Torsades de Pointes in a Case of Hypertrophic Cardiomyopathy with Special Reference to the Pathologic Findings of the Heart Including the Conduction System

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SUMMARY

A clinicopathologic study was performed in a 77-year-old female with hypertrophic cardiomyopathy who had experienced recurrent syncopal attacks due to Torsades de Pointes (TdP) following QT prolongation and atrioventricular block. She died suddenly two years later while eating dinner. Pathologic findings of the heart showed a dilated and hypertrophied left ventricle. The heart weighed 550 g. There were two foci of localized endocardial fibroelastosis (EFE) beneath the aortic valve, one with a size of 3.5×3.5 cm, and the other (2×1 cm) located on the upper ventricular septum. Histologic findings showed hypertrophy and disarray in the left ventricular myocardium. The conduction system using serial sectioning revealed remarkable bilateral bundle branch fibrosis and hypertrophied Purkinje fibers in the left bundle branch adjacent to the EFE on the ventricular septum. These findings were thought to be related to the occurrence of TdP. (*Jpn Heart J* 1999; 40: 233–238)

Key words: Torsades de Pointes, Hypertrophic cardiomyopathy, Conduction system, Purkinje fibers

TORSADES de Pointes (TdP) is a life-threatening ventricular tachyarrhythmia, characterized by a torsion of the spikes of QRS complex around the isoelectric line during repetitive episodes.¹⁾ This characteristic arrhythmia is often associated with advanced or complete atrioventricular (AV) block, hypopotassemia, QT prolongation or appears as an adverse effect of antiarrhythmic drugs such as quinidine, procaineamide or disopyramide. Its initiation is assumed to be induced by the phenomenon of early after depolariza-

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tion. However, knowledge of its histopathologic findings in the heart, including the conduction system, has not been fully elucidated. In this report we performed the following clinicopathologic study in an elderly female patient with hypertrophic cardiomyopathy (HCM) showing TdP and sudden death.

CASE REPORT

A 75-year-old female was admitted because of recurrent attacks of syncope. Her ECG showed complete right bundle branch block (CRBBB) at 71 yrs (Figure 1A) and complete left bundle branch block (CLBBB) at 73 yrs (Figure 1B). In mid-July, 1982 she experienced two episodes of syncope and convulsion. Holter monitoring showed 2:1 AV block without any ventricular tachycardia (VT). On August 23rd, 1982 while an ECG was being taken, she suddenly experienced syncope and convulsions. Her ECG showed 2:1 AV block with QT prolongation ($QT_c = 0.79$ sec) followed by PVC in R on T phenomenon and developed to TdP (Figure 1C). At this time serum K was 3.1 mEq/L, serum Mg 1.94 mEq/L. Advanced AV block was also detected (Figure 1D). HIS bundle electrogram

Figure 1. Electrocardiograms. **A.** Complete right bundle branch block (RBBB) on 12/10/1979. **B.** Complete left bundle branch block (LBBB) on 7/30/1982. **C.** Tracings during syncopal episode (on 8/23/1982). 2:1 AV block occurred with QT prolongation followed by PVC on R on T, developing TdP. **D.** After cessation of VT, advanced AV block developed.

Figure 2. Pathologic findings of the heart. **A.** View of the outflow tract of the left ventricle showing dilatation and hypertrophy of the LV and two foci of endocardial fibroelastosis (EFE) (thick and thin arrows) AO = aorta; AV = aortic valve. **B.** Photomicrograph of EFE (EvG $\times 10$) **C.** Photomicrograph, showing muscle fiber disarray (Azan $\times 100$).

(HBE) demonstrated that AV block was induced by HV block. Thereafter a permanent pacemaker (VVI type) was implanted. At 76 yrs she was readmitted due to a reattack of syncope, but no pacing or sensing failure, and no electrolyte imbalance were detected. She was discharged and spent an uneventful life for 1 year. But at 77 yrs (on March 9, 1984) she died suddenly while eating dinner. Autopsy was performed. The heart weighed 500 g, and marked dilatatory hypertrophy of the left ventricle was observed. No significant coronary arterial stenosis, myocardial infarction, valvular heart diseases, myocarditis or right ventricular dysplasia were found. However, two foci of localized endocardial fibroelastosis

Figure 3. Photomicrographs of the conduction system. **A.** Marked fibrosis (arrows) of the conduction cells in the proximal portion of the left bundle branch (LB) (EvG $\times 10$). **B** = branching portion of the His bundle. **B.** Severe fibrosis (arrows) of the first portion of the right bundle branch (RB) (EvG $\times 5$). **C.** Hypertrophied Purkinje fibers (P; arrows) of the LB (anterior fascicle of the left bundle branch) running just beneath the thick EFE. In Purkinje fibers, the elastic fibers had partially migrated in the EFE (EvG $\times 100$)

(EFE) of unknown etiology were observed beneath the aortic valve (Figure 2, A, B). One was large (3.5×3.5 cm, thick arrows) and the other 2×1 cm (thin arrows). The former was located near the region of the anterior fascicle of the left bundle branch (LB), the latter adjacent to the region of the posterior fascicle of LB. The histologic study revealed myocardial hypertrophy and fiber muscle disarray (Figure 2, C), which was compatible with HCM. The study of the conduction system using Lev's method as previously reported²⁾ revealed normal SA and AV nodes and bundle of His, but the proximal portion of the left bundle branch (LB) and the first portion of the right bundle branch (RB) were severely fibrotic (Figure 3, A, B). In the distal portion of the septum near the EFE, hypertrophic Purkinje fibers of the LB were observed and the elastic fibers had partially migrated (Figure 3C).

DISCUSSION

Histopathologic findings of the heart in cases of "QT prolongation" have not been fully elucidated. Hashiba³⁾ reported the pathologic findings in 2 cases of Romano-Ward syndrome, and insisted that in these cases the conventional AV conduction system was not severely affected, but the subendocardial Purkinje cells were markedly enlarged and associated with noninflammatory degeneration.

Bharati *et al.*⁴⁾ also described the conduction system in 5 patients with a prolonged QT interval, showing that all patients had a certain abnormality in the conduction system, although it was not clear how these changes were related to the disturbance in the repolarization process or prolongation of the QT interval. In contrast, Pellegrino *et al.*⁵⁾ reported that 4 such cases did not show pathologic changes in the conduction system, its vascular supply or the surrounding nerve fascicles. In 1976 Rossi *et al.*⁶⁾ reported two cases of TdP associated with AV block. They postulated that the cyclic changes in the QRS axis were due to the bilateral, uneven and partial disruption of the bundle branches. In our case, typical TdP occurred following 2:1 AV block with QT prolongation modified by slight depletion of serum potassium, and she died suddenly. Pathologically marked fibrosis of the bilateral bundle branches corresponded to advanced AV block induced by HV block on HBE, as seen in elderly cases with advanced or complete AV block.²⁾ In addition, this heart had two peculiar EFE foci beneath the aortic valve, which was similar to cases of healed myocardial infarction associated with ventricular aneurysm showing repetitive VT. From this analogy, we were able to speculate that besides advanced AV block, this case might have morphologic evidence of polymorphic VT (TdP) originating from two foci of hypertrophic Purkinje fibers adjacent to the EFE, as suggested by the original description by Dessertenne.¹⁾

In the past several years, remarkable discoveries regarding molecular genetics and channel pathophysiology, such as KVLQT1-LQT1, KCNE1-LQT5, HERG-LQT2 and SCN5A-LQT3, have been made in terms of inherited long QT syndrome.⁷⁻⁹⁾ Our case appeared before the era of such molecular biology and therefore we were unfortunately unaware of the existence of such channel abnormality. The present case may teach us the importance of investigating the anatomical substrate of ventricular tachyarrhythmias such as TdP.

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