e-ISSN 1941-5923 © Am J Case Rep, 2019; 20: 882-885 DOI: 10.12659/AJCR.915943



Authors' Contribution:

Study Design A

Data Collection B

Statistical Analysis C

Marijuana	Induced	Sick	Sinus	Syndrome:
A Case Rep	port			

Data Interp Manuscript Pre Literatu Funds C	pretation D eparation E ADE re Search F Collection G	E 2 Sohaib Khaleel Mohammed F 1 Salman Muddassir
(Corresponding Autho Conflict of interes	r: Arshad Muhammad Iqbal, e-mail: Arshadiqbal9090@gmail.com t: None declared
	Patient	t: Male, 27
	Final Diagnosis	s: Sick sinus syndrome
	Symptoms	s: Syncope
	Medicatior	n: —
(Clinical Procedure	2: —
	Specialty	y: Cardiology
	Objective	e: Rare disease
	Background	d: Marijuana is a commonly abused illicit drug in the United States (US). Regular marijuana usage has been linked to many adverse cardiovascular effects. Our case describes the association of abusing marijuana and the development of sick sinus syndrome.
	Case repor	t: A 27-year-old male carpenter was admitted to the hospital for recurrent syncopal episodes. He reported 2 episodes of syncope every month for the last 5 years. He denied alcohol or nicotine intake but reports using marijuana daily. He also reported cervical injuries due to syncope in the past. Physical examination was unremarkable. Orthostatic vitals were negative. Electrocardiogram (ECG) showed sinus bradycardia. A series of investigations, including a stress test and tilt table testing, were negative. The drug screen was positive for marijuana. A loop recorder was implanted to evaluate the cause of syncope and was positive for a long sinus pause of more than 3 second, indicative of sick sinus syndrome. The patient was successfully treated with a permanent pacemaker with no further events on follow-up after 6 months.
	Conclusion	5: The case we report here adds to the literature that several reversible etiologies are shown to be associated with the development of sick sinus syndrome, in which marijuana abuse can be one of them. We strongly suspect that marijuana was the cause of this patient's sick sinus syndrome after ruling out all the possible etiologies. The relation between marijuana use and sick sinus syndrome needs to be further investigated in the future.
	MeSH Keywords	s: Bradycardia • Marijuana Abuse • Sick Sinus Syndrome • Syncope
	Full-text PD	F: https://www.amjcaserep.com/abstract/index/idArt/915943





ABCDEF 1 Arshad Muhammad Iqbal CDEF 1 Ateeq Mubarik

- E 1 Venkatesh Gupta Cheetirala
- E 2 Sohaib Khaleel Mohammed

1 Department of Internal Medicine, Oak Hill Hospital, Brooksville, FL, U.S.A. 2 Department of Cardiology, University of Louisville School of Medicine, Louisville, . KY, U.S.A.



Background

Marijuana (cannabis) is a commonly abused substance in the United States (US) and is one of the oldest drugs in use [1]. With more acceptability for its use and the changing laws for legalization of marijuana and the increasing awareness about it as a pain medication has led to increased usage [1]. Smoking marijuana regularly has many adverse cardiovascular effects. In most young and healthy users, the cardiovascular effects are not that serious, although some adverse effects have been reported. In users with cardiac diseases, marijuana use poses health risks because of increased catecholamine levels and cardiac work [2]. Our case describes the relation between marijuana abuse and sick sinus syndrome, a potentially life-threatening side effect of the drug.

Case Report

A 27-year-old male carpenter was admitted to the hospital for recurrent syncopal episodes. He reported 2 episodes of syncope every month for the last 5 years. There was no family history of syncope, ischemic heart disease, sudden death, or any acquired cardiac conditions. He reported an accident in the past, which happened due to a syncopal episode, and resulted in cervical injuries. He denied alcohol or nicotine use but reports using marijuana daily. Physical examination revealed a healthy



NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

appearing male in no acute distress with a resting heart rate at 54 beats per minute, blood pressure 126/74 mmHg and respiratory rate of 16 breaths per minute. Orthostatic vitals were normal. Examination of the cardiovascular system (CVS) did not reveal any abnormality and showed normal heart sounds with no gallops, rubs, or murmurs. There was no cyanosis, clubbing, or peripheral edema. The chest was clear to auscultation. Initial laboratory tests, including complete blood count, cardiac troponins, thyroid stimulating hormone, and electrolytes, were normal. The urine drug screen was positive for marijuana. Resting electrocardiogram (ECG) showed sinus bradycardia with ventricular rate of 43 beats/minute with no evidence of atrioventricular block, sinus pause, or ischemic changes (Figure 1). The transthoracic echocardiogram performed during hospitalization showed a normal ejection fraction, without any structural, valvular, and/or wall motion abnormalities. Additionally, myocardial perfusion stress test and tilt table test were also insignificant. Interestingly, no syncopal episodes were observed during his initial hospitalization, so the patient was discharged with a loop recorder. The patient was readmitted within 1 week of discharge with another episode of syncope. Recordings from a loop recorder found sinus pause of more than 3 seconds (Figure 2). Occasional runs of atrial fibrillation were detected on cardiac monitor during hospitalization. Sick sinus syndrome was diagnosed based on these findings. Given his occupation and the previous history of a road traffic accident, he subsequently underwent implantation of a dual

> Figure 1. Twelve lead electrocardiogram (ECG) showing sinus bradycardia with the heart rate of around 43 beats/ minute. There is no ST segment changes except some non-specific T wave inversion in lead aVL. There is no evidence of atrioventricular block, sinus pause or ischemic changes.



chamber permanent pacemaker. Post-discharge, the patient was followed for 6 months, but there was no syncopal recurrence or any new symptoms.

Discussion

Sick sinus syndrome is characterized by the inability of heart to perform its pacemaking function. It encompasses various arrhythmias like bradyarrhythmias with or without associated tachyarrhythmias [3]. Marijuana is now legalized in most of the states in the US and is one of the commonly abused illicit drugs [4]. The cardiovascular effects of marijuana include bradycardia, sinus pauses, tachycardia, and orthostatic hypotension [3]. The underlying mechanism of this is either sympathetic or parasympathetic drive [5]. Marijuana decreases the amplitude of P-wave, significantly decreases the mean sinoatrial time, and mean atrioventricular conduction time. It causes atrial and ventricular arrhythmias [5].

Sick sinus syndrome can be caused by intrinsic and/or extrinsic factors which interrupt with the sinoatrial nodal function [6–10]. Intrinsic causes include sinoatrial nodal remodeling, ion channel dysfunction, and sinoatrial nodal fibrosis [6,7,10]. Extrinsic factors include metabolic disturbances, autonomic dysfunction, and medications including calcium channel blockers, antiarrhythmics, beta blockers, sympatholytic medications, digoxin, and lithium [10,11].

Sick sinus syndrome is often asymptomatic in its early course, but advanced disease presents with end-organ hypoperfusion symptoms, the most common being cerebral hypoperfusion which causes syncope [7,12]. Other manifestations include fatigue, transient lightheadedness, palpitations, angina,

References:

- 1. Hasin DS: US epidemiology of cannabis use and associated problems. Neuropsychopharmacology, 2018; 43(1): 195–212
- 2. Jones RT: Cardiovascular system effects of marijuana. J Clin Pharmacol, 2002; 42(S1): 58S-63S
- 3. Semelka M, Gera J, Usman S: Sick sinus syndrome: A review. Am Fam Physician, 2013; 87(10): 691–96
- 4. Rezkalla S, Kloner RA: Cardiovascular effects of marijuana. Trends Cardiovasc Med, 2018 [Epub ahead of print]
- Huestis MA: Pharmacokinetics and metabolism of the plant cannabinoids, delta9-tetrahydrocannabinol, cannabidiol and cannabinol. Handb Exp Pharmacol, 2005; (168): 657–90
- Dobrzynski H, Boyett MR, Anderson RH: New insights into pacemaker activity: Promoting understanding of sick sinus syndrome. Circulation, 2007; 115(14): 1921–32
- 7. Adán V, Crown LA: Diagnosis and treatment of sick sinus syndrome. Am Fam Physician, 2003; 67(8): 1725–32

confusion, congestive heart failure, transient ischemic attacks, stroke, gastrointestinal symptoms, and/or oliguria [7,12,13].

ECG findings for consideration of sick sinus syndrome requires bradyarrhythmias like sinoatrial pauses, sinoatrial exit block, sinus bradycardia, or sinus arrest [6–8]. However, in early disease course, these findings are often normal [8,14,15].

Sick sinus syndrome is diagnosed by associating the end-organ hypoperfusion symptoms like syncope with bradycardia [7]. Only marked bradycardia is not the diagnostic of sick sinus syndrome in the absence of other symptoms [8,16]. Cardiac monitoring is done when ECG is not diagnostic [14]. Sinoatrial nodal pause of more than 3 seconds on carotid massage, also suggest sinoatrial node dysfunction [7,14,17].

Permanent pacemaker placement is the recommended treatment for sick sinus syndrome. In chronic sick sinus syndrome that is not due to extrinsic factors, it is the only effective intervention [6,7,15].

Conclusions

The case we report here adds to the literature that several reversible etiologies are shown to be associated with the development of sick sinus syndrome, in which marijuana abuse can be one of them. We strongly suspect that marijuana was the cause of this patient's sick sinus syndrome after ruling out all the other possible etiologies. Marijuana induced asystole, vasovagal syncope, and cardiac arrest have been documented in the past, but sick sinus syndrome has not yet been reported [18,19]. The relation between marijuana use and sick sinus syndrome needs to be further investigated in the future.

- 9. Demoulin JC, Kulbertus HE: Histopathological correlates of sinoatrial disease. Br Heart J, 1978; 40(12): 1384–89
- Mangrum JM, DiMarco JP: The evaluation and management of bradycardia. N Engl J Med, 2000; 342(10): 703–9
- 11. Oudit GY, Korley V, Backx PH, Dorian P: Lithium-induced sinus node disease at therapeutic concentrations: Linking lithium-induced blockade of sodium channels to impaired pacemaker activity. Can J Cardiol, 2007; 23(3): 229–32

Epstein AE, DiMarco JP, Ellenbogen KA et al: ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons [published corrections appear in J Am Coll Cardiol, 2009; 53(16): 1473, and J Am Coll Cardiol, 2009; 53(1): 147]. J Am Coll Cardiol, 2008; 51(21): e1–e62

- 12. Zipes DP, DiMarco JP, Gillette PC et al: Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. (Committee on Clinical Intracardiac Electrophysiologic and Catheter Ablation Procedures). Developed in collaboration with the North American Society of Pacing and Electrophysiology. J Am Coll Cardiol, 1995; 26(2): 555–73
- 13. Rodriguez RD, Schocken DD: Update on sick sinus syndrome, a cardiac disorder of aging. Geriatrics, 1990; 45(1): 26–30, 33–36
- 14. Keller KB, Lemberg L: The sick sinus syndrome. Am J Crit Care, 2006; 15(2): 226–29
- Lamas GA, Lee KL, Sweeney MO et al: Mode selection trial in sinus node dysfunction. Ventricular pacing or dual-chamber pacing for sinus node dysfunction. N Engl J Med, 2002; 346(24): 1854–62
- Hilgard J, Ezri MD, Denes P: Significance of ventricular pauses of three seconds or more detected on twenty-four-hour Holter recordings. Am J Cardiol, 1985; 55(8): 1005–8
- Moya A, Sutton R, Ammirati F et al: Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS). Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J, 2009; 30(21): 2631–71
- Akins D, Awdeh MR: Marijuana and second-degree AV block. South Med J, 1981; 74(3): 371–73
- 19. Dockery BK, Newman KP: Exercise-induced asystole with syncope in a healthy young man. Am J Med Sci, 2007; 334(2): 145–48