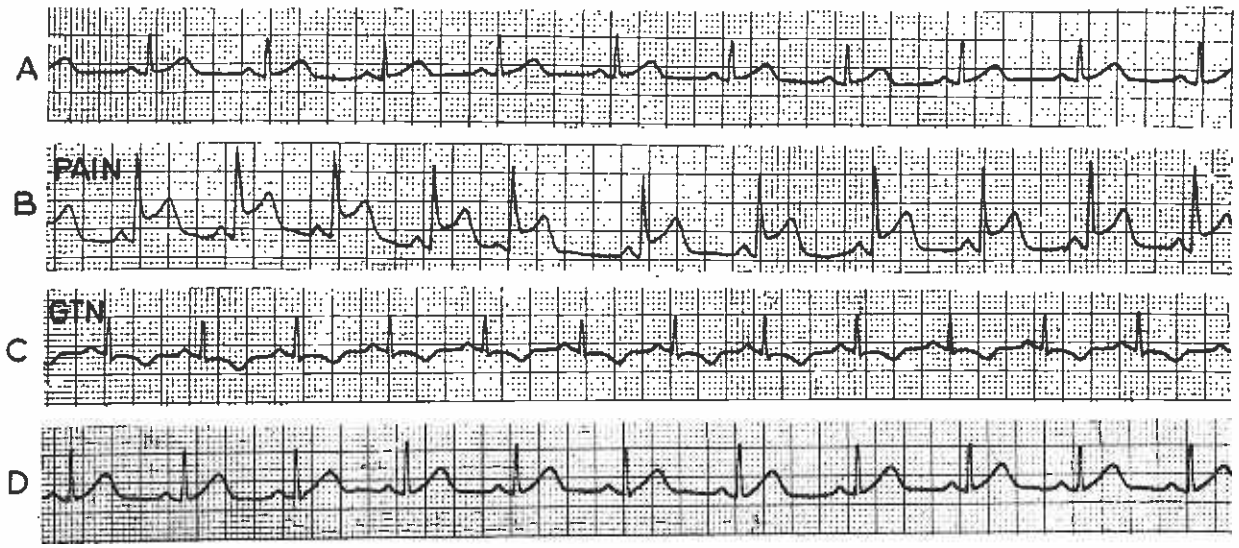

Fig. 11 Monitoring strips (lead II) of Case 3 showing ST segment elevation during chest pain (B), T wave inversion after sublingual nitroglycerin (C) and subsequent normalization of ECG (D).

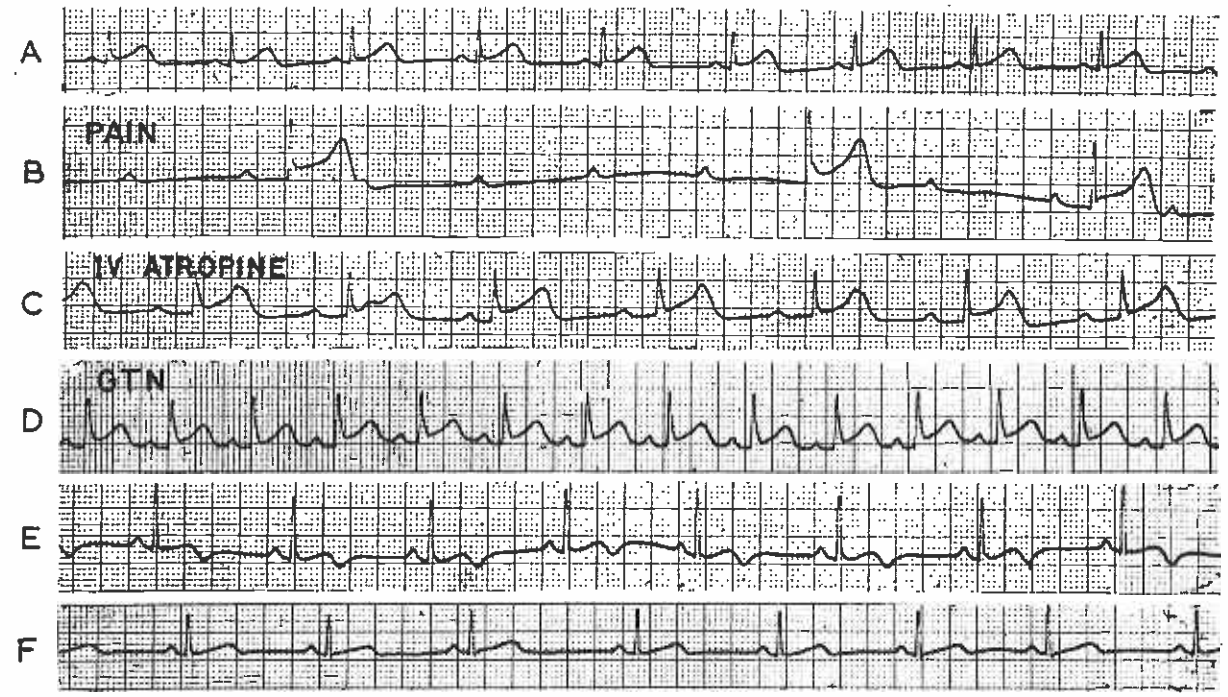

Fig. 12 Monitoring strips (lead II) of Case 3 showing transient complete heart block during chest pain (B).

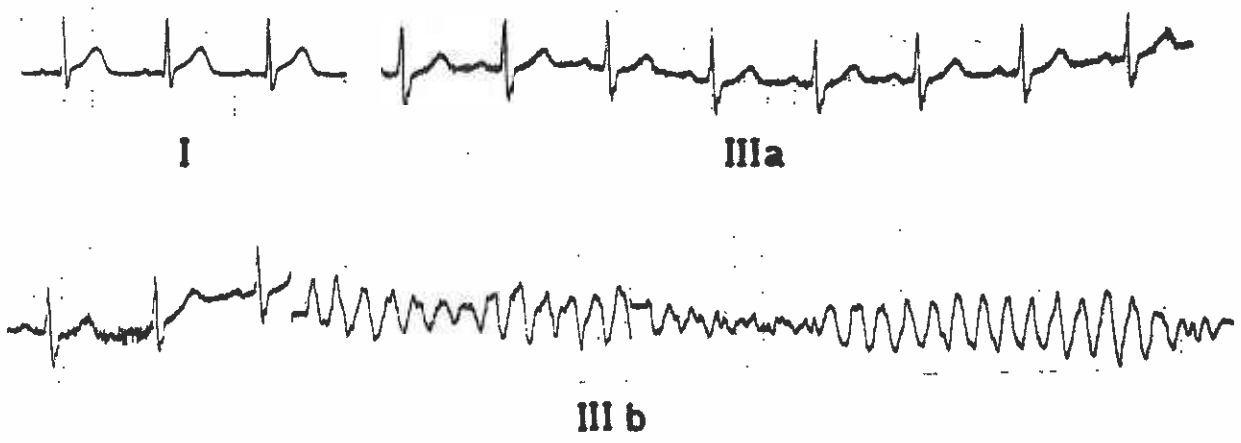

Fig. 13 Electrocardiogram of Case 4 showing onset of ventricular fibrillation during chest pain.

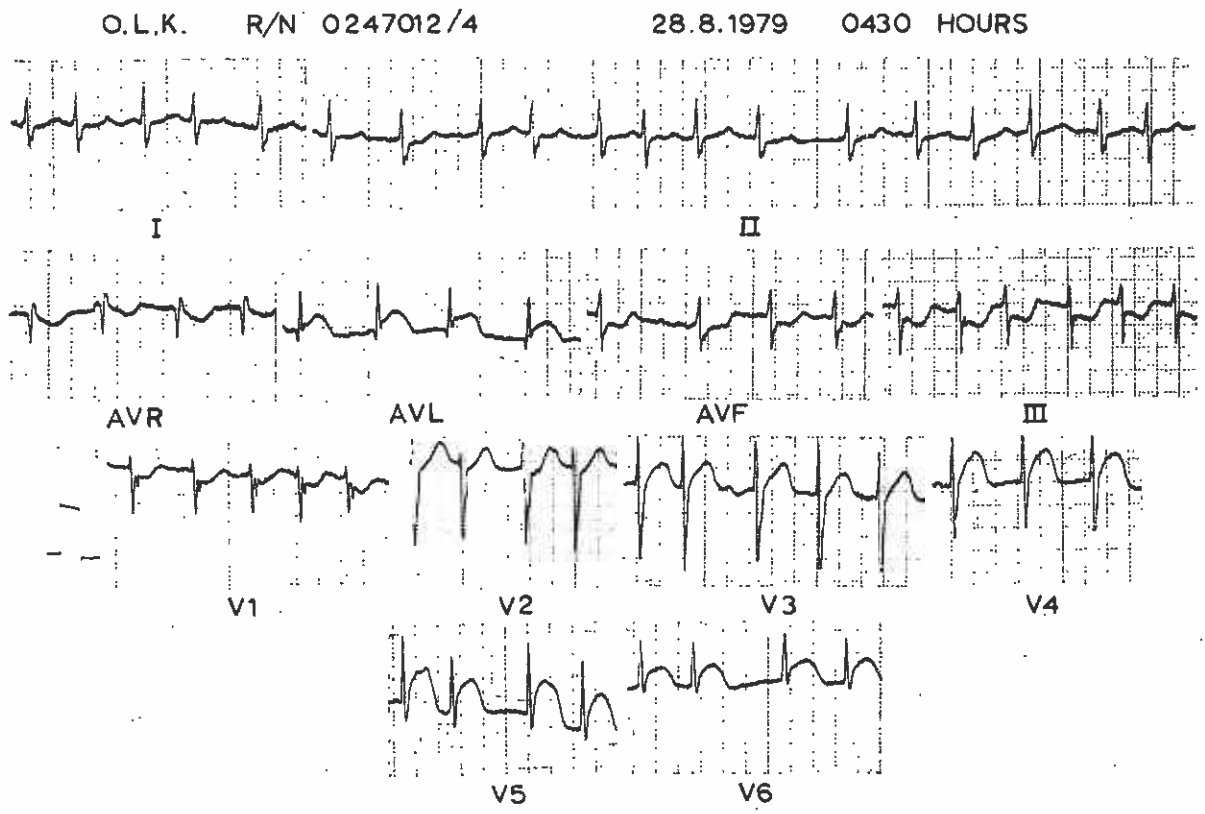

Fig. 14 Twelve lead ECG of Case 4 (recorded shortly after electrocardioversion) showing atrial fibrillation and raised ST segments.

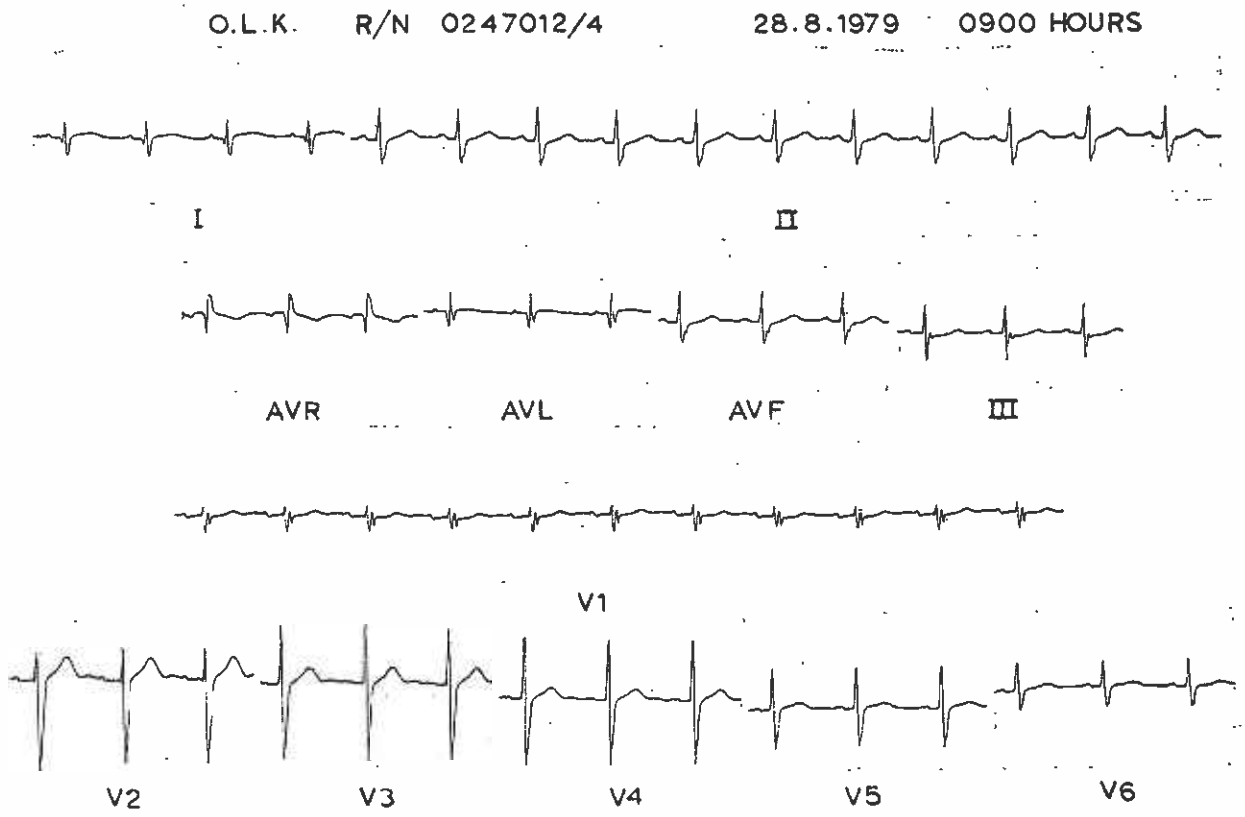

Fig. 15 Twelve lead ECG of Case 4 five hours after electrocardioversion showing isoelectric ST segments.

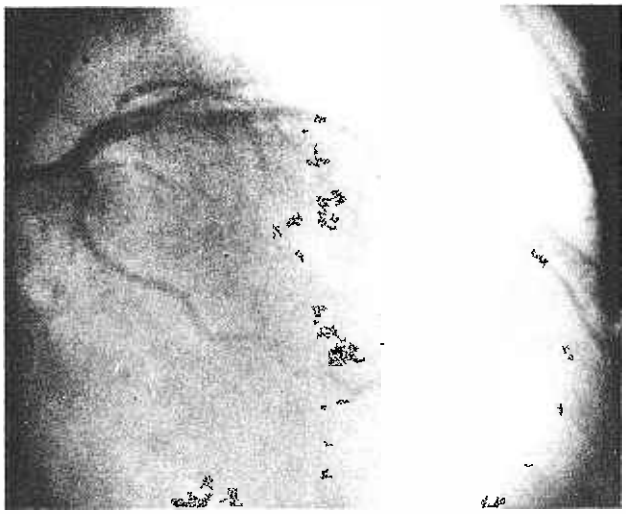

Fig. 16 Right anterior oblique view of left coronary angiogram showing normal left coronary artery.

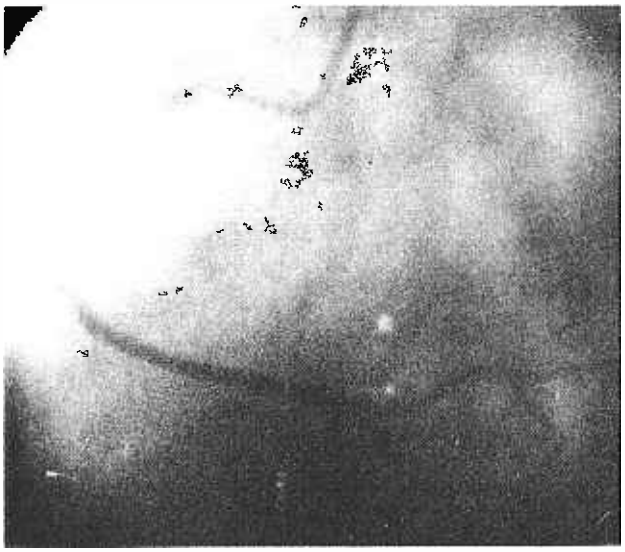

Fig. 17 Left anterior oblique view of right coronary angiogram showing normal right coronary artery.

patient during each attack. A similar observation was found in the 30 patients reported by the Cleveland Clinic implying spasm occurring repeatedly in the same artery for each patient (7).

Although coronary spasm was not demonstrated in any of our patients, its occurrence has been assumed. The ergonovine maleate provocative test for coronary spasm introduced by the Cleveland Clinic group in 1972 has been shown to be highly sensitive and specific for demonstrating coronary spasm during coronary angiography (8).

Major arrhythmias have been known to be common in Prinzmetal's angina (7, 9) particularly ventricular fibrillation, as demonstrated by 2 of our patients. Complete heart block which occurred in our 3rd case, is less common, and occurred in only 2 of the 30 patients reported by the Cleveland Clinic group (7). Sudden death has been reported to occur in Prinzmetal's angina, probably due to ventricular fibrillation (10). Indeed, our two patients with ventricular fibrillation would certainly have suffered the same fate if it had occurred before they were admitted to hospital.

Acute transmural myocardial infarction, which was a complication in Case 3, has been reported in Prinzmetal's angina with normal coronaries but it is rare (7, 10).

Nifedipine, a calcium antagonist, has been shown to be effective in preventing further episodes of Prinzmetal's angina in our four patients. Since the report by Hosoda et al on the efficacy of Nifedipine in Prinzmetal's angina, a few further reports have also confirmed its usefullness (5, 8, 11). Nifedipine is believed to relax coronary smooth muscle by blocking the transmembrane calcium influx, causing the coronary arteries to be less sensitive to vasoconstricting stimuli.

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