Ventricular Fibrillation Occurring on Arousal from Sleep by Auditory Stimuli

By Hein J. J. Wellens, M.D., Aart Vermeulen, M.D., and Dirk Durrer, M.D.

SUMMARY
A patient is described having syncopal attacks on being awakened from sleep by auditory stimuli. The electrocardiogram registered during these episodes showed Q-T-segment changes followed by ectopic ventricular activity and spontaneously ending attacks of ventricular fibrillation. Aside from the attacks, her ECG only showed abnormalities of the S-T segment with marked U waves. Hemodynamic and electrophysiologic studies showed no abnormalities. Coronary angiograms were normal. Following therapy with propranolol and diphenylhydantoin she has been free from syncopal episodes for the past 11 months. The mechanism responsible for the Q-T-segment changes and ventricular tachyarrhythmias is not understood.

Additional Indexing Words: Syncopal attacks Q-T-segment changes Tachyarrhythmias

We recently studied a patient who suffered from repeated attacks of ventricular fibrillation. Initiation, course, and spontaneous termination of the arrhythmia were registered several times. The only abnormality found outside the arrhythmia were abnormalities of the ST-T segment.

Case Report

The patient, a girl, was 14 years old when she lost consciousness for the first time on being awakened one night by a thunderclap. When she regained consciousness a few minutes later, it was noted that she had been incontinent for urine. Thereafter, similar episodes occurred, always on waking up, usually following the noise of the alarm clock. She was admitted elsewhere 4 years later under a tentative diagnosis of epilepsy. The attending cardiologist (Dr. T. Bloem) found that during her fainting spells ventricular fibrillation was present and that the attacks could be provoked by setting off an alarm clock. Thereafter the patient was referred to our department. Physical examination was normal, as were detailed blood and urine laboratory tests, an encephalogram, an electromyogram, and audiometrics.

The ECG showed sinus rhythm, with normal P-Q interval and QRS width. There were S-T-segment changes with marked U waves. The family history was unremarkable. The ECGs of the parents and five siblings of the patient showed normal Q-T segments at rest and following exercise. During the observation period it was repeatedly possible to evoke ventricular fibrillation by awakening her with an auditory stimulus (alarm clock, falling bedpan, rock-and-roll music, etc.). The electrocardiographic events following the auditory stimulus are shown in figure 1. A slight increase in heart rate was accompanied by Q-T prolongation, and T-wave inversion appeared 8 sec after the alarm signal. This was followed by premature beats and further bizarre changes in the Q-T segment. The combination of these Q-T-segment abnormalities and ectopic activity resulted in ventricular premature beats following shortly after the summit of the T wave, leading to ventricular fibrillation. Seven of these episodes were recorded. All ended spontaneously. The longest one lasted 2 min 11 sec. These attacks could not be provoked by exercise, hyperventilation, Valsalva

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maneuver, carotid sinus massage, or frightening her when she was awake. No arrhythmia occurred when she awakened spontaneously.

Right- and left-sided heart catheterization revealed normal hemodynamics during both rest and exercise. No abnormalities were noted in cineangiograms of the left ventricle and coronary arteries. The functional properties of the A-V conduction system as measured by the extrastimulus method were normal. Thereafter the functional refractory period was determined at different sites in right and left ventricle at different driving rates. The stimulus strength of the test pulse was two times diastolic threshold. Recordings were made following at least 200 beats of the new regular driven rhythm.

As shown in table 1, under these circumstances the maximal difference in functional refractory period between different points in right and left ventricle at identical driving rates was 35 msec. During this study no ventricular arrhythmias were initiated, not even by two ventricular premature beats given in the closest possible succession. Following these investigations we started our patient on propranolol, 20 mg four times daily.

The ST-T-segment changes during sinus rhythm seemed to be less than prior to propranolol therapy. Arousal with the alarm clock resulted now only in Q-T changes, but not in ectopic ventricular activity (fig. 2). After this was registered several times she was discharged on propranolol. Three months later she reported to have suffered from another attack. We then added 50 mg diphenylhydantoin four times daily. Since then she has remained free from attacks for the past 11 months.

Discussion

In 1957 Jervell and Lange-Nielsen described a heritable syndrome consisting of syncope and sudden death in patients with deaf mutism and a prolonged Q-T interval. Fraser et al. pointed to the cardiac origin of the syncopal episodes.

Since then patients have been reported with Q-T prolongation and ventricular tachyarrhythmias, but without deafness. In view of the absence of other apparent abnormalities

Table 1

<table>
<thead>
<tr>
<th>Basic cycle length (msec)</th>
<th>Right ventricle</th>
<th>Left ventricle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Apex</td>
<td>Inflow tract</td>
</tr>
<tr>
<td>850</td>
<td>290</td>
<td>290</td>
</tr>
<tr>
<td>667</td>
<td>270</td>
<td>245</td>
</tr>
<tr>
<td>500</td>
<td>230</td>
<td>230</td>
</tr>
</tbody>
</table>

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VENTRICULAR FIBRILLATION

II

V J

400 msec

1000 msec

400 msec

After propranolol therapy no ventricular ectopic activity follows the auditory stimulus.

(such as electrolyte disturbances) these patients have been called examples of the idiopathic Q-T-prolongation syndrome by James. In most, direct familial transmission of the abnormality was assumed, with an autosomal dominant mode of inheritance. The anatomic and pathophysiologic basis for the Q-T prolongation and the arrhythmias is not clear. In patients with the syndrome that came to autopsy changes in conducting tissue and Purkinje fibers have been described by Fraser et al. and Philips and Ichinose.

Both groups considered pathology of the small coronary vessels the most likely cause for their findings. Other theories offered to explain the idiopathic Q-T prolongation include: abnormalities in repolarization of the myocardium caused by metabolic disturbances, a neurogenic etiology with paroxysmal discharges from the central nervous system, and assymetric sympathetic neural stimulation of the ventricular muscle. In favor of the last theory is the observation by Moss and McDonald that right-sided stellate ganglion block resulted in Q-T prolongation, while left-sided stellate ganglion block gave definite shortening of the Q-T interval. In their patient with Q-T prolongation and syncope caused by ventricular tachyarrhythmias a left-sided cervicothoracic sympathetic ganglionectomy resulted in marked shortening of the Q-T interval and disappearance of the syncopal episodes. As a possible mechanism for ventricular tachyarrhythmias and sudden death in patients with idiopathic Q-T prolongation, James postulated abnormalities in the A-V conducting system. He thought that these could lead to a change in properties in the A-V conducting system enabling an early supraventricular impulse to arrive in the vulnerable period of the preceding ventricular complex.

The ECG of our patient showed definite abnormalities of the ST-T segment. The marked U waves made it impossible to determine the true length of the Q-T interval. When auditory stimuli were applied during sleep there were changes in the ST-T segment suggesting marked prolongation of the Q-T interval. This led us to believe that our patient represents another example of the Q-T-prolongation syndrome. Hemodynamic studies and coronary angiography were normal. The A-V conducting system behaved normally when tested by the extrastimulus method.

We examined the possibility that the prolonged Q-T segment was suggestive of increased asynchrony in refractoriness of
different areas of ventricular muscle, predisposing to reentrant ventricular activity.\textsuperscript{13} As shown in table 1, the differences in functional refractory period at identical driving rates at different points of the endocardium of the right and left ventricle were not greater at slow driving rates (70 beats/min) as compared to a faster driving rate (120 beats/min). The greatest difference in refractory period was 35 msec. During these stimulation studies we never were able to initiate a short burst of ventricular premature complexes, not even by two ventricular premature beats given in the closest possible succession. As far as we know, nobody has ever determined functional refractory periods at different ventricular endocardial sites at identical driving rates in the human heart. Data from the ventricular myocardium of the dog heart, however, suggest that our findings might well be in the normal range.\textsuperscript{14-16}

It is obvious, however, that this does not exclude the possibility that in our patient asynchrony in refactoriness of ventricular muscle was present between subendocardial and subepicardial layers, nor that this occurred following neural stimulation or during the first beats following sudden changes in heart rate.

Although it is tempting to speculate upon a relation between strong auditory stimuli and neurophysiologically induced changes in the heart leading to Q-T-segment changes and ventricular ectopic activity, we do not understand the true mechanism leading to the arrhythmia in our patient. As far as we know, the initiation of ventricular tachyarrhythmias by auditory stimuli in patients with the idiopathic Q-T-prolongation syndrome has never been reported. Drug therapy of the syndrome has been disappointing in most cases.\textsuperscript{3-8} Following the suggestion of Garza et al.\textsuperscript{6} we treated our patient with propranolol. As reported above this prevented her from arrhythmias following auditory stimuli during sleep while in the hospital. Three months after discharge, however, she had another syncopal episode. Fortunately the addition of diphenylhydantoin prevented her from further attacks. In case of new occurrences of symptomatic tachyarrhythmias one might consider regular driving of the heart at a relatively fast rate (100 beats/min) to prevent ectopic activity or the intervention described by Moss and McDonald.\textsuperscript{9}

References


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