Sudden Cardiac Death during Ambulatory Holter Monitoring

Report on 3 Documented Cases

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SUMMARY

Three cases are presented who died suddenly while being continuously monitored on ambulatory Holter ECG. Two patients with coronary artery disease and severe left ventricular dysfunction after multiple myocardial infarctions died instantly from ventricular fibrillation; this was preceded by a rapid uniform ventricular tachycardia in one patient with normal Q-T interval and by polymorphic ventricular tachycardia in the other whose Q-T was prolonged on combined antiarrhythmic therapy with propafenone and mexiletine. The third patient died from rapidly progressive circulatory failure and acute pulmonary edema due to secondary cardiomyopathy. Despite its occurrence within 30 min after the onset of symptoms, death was not primarily arrhythmic in origin.

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SUDDEN death outside the hospital is believed to be caused predominantly by cardiac arrhythmias, in particular ventricular fibrillation (VF).\textsuperscript{1} The evidence for this has mainly been derived from the presence of VF on institution of electrocardiographic monitoring in victims of cardiac arrest. Assessment of the exact mechanism of sudden death, however, requires documentation of the electrocardiogram at the onset of the arrhythmia which has only recently been possible in a rapidly growing number of cases fortuitously wearing an ambulatory Holter tape.\textsuperscript{2)--151}

This report describes the electrocardiographic findings in 2 patients with documented VF during ambulatory monitoring; in a third case death was found not to have been primarily arrhythmic in origin.
METHODS

Continuous ambulatory electrocardiographic monitoring was obtained using a two-channel tape recorder (Medilog, Oxford Ltd). Analysis of the tapes was performed semiautomatically on a digital computer program (Pathfinder II, Reynolds Ltd) carefully controlled by visual inspection. Original strips were prepared, at a paper speed of 25 mm/s, of each episode of any ventricular arrhythmia for determination of prematurity of ventricular premature contractions (VPCs). Since there is considerable technical difficulty in accurately determining the Q-T interval from single leads at low paper speed the exact Q-T interval was obtained from portions with distinct T waves of a standard 12-lead electrocardiogram recorded routinely at 100 mm/s immediately prior to institution of Holter monitoring. After correction for rate according to Bazett's formula \( Q-T_c = Q-T/\sqrt{R-R} \), this computed Q-T interval together with the actual R-R interval was used to calculate the Q-T of each QRS complex on the tape that was followed by a ventricular premature contraction. Additional direct measurements of Q-T from the 25 mm/s strips confirmed that no significant changes of Q-T had occurred during the monitoring period in any patient. Prematurity of an extrasystole was determined by the R-R'/Q-T ratio. Evaluation of prematurity indices within ectopic pairs or salvos was not considered feasible since the Q-T of consecutive premature beats cannot be accurately delineated.

CASE REPORTS

Case 1

A 58-year-old plumber with a long-term history of angina pectoris had developed severe impairment of left ventricular function (radionuclide EF < 20%) following two myocardial infarctions in 1978 and 1980. After he had experienced a brief blackout concomitant with signs of mild pulmonary congestion, continuous Holter ECG recording was begun on June 2, 1981 at 2 p.m. Q-T was 365 ms. The following morning he went to a meadow in the vicinity of his home where he used to scythe the grass; this activity had consistently provoked severe chest pain on previous occasions. Two hours later, he was found dead with the scythe lying beside him.

Review of the tape revealed regular sinus rhythm throughout almost 22 hours until shortly prior to death. There were frequent multiform premature ventricular contractions (VPCs) especially in the daytime (29–71 VPCs/hour) many of which were early coupled (prematurity index 1.0–1.2) but none of them encroached upon the T wave of the preceding complex (Fig. 1). Apart
Fig. 1. Case 1. Review of premature ventricular contractions and their prematurity indices (R-R'/Q-T) during the recording period. C=couplet; VF=ventricular fibrillation; VT=ventricular tachycardia.

Fig. 2. Case 1. Terminal arrhythmia sequence. The upper 2 panels are recorded continuously. Paper speed: 25 mm/s.

from one pair with late coupling during the night, no repetitive ectopic activity was noted nor could any increase in VPC frequency be detected until immediately before death.
The terminal episode was preceded by an abrupt increase in sinus rate to 140 beats/min lasting for 40 sec. There were two bidirectional ventricular couplets with the second complex of each pair falling on the T wave of the preceding one (Fig. 2a); such short coupling intervals had never previously been observed. Ten seconds later, an early coupled VPC with a prematurity index of 0.95 occurred followed by a second one in the vulnerable period that initiated a rapid uniform ventricular tachycardia (VT) at a rate of 272/min (Fig. 2a). After 1 min, this degenerated into coarse (Fig. 2b, c) and, 13 min later, into fine VF (Fig. 2d). After a duration of 15 min, VF subsided and was followed by a brief period with distinct aberrant ventricular complexes at decreasing rate (Fig. 3a) that suddenly changed into ventricular standstill with complete A-V block; atrial activity at 31 beats/min was clearly discernible (Fig. 3a, b). Asystole was occasionally interrupted by brief episodes of slow
ectopic ventricular rhythms (Fig. 3b–d). The last electrical activity was recorded 72 min after the onset of VT. The course of the arrhythmic sequence is illustrated in Fig. 4.

Case 2

This 49-year-old electrical engineer had developed a large ventricular aneurysm after two myocardial infarctions in 1974. Because of multiple peripheral involvement of all major coronary arteries and markedly depressed left ventricular function (EF 10%) surgery was not advised. Three months prior to death he suffered a syncopal attack. During the following hospitalization Holter ECG revealed advanced grade ventricular arrhythmias including episodes of nonsustained VT that were effectively suppressed by oral propafenone, 900 mg daily. Over the 4-week course of this therapy he developed gradual prolongation of the Q-Tc interval from 436 to 468 ms concomitant with Q-R-S widening from 0.16 to 0.18 s. On hospital discharge mexiletine, 400 mg daily, was added to the drug regimen. Eighteen days later, on September 9, 1981, he presented for ambulatory rhythm recording that was begun at 2 p.m.; Q-Tc had slightly prolonged to 490 ms, Q-R-S duration was unchanged. The next morning, he suddenly collapsed while walking to the outpatient clinic to have his recorder taken off.

Review of the ambulatory recording disclosed multiform VPCs at a rate of 8 to 81 (mean 24)/hour that were mostly early coupled with frequent R on T phenomena, in particular at night when prematurity indices of as low as 0.79 were noted. In addition, ten couplets and two short runs of VT were
observed (Fig. 5).

Within 1 min prior to the terminal arrhythmia there was an increase in sinus rate from 82 to 100 beats/min. After a short run of VT a relatively late coupled VPC (R-R'/Q-T 1.23) triggered a sustained VT (Fig. 6a) with slightly changing morphology and rate but without a specific pattern of sequential oscillation (Fig. 6a, b). Interelectrogram intervals varied between 300 and 400 ms. This polymorphous VT organized into a tachycardia of uniform morphology (Fig. 6c) that progressed into coarse (Fig. 6d) and, 4 min later, into fine VF (Fig. 6e). After a further 10 min period distinct complexes of irregular ventricular activity with a background of atrial fibrillation (Fig. 6f) and eventually atrial flutter (Fig. 6g) appeared. Following a gradual decrease of ventricular rate, asystole then supervened. At 11:28 a.m. two short runs of rapid ventricular ectopics occurred; this was the last electrical activity recorded.

Case 3

This was a 54-year-old housewife with a history of congestive heart failure. Clinical and non-invasive investigational findings were consistent with
congestive cardiomyopathy. Because of single VPCs on resting electrocardiogram continuous Holter recording was begun on February 17, 1982 at 3:20 p.m. The following morning she suddenly experienced severe shortness of breath while driving her car. She was taken home where she arrived with typical signs of pulmonary edema. She was able to maintain a sitting position for about 20 min until complete circulatory collapse resulted in unconsciousness. Attempts to resuscitate her were unsuccessful. Autopsy revealed moderate biventricular hypertrophy and dilation and acute pulmonary edema. On histologic examination diffuse patchy myocardial fibrosis was present, which was most compatible with healed inflammatory lesions. The coronary arteries were normal.

During the previous 18 hours of ambulatory monitoring multiform VPCs (average rate 18/hour), R on T phenomena and two couplets were recorded. The terminal episode consisted of marked sinus tachycardia at a rate of 150 to 170/min that persisted for 30 min and was occasionally interrupted by short runs of VT (Fig. 7a). Thereafter, with gradual slowing of the sinus rate, junctional (Fig. 7b) and ventricular (Fig. 7c) escape rhythms appeared that

![Fig. 7. Case 3. Terminal electrocardiographic sequence. Paper speed: 25 mm/s.](image)
further slowed down and were followed by asystole (Fig. 7d), eventually interrupted by brief periods of VF (Fig. 7e) and the artifacts of closed chest massage (Fig. 7f).

DISCUSSION

Among the hitherto reported cases in whom sudden cardiac death outside the hospital was documented on ambulatory Holter electrocardiogram, VF was the prevailing cause of death; only approximately 10% of patients died of bradyarrhythmias. Some additional subjects included in recently published series on "sudden cardiac death" suffered from self-terminating torsade de pointes and did actually not die. The cases described in this report represent additional documentation of fatal VF and its progression into asystole. Moreover, they contain, to our knowledge, the first report of a case of death in circulatory failure documented on ambulatory recording.

Our first 2 cases fit into a category of patients with advanced coronary disease and severe infarct-related depression of left ventricular function who are well known to be at high risk for sudden death due to ventricular tachyarrhythmias, in particular in the presence of advanced grades of ventricular ectopy. Little information, however, is available about the triggering factors that might precipitate the terminal arrhythmic event. Although in both of our cases a certain degree of electrical instability was evident during the hours preceding the terminal event they remained virtually stable until the last minute prior to death. Then, a sudden rise in sinus rate was accompanied by increased ectopic complexity, possibly suggesting an ischemic mechanism in both patients. The type of VT, however, that finally initiated VF was different in the 2 cases. In the first case a uniform tachycardia was triggered by a VPC with high prematurity. In contrast, the second patient exhibited a polymorphous VT precipitated by a relatively late coupled VPC. This observation raises the possibility of a paradoxic arrhythmogenic effect of propafenone and/or mexiletine administration. Even though typical features of quinidine toxicity such as marked Q-T prolongation and classical torsade de pointes morphology were lacking, drug induced polymorphous VT has been encountered with virtually all other antiarrhythmic agents including mexiletine, even in the absence of significant Q-T prolongation. It cannot, however, be excluded that the polymorphous VT in our patient simply represents a variant form of spontaneous VT without implying a specific pathogenesis.

The continuing recording after establishment of VT enabled us to study
a rather uniform sequence of terminal arrhythmic events in patients 1 and 2. Within 1 to 3 min VT degenerated into coarse and, after a further period of 4 and 13 min, respectively, into fine VF. Spontaneous defibrillation into bradycardia and asystole occurred 16 and 19 min, respectively, following initiation of VT. Even 72 and 45 min respectively after the onset of VT, sporadic electrical activity was still recorded. These data may provide some clue to the utility of resuscitative efforts in a victim of cardiac arrest and are supported by recently published findings of a substantially higher survival rate in patients discovered with coarse compared to those with fine VF.\textsuperscript{22)

In contrast to the arrhythmic mode of death described above, the third patient died in rapidly progressive circulatory failure within 30 min after the onset of symptoms of acute pulmonary edema. Although the presence of advanced grade ventricular arrhythmias during the previous hours of recording was indicative of considerable electrical instability, a hemodynamically compromising rhythm disturbance did not occur until complete circulatory collapse resulted in unconsciousness and gradual slowing of heart rate. The subsequent VF must be considered a secondary event in this context. In agreement with similar observations by Hinkle and Thaler\textsuperscript{33)} these findings demonstrate that even witnessed death within 1 hour after onset of acute symptoms\textsuperscript{34)} does not necessarily imply a primarily arrhythmic mechanism. The latter could be more specifically characterized by using more restrictive definition criteria of sudden cardiac death such as instantaneous death or collapse within 5 min;\textsuperscript{33)} this seems reasonable in particular for intervention studies with antiarrhythmic drugs.

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**References**