Cardiology in the Young

cambridge.org/cty

Immunosuppressant associated torsades de pointes after acute heart rejection in an 8-year-old boy

Liu Hsin-Ming[1], Tseng Wei-Chieh[1] and Chiu Shuenn-Nan[2]

[1]Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan and [2]Department of Pediatrics, National Taiwan University Children's Hospital, Taipei, Taiwan

Brief Report

Cite this article: Hsin-Ming L, Wei-Chieh T, and Shuenn-Nan C (2020) Immunosuppressant associated torsades de pointes after acute heart rejection in an 8-year-old boy. *Cardiology in the Young* **30**: 1194–1195. doi: 10.1017/S1047951120001602

Received: 5 December 2019
Revised: 16 May 2020
Accepted: 28 May 2020
First published online: 30 June 2020

Keywords:
Torsades de pointes; graft rejection; heart transplantation

Author for correspondence:
Dr Chiu Shuenn-Nan, Department of Pediatrics, National Taiwan University Hospital, No. 7, Chung Shan S. Rd. (Zhongshan S. Rd.), Zhongzheng Dist., Taipei 10002, Taiwan. Tel: +886 2 23123456#71710; Fax: +886 2 23147450. E-mail: michael@ntuh.gov.tw

Abstract

Torsades de pointes is a kind of life-threatening ventricular tachyarrhythmia. We report a case of torsades de pointes in an 8-year-old boy with acute rejection after orthotopic heart transplantation. The causes of torsades de pointes could be either congenital or acquired. In this case, various causes including acute rejection-related repolarisation heterogeneity, dose-dependent acquired long QT resulting from treatment with immunosuppressants, and AKAP9 (A-kinase anchoring protein 9) genetic variants are the possible mechanisms.

We report the case of an 8-year-old boy who exhibited torsades de pointes and describe the subsequent treatment. He visited our emergency room presenting with nausea, abdominal distension, and dyspnoea on exertion. He had undergone orthotopic heart transplantation without complications for restrictive cardiomyopathy 2 months earlier. Echocardiography showed a left ventricular ejection fraction of 32%, and endomyocardial biopsy revealed grade 2 moderate acute cellular rejection per the International Society for Heart and Lung Transplantation. We started him on steroid pulse therapy and everolimus. Tacrolimus was titrated to a higher dosage of 0.08 mg/kg daily. The second myocardium biopsy on the 7th day of admission showed decreased cellular rejection (International Society for Heart and Lung Transplantation 1R).

The next day, the boy suddenly collapsed in the paediatric intensive care unit with generalised tonic–clonic movements. The electrocardiogram during the episode showed a pattern of complex T-wave alternans and torsades de pointes triggered by a premature ventricular beat on the T wave (Fig 1). Cardiopulmonary resuscitation was performed immediately. After 3 minutes of resuscitation, spontaneous circulation resumed, and a normal sinus rhythm with QTc of 482 ms was restored, per electrocardiography (Fig 2). Serum electrolyte levels were within the normal ranges, and the serum levels of tacrolimus and everolimus at 8.7 and 3.3 ng/ml, respectively, were within the therapeutic range. His medical records showed his QTc at 401 ms at the time of admission. Two more episodes of torsades de pointes occurred in the subsequent 3 days despite treatment with oral propranolol (1.25 mg/kg daily) and intravenous lidocaine (30 μg/kg per min). We then implanted an implantable cardioverter defibrillator. More than 20 episodes of defibrillator-appropriate shock were recorded in the following 4 days when the serum level of tacrolimus was above the upper limit of the normal range. We therefore tapered tacrolimus to 0.04 mg/kg daily. No more episodes of arrhythmia were documented in the 5 days after defibrillation. The acute rejection subsided, and his heart function returned to normal. Whole-exome sequencing (targeting all reported long QT syndrome and channelopathy genes) showed a non-frameshift insertion (K1335_L1336insQ) in the AKAP9 (A-kinase anchoring protein 9) gene. No further episodes of ventricular tachyarrhythmia or acute rejection were encountered during 2 years of follow-up.

Discussion

Torsades de pointes is a life-threatening ventricular tachyarrhythmia characterized by a continuously changing QRS complex morphology with the electrical axis twisting around the isoelectric line.[1] It is associated with a prolonged QT interval and may be preceded by T-wave alternans, which could be either congenital or acquired.[2,3] The common aetiologies of acquired long QT include electrolyte imbalance and drugs.

In our case, torsades de pointes developed while the dosages of immunosuppressants were being escalated to control acute rejection; however, the drug levels were still within the normal ranges. We attribute the development of long QT to various causes including dose-dependent acquired long QT resulting from treatment with tacrolimus and everolimus, rejection-related repolarisation heterogeneity, and AKAP9 genetic variants. Firstly, tacrolimus and everolimus have been shown to increase the risk of torsades de pointes in a dose-dependent manner.[4,5] Secondly, acute rejection was reported to prolong QT[6] and may increase electrical instability

CAMBRIDGE UNIVERSITY PRESS

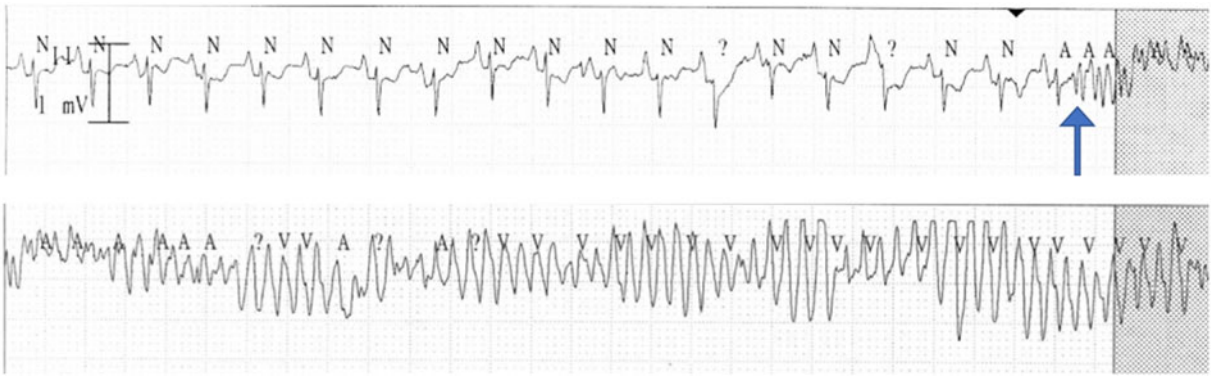

Figure 1. Complex T-wave alternans shown on the electrocardiogram. Torsades de pointes was triggered by a premature ventricular beat (R on T, arrow).

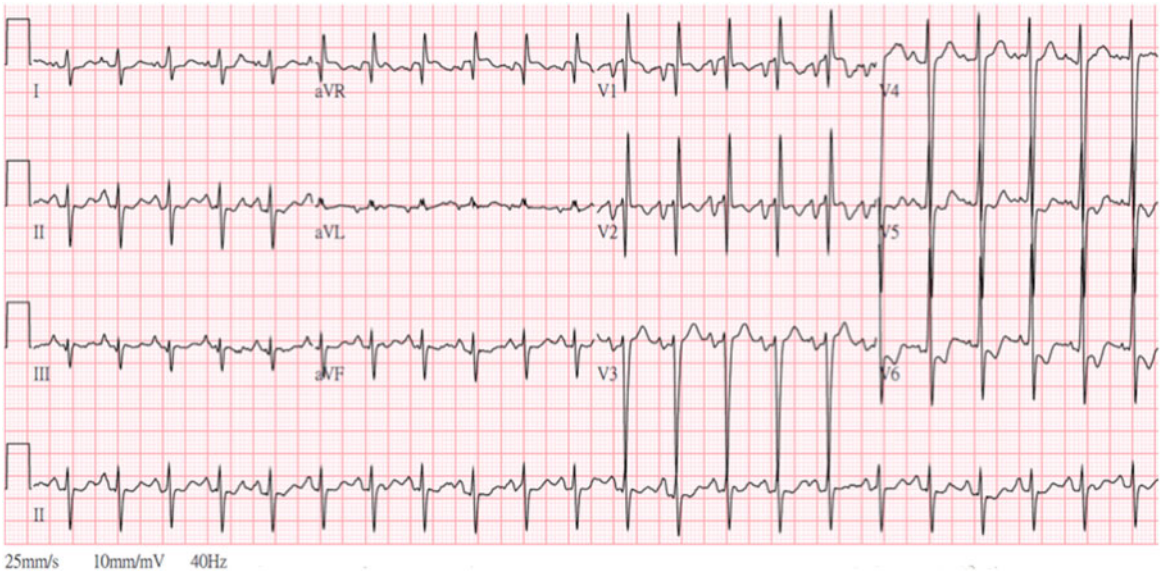

Figure 2. Electrocardiogram after spontaneous circulation was restored. Prolonged QT interval with QTc of 482 ms was observed. Left atrial enlargement, left superior axis deviation, and ST depression at V5 and V6 were also seen.

and repolarisation heterogeneity, contributing to the development of torsades de pointes. Finally, previous studies have suggested that genetic variants, which may not be pathogenic, increase the risk of acquired long QT syndrome.[7] In our case, an AKAP9 variant was speculated to be the culprit. The aforementioned factors combined may have contributed to acquired QT prolongation and repolarisation heterogeneity, causing torsades de pointes ventricular arrhythmia in our patient.

Acknowledgements. None.

Financial Support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflict of Interest. None.

References

1. Dessertenne F. La tachycardie ventriculaire a deux foyers opposes variables. Arch Mal Coeur 1966; 59: 263–272.
2. Takasugi N, Goto H, Takasugi M, et al. Prevalence of microvolt T-wave alternans in patients with long QT syndrome and its association with torsade de pointes. Circ Arrhythm Electrophysiol 2016; 9: e003206.
3. Kukla P, Jastrzębski M, Fijorek K, et al. Evolution in patients with acquired long QT syndrome and torsades de pointes. Ann Noninvasive Electrocardiol 2016; 21: 572–579.
4. Hodak SP, Moubarak JB, Rodriguez I, et al. QT prolongation and near fatal cardiac arrhythmia after intravenous tacrolimus administration: a case report. Transplantation 1998; 66: 535–537.
5. Ikitimur B, Cosansu K, Karadag B, et al. Long-term impact of different immunosuppressive drugs on QT and PR intervals in renal transplant patients. Ann Noninvasive Electrocardiol 2015; 20: 426–432.
6. Richartz BM, Radovancevic B, Bologna MT, Frazier OH. Usefulness of the QTc interval in predicting acute allograft rejection. Thorac Cardiovasc Surg 1998; 46: 217–221.
7. Chiu SN, Huang SC, Wang JK, et al. Implantable cardioverter defibrillator therapy in repaired tetralogy of Fallot after pulmonary valve replacement: Implications for the mechanism of ventricular arrhythmia. Int J Cardiol 2017; 249: 156–160.

https://doi.org/10.1017/S1047951120001602 Published online by Cambridge University Press