Silent Myocardial Ischemia and Late Ventricular Repolarization in the Genesis of Ventricular Fibrillation in Humans

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Background: We report a well-documented case of a patient, a 62-year-old man, with severe and asymptomatic left main coronary artery disease who had several episodes of silent myocardial ischemia and a syncopal attack during Holter recording.

Methods and Results: Ambulatory monitoring showed isolated giant U waves separated from the T wave 60 minutes before syncope that was due to reversible ventricular fibrillation lasting about 4 minutes and spontaneously reverting to asystole (7 seconds) and then to atrial fibrillation

Conclusion: Our experience suggests that myocardial ischemia may differently affect the repolarization times within the myocardium leading to widely disparate repolarization gradients that may represent the arrhythmogenic substrate for the occurrence of life-threatening ventricular tachyarrhythmias.

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myocardial ischemia; repolarization; ventricular fibrillation

Recent studies have provided evidence of a substantial mass of M cells occupying up to 40% of the left ventricular myocardium and their role in the generation of the U wave.[1-3] Recently, we have discovered a clear relationship between isolated U waves and the onset of VF in a 62-year-old man with significant coronary artery disease (CAD) and frequent episodes of silent myocardial ischemia.[4] After the discovery of the M cells and their relationship with the U wave, we reconsidered the possibility that acute myocardial ischemia may differently affect the repolarization times of myocardium layers including the late repolarization region (M cells), leading to reentrant life-threatening ventricular tachyarrhythmias.

CASE REPORT

Six months before admission the patient, a 62-year-old man, had an uncomplicated anteroseptal myocardial infarction and was referred for a recent brief episode of chest pain at rest. Coronary arteriography showed 90% diameter stenosis of the right coronary artery at origin and 80% diameter stenosis of the left main coronary artery with preserved ventricular function. During Holter monitoring, the patient had a syncopal attack due to a prolonged episode of spontaneously reversible ventricular fibrillation (VF) lasting about 4 minutes and preceded by isolated giant U waves. He was not on pharmacological therapy at the time. VF reverted to an AF at rapid ventricular response. An accurate analysis of Holter recordings revealed frequent episodes of silent myocardial ischemia characterized by both ST-segment elevation and depression; in addition, we observed some interesting findings concerning the U wave: first, isolated giant U waves preceded the onset of VF and appeared to be

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distinct, separate, and opposite from the T waves in the absence of ST change and QT prolongation (Fig.1); second, about 1 minute before the onset of VF, Holter recording documented a postpause augmentation of the U wave with concomitant postpause augmentation of the T wave (Figs. 2A and B), resulting in a more marked and distinct separation of the U wave from the T wave; third, the U waves remained late (600 ms from the QRS complex), again distinct and separate from the T wave in the presence of ST elevation (Fig. 2C) and depression (Fig. 2D); fourth, there was a rate dependency of the amplitude and duration of the U wave (Figs. 2A-C); fifth, the last 2 beats before VF reversion showed uniform QRS morphology, which was totally different from the previous disorganized fibrillation waves (Figs. 3A-B) suggesting a reentry as the mechanism of VF. Creatine phosphokinase isoenzymes and laboratory findings including serum electrolytes were within normal range at the time syncope occurred. The patient underwent immediate surgical bypass graft and was well (follow-up 3 years).

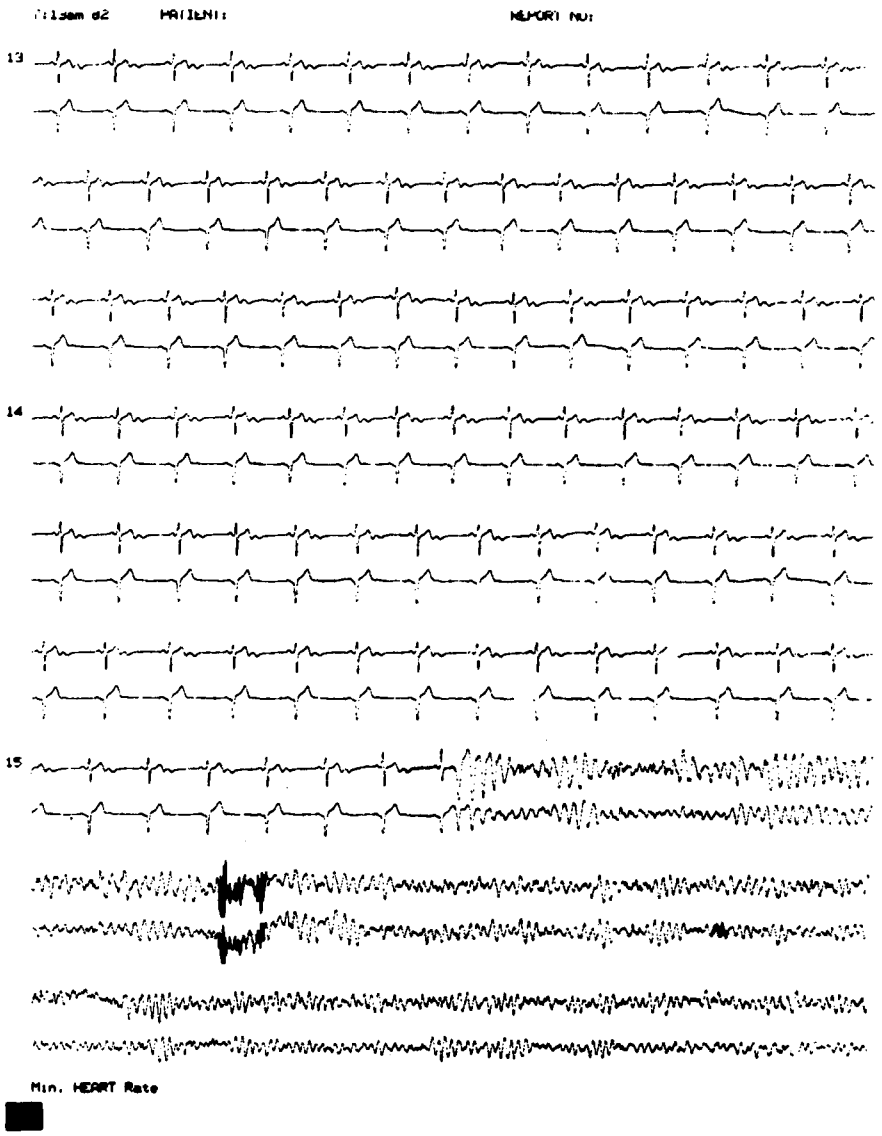

Figure 1. Continuous low speed Holter recording. Note isolated giant U waves before the onset of ventricular fibrillation (VF). The U waves appear to be quite late (600 ms after the onset of the QRS complex) and separate from the T waves.

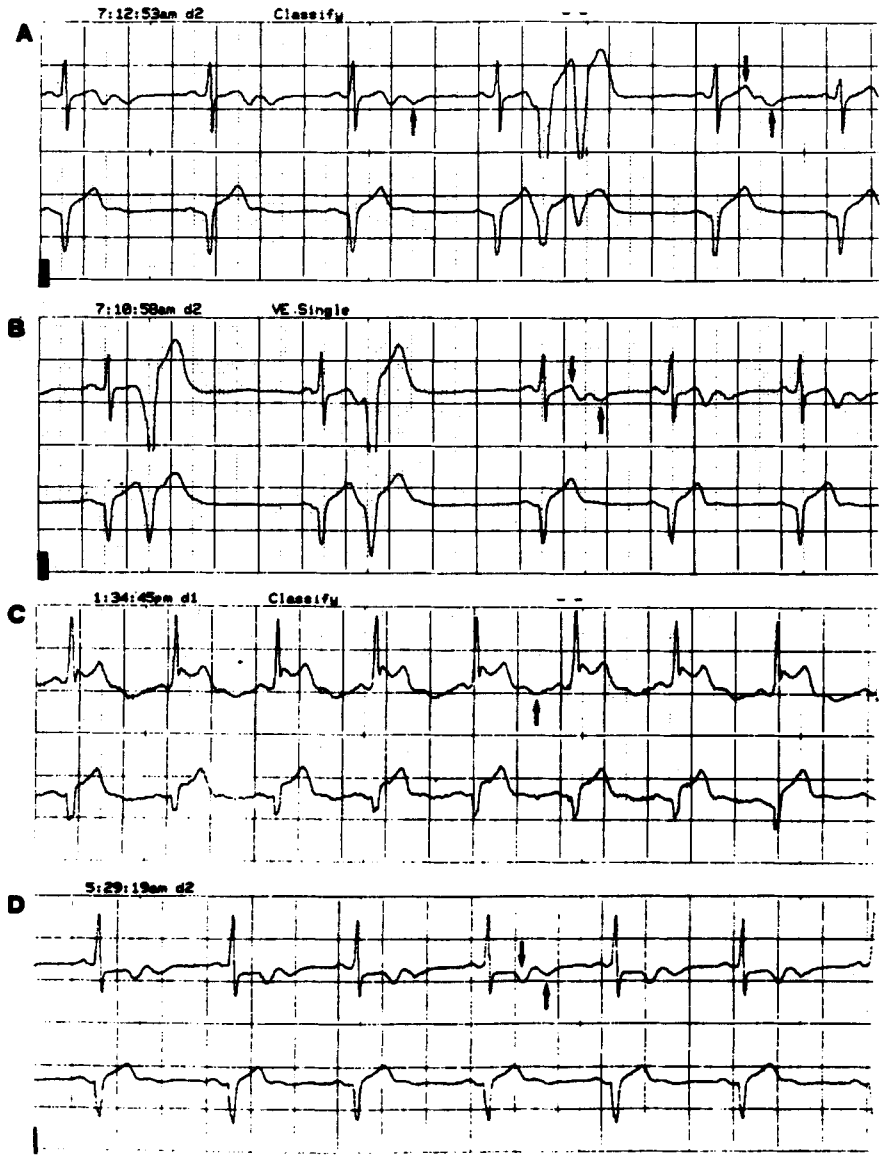

Figure 2. (A, B) Note a postpause augmentation of the U wave (arrow) with concomitant postpause augmentation fo the T wave (arrow) resulting in a more marked separation of the U from the T wave. The U wave remained quite late (600 ms from the QRS complex) and separate from the T wave in the presence of ST elevation (C) and depression (D).

To our knowledge, a well-documented relationship between an isolated giant U wave and the onset of VF has never been reported. The U wave appeared quite late and separate from the T wave, and this would suggest that ventricular repolarization abnormalities in the absence of ST-segment changes may play an important role in precipitating VF in patients with CAD. Our experience appears to be more important after the discovery of M cells, especially when their documented relationship with the U wave on the ECG and supposed potential role in ventricular arrhythmogenicity is considered.[3] It is conceivable that only acute myocardial ischemia of sufficient magnitude, as observed in our case, may affect the substantial mass of M cells (up to 40% of the left ventricular

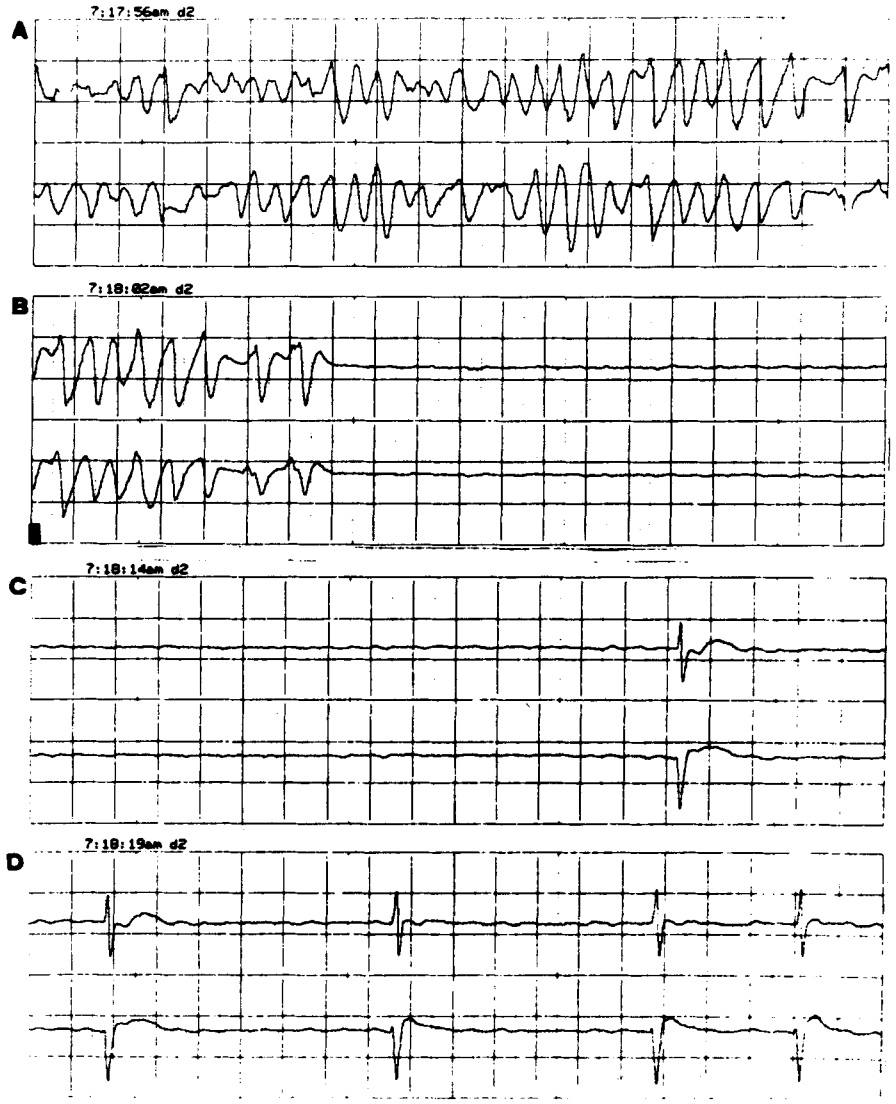

Figure 3. Continuous Holter recording at the time of spontaneous conversion of ventricular fibrillation (VF). Irregular VF waves (A) suddenly change into a more uniform morphology (last 2 beats) just before asystole (B).

wall) producing U waves on the body surface ECG. In our case, the U wave was quite late, peaking approximately 600 ms after the QRS complex (Fig. 2). Therefore, an early premature beat that initiated VF occurring at the peak of the T wave must have propagated irregularly and encountered areas of block from very late repolarizing cells producing opportunities for reentry around the sites of block. Another interesting observation is the finding of U waves separate from T waves (Figs. 1 and 2) that would suggest a relative electrical isolation of the late repolarization region. Since the mass of M cells appears to be substantial, it is conceivable that their electrical isolation could lead to a mid-myocardial "column" of functional refractoriness as hypothesized by Antzelevitch and Sicouri.[2] This, in turn, could explain the development of this very unusual sustained and spontaneously reversible VF. Another interesting finding was a postpause augmentation of the U wave with concomitant postpause augmentation of the T wave (Figs. 2A and B) resulting in a more marked and distinct separation of the U wave from the T wave. This

suggests the presence of widely disparate repolarization times within the myocardium. Immediately before VF reversion, the VF waves appeared to suddenly become more uniform (Fig. 3B), suggesting a reentry as the mechanism of this unusual VF.

CONCLUSION

Our unique experience constitutes strong evidence that very late and widely disparate repolarization times characterized by the presence of isolated U waves distinct from T waves can lead to life-threatening ventricular tachyarrhythmias and sudden death, especially in patients with CAD.

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