

Journal of Atrial Fibrillation



www. jafib.com

Monomorphic Outflow Tract Ventricular Tachycardia: Unique Presenting Manifestation of Gitelman's Syndrome

Subba Reddy Vanga, MD*, Chandra Annapureddy, MD⁺, Mazda Biria, MD*, Dhanunjaya Lakkireddy, MD FACC*.

*Mid America Cardiology @ University of Kansas Hospital, Kansas City, KS. + Howard University Hospitals, ashington, DC.

Introduction

Outflow Tract Ventricular Tachycardia (OTVT) is typically seen in young to middle aged people with structurally normal hearts. These arrhythmias are triggered by emotional or stress factors and that responds to medications. Electrolyte abnormalities rarely cause ventricular arrhythmia. Gitelman's syndrome, a rare autosomal recessive renal disorder causes hypokalemia, metabolic alkalosis and hypomagnesaemia.¹ This disorder is often benign with mild clinical symptoms and excellent long-term prognosis. We present a case of Gitelman's syndrome with symptomatic OTVT as initial manifestation.

Case description

A 27-year old male presented for arrhythmia evaluation after multiple ER visits with symptoms of palpitations, light headedness and near syncope over a period of 2 months. Typical episodes were spontaneous in onset and were not associated with activity or exercise or caffeine intake. They lasted from few seconds to few minutes and are associated with lightheadedness. His past medical history was otherwise unremarkable. His family history is negative for coronary artery disease or sudden death. His alcohol and caffeine intake were not significant and he denied tobacco or illicit drug use. His only medication includes potassium supplements at 20 mEq per day for documented hypokalemia (Serum K+ 3.1 mEq/L; Normal: 3.5 -5.0 mEq/L) during one of his ER visits. Cardiovascular examination revealed a normotensive male with regular rhythm and rate without any murmur or clicks. A 12 lead EKG obtained during his initial office visit showed normal sinus rhythm and QT interval without any obvious pre-excitation or PR prolongation to suggest AV nodal dysfunction. Patient was sent home on a continuous looping event monitor.

Two weeks later he presented to the ER with another episode of palpitations with documented sustained VT. He was found to have hypokalemia (Serum K+ 2.8mEq/L, Normal: 3.5 – 5.0mEq/L) and hypomagnesaemia (Serum Mg++ 0.7 mEq/L; Normal: 1.3 -2.1 mEq/L) during the work up in the ER and was admitted for further evaluation. On repeat questioning, he denied diuretic or laxative abuse. Interim review of his event monitor showed significant arrhythmia burden which accounted for more than 14% of his monitored period, with bigeminy, trigeminy, non sustained and sustained VT. All of his non-sustained and majority of sustained VT were asymptomatic. ECG obtained dur-

Corresponding Address : Dhanunjaya Lakkireddy MD, FACC Associate Professor of Medicine, Director, Center for Excellence in AF & EP Research, Bloch Heart Rhythm Center, Mid America Cardiology @ University of Kansas Hospitals, 3901 Rainbow Blvd, Suite G600, Kansas City, KS 66160.

Journal of Atrial Fibrillation

Figure 1: 12 lead EKG of the patient with Gitelman's Syndrome showing monomorphic Ventricular tachycardia.



ing an episode of VT revealed left bundle branch block morphology with transition in V2/V3 and an inferior axis suggesting the origin from ventricular outflow tract [Figure 1]. The transition in V2/ V3 makes it difficult to diagnose the origin of VT without an EP study.

His biochemistry panel also showed metabolic alkalosis. In the absence of diuretic use and GI losses, it triggered further workup which demonstrated hypocalciuria. His urinary prostaglandins were normal. Plasma renin-activity, aldosterone and cortisol levels were in the upper normal range. Patient had a Thiazide test which demonstrated a blunted diuretic response to thiazide diuretic with lower than the normal (2.2%) fractional chloride clearance.² These findings were suggestive of Gitelman's syndrome. His 2D-Echocardiogram was normal and cardiac MRI ruled out arrhythmogenic right ventricular dysplasia. His arrhythmia improved with intravenous electrolyte replacement alone and hence an electrophysiology study was not undertaken. He required 80 mEq of potassium, 2 grams of magnesium supplements every day and spironolactone was added to maintain his serum potassium and magnesium levels within normal range. Patient remained asymptomatic on oral electrolyte supplementation alone and 24Hour Holter monitor demonstrated less than 10 premature ventricular contractions without arrhythmia at one year follow up.

Discussion

Gitelman's syndrome, also called as familial hypokalemia hypomagnesemia, is a autosomal recessive disorder resulting from a gene (SLC12A3) defect that encodes the renal thiazide-sensitive sodiumchloride co-transporter.^{1,3,4} Secondary to this defect, the biochemical abnormalities closely mimic chronic thiazide diuretic abuse characterized by hypokalemic metabolic alkalosis with significant hypomagnesemia and low urinary calcium excretion. The differential diagnosis of Gitelman's syndrome includes Barter's syndrome and Hereditary Magnesium loosing nephropahthy.⁵ Barter's syndrome is not associated with hypomagnesemia and hypocalcuria while the magnesium loosing nephropathy does not present with hypokalemia. The diagnosis is made on clinical symptoms and biochemical abnormalities. Although genetic testing is available, it is not recommended because of excellent long-term prognosis of this syndrome. Gitelman's syndrome typically adolescence and adulthood manifests during with symptoms of fatigue, muscle weakness,

Journal of Atrial Fibrillation

cramps, and tetany from hypomagnesemia. Acute fluid and electrolyte losses such as dehydration, vomiting or diarrhea can exaggerate or precipitate these symptoms. Gitelman's Syndrome is hereditary, no other first degree relatives of this patient had electrolyte abnormalities.

The mechanism of arrhythmogenesis in Gitelman's syndrome is not clear. Chronic hypokalemia can predispose but not sufficient to generate a symptomatic ventricular arrhythmia. Electrocardiographic abnormalities were studied in Barter's syndrome patients who have predominantly hypokalemia.⁶ Electrocardiograms demonstrated prolongation of QT interval and frequent premature ventricular contractions were noted in 2 patients on Holter monitor. No arrhythmia was documented. Another study specifically looking at cardiac workup in Gitelman's syndrome, found out that QT interval is often prolonged but 24 hour Holter, treadmill exercise, echocardiographic data was unchanged.⁷ Similar changes in QT interval were reported from other study without any documentation of arrhythmia.8

Magnesium deficiency can potentially result in torsades-de-pointes and cardiomyopathy.⁹ Similarly VT was documented in a patient with Magnesium deficiency.¹⁰ A rare case of exercise induced VT in Gitelman's syndrome was that disappeared with electrolyte replacement was reported.¹¹ In another case report VT in a patient with Gitelman's syndrome did not respond to electrolyte replacement but required multiple antiarrhythmic medications and ICD therapy.¹² Rarely this syndrome can present as sudden cardiac death.¹³ Autonomic system imbalance can cause arrhythmia and this patient did not demonstrate any signs or symptoms suggestive of such problem. It is unlikely that this patient had a concurrent idiopathic monomorphic OTVT because the arrhythmia was suppressed with simple electrolyte replacement alone. Premature ventricular contraction might have probably precipitated the arrhythmia in this patient whose substrate was modified from chronic electrolyte imbalance. Recent study supports the role of microvascular dysfunction and myocardial perfusion abnormalities as triggering factors precipitating malignant ventricular arrhythmias in the context of chronic hypokalemia usually present in Gitelman's syndrome patients.¹⁴

Conclusions

Electrolyte imbalance is an easily correctable cause that could be the potentially precipitate or exaggerate an arrhythmia. Every effort should be taken to correct hypokalemia and hypomagnesemia early in the management of an arrhythmia. Rare causes of electrolyte disorders should be kept in differential diagnosis in such cases as these problems will recurs if not treated appropriately. Gitelman's syndrome, a rare cause of hereditary hypokalemic, hypomagnesemic metabolic alkalosis is gaining recognition for its association with cardiac arrhythmia.

Key Words : Gitelman's Syndrome, VT.

References

1. Gitelman, H.J., J.B. Graham, and L.G. Welt, A new familial disorder characterized by hypokalemia and hypomagnesemia. Trans Assoc Am Physicians, 1966. 79: p. 221-35.

2. Colussi, G., et al., A thiazide test for the diagnosis of renal tubular hypokalemic disorders. Clin J Am Soc Nephrol, 2007. 2(3): p. 454-60.

3. Riveira-Munoz, E., et al., Transcriptional and functional analyses of SLC12A3 mutations: new clues for the pathogenesis of Gitelman syndrome. J Am Soc Nephrol, 2007. 18(4): p. 1271-83.

4. Sabath, E., et al., Pathophysiology of functional mutations of the thiazide-sensitive Na-Cl cotransporter in Gitelman disease. Am J Physiol Renal Physiol, 2004. 287(2): p. F195-203.

5. Konrad, M. and S. Weber, Recent advances in molecular genetics of hereditary magnesium-losing disorders. J Am Soc Nephrol, 2003. 14(1): p. 249-60.

6. Blomstrom-Lundqvist, C., et al., Electrocardiographic findings and frequency of arrhythmias in Bartter's syndrome. Br Heart J, 1989. 61(3): p. 274-9.

7. Foglia, P.E., et al., Cardiac work up in primary renal hypokalaemia- hypomagnesaemia (Gitelman syndrome). Nephrol Dial Transplant, 2004. 19(6): p. 1398-402.

8. Bettinelli, A., et al., Electrocardiogram with prolonged QT interval in Gitelman disease. Kidney Int, 2002. 62(2): p. 580-4.

9. Bloom, S., Magnesium deficiency cardiomyopathy. Am J Cardiovasc Pathol, 1988. 2(1): p. 7-17.

10. Phan, T.T., et al., Ventricular tachycardia associated with hereditary magnesium-losing nephropathy. Int J Cardiol, 2006. 113(2): p. e42-3.

11. Nakane, E., et al., Gitelman's syndrome with exercise-induced ventricular tachycardia. Circ J, 2004. 68(5): p. 509-11.

12. Pachulski, R.T., F. Lopez, and R. Sharaf, Gitelman's not-sobenign syndrome. N Engl J Med, 2005. 353(8): p. 850-1.

13. Scognamiglio, R., C. Negut, and L.A. Calo, Aborted sudden cardiac death in two patients with Bartter's/Gitelman's syndromes. Clin Nephrol, 2007. 67(3): p. 193-7. 14. Scognamiglio, R., et al., Myocardial perfusion defects in Bartter and Gitelman syndromes. Eur J Clin Invest, 2008. 38(12): p. 888-95.