Spontaneous remission in variant angina*

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SUMMARY Four cases of variant angina are reported, in which total remission of anginal pain was documented during a follow-up of seven months, four years, five years, and 15 years, respectively. During this relatively long follow-up, the clinical course of the disease was apparently benign. The possibility of spontaneous and complete recovery may be postulated. The natural history of relatively benign forms of variant angina is poorly known and understood.

Since 1959, when Prinzmetal et al. described the variant form of angina pectoris, several studies have been devoted to the clinical and pathophysiological aspects, angiographic features, detection by provocative tests, and results of different forms of treatment. While the clinical course is usually severe, including the possible occurrence of acute myocardial infarction, malignant arrhythmias, and sudden death, the natural history of relatively benign forms is unknown. Further research into this important aspect of the disease is hindered mainly by recent developments. One is the availability of safe surgical procedures which are resorted to early in case of doubt. The other is that several forms of medical treatment are also available, and one or both are used to alter a spontaneous behaviour which has not really been established. Even medical intrusion or aggressive diagnostic procedures might be expected to modify the response pattern of patients known to be highly susceptible to emotional and neurogenic influence. For these reasons it is important to report the retrospective analysis of four cases of variant angina in which prolonged spontaneous remission of symptoms was documented.

Case reports

CASE 1
A 29-year-old man was well until April 1979, when he began experiencing severe epigastric pain at rest, lasting around 10 minutes. For 10 days these episodes occurred at an average frequency of twice a day. He was admitted to the coronary care unit where several episodes were promptly controlled with sublingual glyceryl trinitrate. An electrocardiogram recorded during one of the episodes (Fig. 1a) showed signs of transmural myocardial ischaemia, which consisted of ST segment elevation in leads V2 to V5, with small or absent S waves in

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Fig. 1 Case 1. (a) Electrocardiogram during anginal attack; (b) one hour later; (c) seven months later.
the same leads. All these changes subsided rapidly after disappearance of pain. The tracing recorded one hour later (Fig. 1b) was normal. Nifedipine was administered (20 mg every eight hours) and the anginal attacks disappeared from the first day of treatment. After 10 days, treatment was discontinued to perform an exercise test which was negative. The patient remained totally asymptomatic despite the fact that he did not resume treatment (his own decision), and an electrocardiogram recorded seven months later (Fig. 1c) was also normal.

CASE 2
In March 1973, a 47-year-old man had, unexpectedly, an episode of severe retrosternal pain followed by syncope. For the next 12 months he had approximately monthly episodes of less severe chest pain, not accompanied by neurological symptoms. During this interval he did not receive any medication. In March 1974, during a second episode of pain followed by syncope, an electrocardiogram recorded while he was unconscious (Fig. 2a) showed signs of inferior wall transmural ischaemia, consisting of severe ST segment elevation and increased R waves in leads II, III, and aVF, with pronounced ST segment depression in the anterior chest leads. The heart rate was 50 beats/min. A few minutes later (Fig. 2b) the electrocardiogram was normal. An exercise test was negative. He was treated with oral amiodarone 200 mg/day, and for the next 12 months he experienced isolated episodes of chest pain rapidly controlled by sublingual glyceryl trinitrate. Since March 1975 when he discontinued treatment, until September 1979, the patient remained totally free of symptoms and his electrocardiogram remained normal (Fig. 2c).

CASE 3
A 53-year-old man was well until 6 January 1974, when he was awakened between 5 and 6 am by severe retrosternal pain which lasted for about 10 minutes. Similar episodes occurred every night during the following 20 days. He was then admitted to the coronary care unit, where several episodes were recorded electrocardiographically and showed (Fig. 3a) ST segment elevation and tall T waves in leads V2 to V5. The chest pain and acute electrocardiographic changes subsided rapidly after the sublingual administration of isosorbide dinitrate 5 mg. The electrocardiogram under resting conditions showed inverted T waves in leads I and V3 to V6 (Fig. 3b). Serial determination of cardiac enzymes was normal. The episodes of chest pain disappeared after 10 days of treatment with isosorbide dinitrate (5 mg every three hours) and the electrocardiogram became normal. A few days later the patient interrupted treatment, and this was followed by reappearance of the episodes of night chest pain which, however, began to diminish in number until they finally ceased to occur after three months. He remained asymptomatic for the next five years, and his electrocardiogram also remained normal (Fig. 3c). During his last control, on 14 August 1979, attempts to provoke coronary spasm by hyperventilation or the injection of ergonovine intravenously proved unsuccessful (Fig. 3d and e). Further studies were refused.

CASE 4
A 56-year-old man began experiencing angina pectoris both on effort and at rest in 1960, with variable frequency, not uncommonly several times during the same day. An electrocardiogram recorded during one episode occurring at rest (Fig. 4a) showed severe ST segment elevation in leads V1 to V6 accompanied by QRS changes including left anterior hemiblock, and ventricular extrasystoles. Ten minutes later, pain had subsided and the electrocardiogram was normal (Fig. 4b). He continued having anginal pain for three months,
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after which he became asymptomatic and led a normal life for many years. In 1975, a clinical check-up indicated that he had been free of symptoms and an electrocardiogram was similar to the one recorded under resting conditions in 1960 (Fig. 4c). He died in 1978, at the age of 74, of carcinoma of the bladder.

Discussion

Although no angiographic proof can be provided, it seems plausible that the four patients had naturally occurring episodes of transmural myocardial ischaemia resulting from spasm of a major coronary artery. Since coronary arteriography was not carried out, we do not know whether or not the patients had atherosclerotic coronary stenoses. Clearly, this may be important in terms of prognosis. The negative exercise test in two patients, however, and the benign course of the disease in all of them, suggest that the four patients probably belonged to the subgroup of variant angina in which critical coronary stenoses do not play a prominent role. Also none of the four patients developed signs of myocardial infarction subsequently. Though the classical pattern including nocturnal pain at a fixed hour and lack of angina on effort was not present in every case, it is now widely admitted that variant angina may cover a much wider spectrum of clinical manifestations.

In case 1, a follow-up of only seven months precludes further prognostic considerations. In cases 2, 3, and 4, however, in which anginal pain disappeared entirely during a follow-up of four, five, and 15 years, respectively, the course of the disease was indeed uneventful. The question arises as to whether such patients may have had episodes of painless coronary spasm and, though this possibility cannot be ruled out, it does not detract from the fact that even if such minor episodes did occur, they do not appear to have changed the clinical course of the disease. For all practical purposes, the course of the disease was benign, and even the possibility of spontaneous and total recovery might be postulated. This possibility is favoured in case 4 by the long follow-up until a death from non-cardiac causes occurred at an advanced age, and in case 3 by the fact that provocative tests were negative. Others have reported that variant angina shows a natural tendency for “waxing and waning of the disease” MacAlpin et al. stressed that “periods of weeks or months when multiple attacks occurred daily alternated with periods of weeks, months and even years when there were no attacks at all”; and of a series of 20 patients, they refer to seven who became entirely free of anginal attacks at rest. In one of these patients, myocardial infarction “cured” his angina, but precise indications as to the length of time of the apparent cure were not given. Long lasting...
remissions but not total disappearance of symptoms were also mentioned by Robertson et al., and one of three patients was reported to have had no recurrences for 18 months. Gaquiere and Quillet reported a 20-year follow-up of a patient assumed to have variant angina. After this interval, the patient had an acute myocardial infarction, but there are doubts as to whether a non-transmural infarction occurred or was present when the first anginal attack was recorded. It is worth mentioning that in the classical form of angina, 30 per cent of patients may show complete abatement of anginal symptoms with advanced age.

Several new drugs have been shown to be effective in the treatment of variant angina. In the light of our observations, it may be advisable to withdraw the apparently useful drug after a certain time of treatment (provided the episodes can be safely controlled with sublingual vasodilators), in order to determine whether the drug is still needed, or whether or not spontaneous remission has occurred. In view of the observation made by MacAlpin et al. that the first three months of variant angina seem to be the time when complications are more likely to occur, treatment should probably not be interrupted before this interval. In addition to allowing a more precise evaluation of the effects of drugs, this approach should also contribute to a better knowledge of the natural history of this form of angina pectoris.

Fig. 4 Case 4. (a) Electrocardiogram during anginal attack; (b) a few minutes later; (c) 15 years later.

References
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