Transient sinus node dysfunction with acute hepatitis of unknown etiology

Ahmed R. Al-Fagih, MBBS, ABIM, *Saleh A. Al-Ghamdi,* MBBS, CABP, *Khaled G. Dagriri,* MBBS, CABP, *Ahmed S. Al-Malki,* MBBS, ABIM.

ABSTRACT

نعرض حالة مريض ذكر يبلغ من العمر 72 عام، مصاب بداء السكري المعتمد على الأنسولين، وقد أحيل إلينا كحالة إحصار أذيني بطيني تام. وقد تبين أن المريض مصاب بالتهاب كبدي حاد بالإضافة إلى إصابته خلال ذلك بعدم انتظام قلبي أذيني عابر، واعتلال العقدة الجيبية الأذينية. وقد زالت الأعراض القلبية تماماً بعد تحسن الالتهاب الكبدي لديه، إذ أظهرت جميع فحوصاته القلبية التي شملت مخطط القلب الكهربائي، والأشعة الصوتية، واختبار جهد الثاليوم نتائج طبيعية. ولم تظهر نتائج متابعة فحوص الهولتر التي أجريت له خلال مراجعته للعيادة بعد 3 شهر، و 6 شهر وجود عدم انتظام في ضربات القلب. كما أفاد المريض عدم تعرضه للخفقان القلبي، أو أعراض ما قبل الإغماء. وقمنا من خلال هذا البحث باستعراض منهجي بشأن العلاقة بين التهاب الكبد وعدم انتظام ضربات القلب.

We reported a case of a 72-year-old male, known diabetic on insulin, referred because of complete atrioventricular block. He was found to have acute hepatitis during which he developed transient atrial arrhythmia, and sinus node dysfunction. His cardiac symptoms disappeared completely after hepatitis improvement. All of his cardiac investigations were normal including electrocardiogram, echocardiography and thalium stress test. At 3 and 6 months follow up, his Holter monitoring did not show any further arrhythmia, and he denied any further episodes of palpitation or pre-syncope. We reviewed the literature regarding the relationship between hepatitis and atrial arrhythmia.

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From the Department of Adult Cardiology (Al-Fagih, Al-Ghamdi, Dagriri), Prince Sultan Cardiac Center and the Department of Gastroenterology (Al-Malki), Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Ahmed R. Al-Fagih, Department of Adult Cardiology, Prince Sultan Cardiac Center, Riyadh, Kingdom of Saudi Arabia. Tel. +966 (1) 4777714. Ext. 8765. Fax: +966 (1) 4778771. E-mail: aafagih@yahoo.com

Wide ranges of cardiac manifestations during the course of acute hepatitis have been reported in small retrospective studies[1-3] mostly associated with electrocardiogram (ECG) changes. Most commonly associated manifestations were clinically non significant and very unlikely to be associated with hemodynamic instability. Multiple mechanisms might be involved in acute hepatitis that can affect the cardiac system, including autoimmune mechanism, medication, and electrolyte disturbance, especially in older age.[4] In our case, we describe sinus node dysfunction (SND) secondary to acute hepatitis, which is very rare and transient, completely recovered with supportive management.

Case Report. A 72-year-old male, known diabetic on insulin, referred as a case of complete atrioventricular (AV) block with possible inferior myocardial infarction. He reported sudden onset epigastric pain associated with nausea and frequent vomiting for one day. Initial 12 lead ECG from another hospital showed junctional escape rhythm at the rate of 48/minute, with no evidence of ischemic changes (**Figure 1**). His blood pressure was 70/40 mm Hg and his temperature was 38.5˚C. He was resuscitated with intravenous fluid and atropine. Initial blood investigations were within normal limits and septic work-up and ultrasound imaging did not identify an infective cause. One day after arrival to our hospital, his 12 lead ECG showed normal sinus rhythm, total creatinine kinase was normal, and cardiac troponin was negative. Other blood investigations are shown in **Table 1**. Screening for hepatitis A, B, and C were negative as well as for Epstein-Barr virus and cytomegalovirus. Autoimmune markers such as anti-nuclear antibody and anti double-stranded DNA were negative. During telemetry, he had episodes of atrial arrhythmias and prolonged pauses (**Figures 2a & 2b**). His echocardiography as well as Persantine thallium stress test were essentially normal. All of his blood parameters returned to the normal limits within a one-week period, and there was no arrhythmia reported afterward. His 12 leads ECG on discharge showed sinus

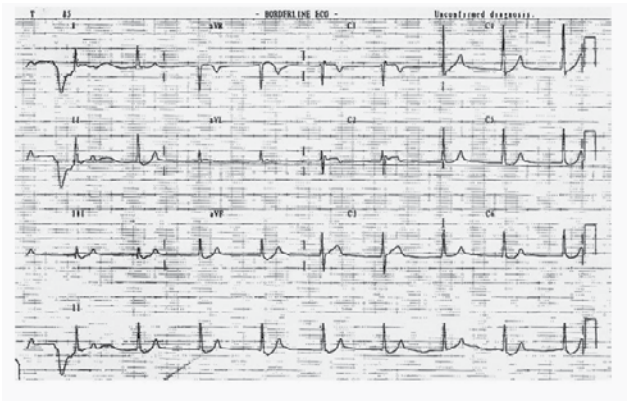

Figure 1 - Twelve-lead electrocardiogram showed junctional escape rhythm at a rate of 55/minute.

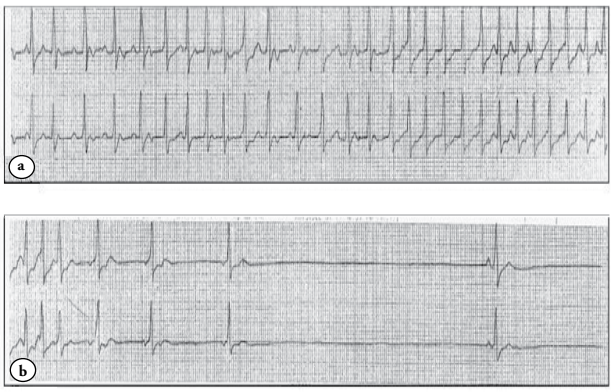

Figure 2 - Rhythm strip shows **a)** atrial arrhythmia with rapid ventricular response and **b)** prolonged sinus arrest for 4.8 seconds.

Table 1 - Results of blood investigations at presentation and on discharge.

Parameter	At presentation	On discharge	Normal range
Aspartate transaminase (U/L)	2215	18	2 - 37
Alanine transaminase (U/L)	5205	78	2 - 40
Alkaline phosphatase (U/L)	259	112	40 - 129
Total Bilirubin (umol/L)	44	9	2 - 22
Lactate dehydrogenase (U/L)	1223	149	135 - 225
Total creatine kinase (U/L)	63	18	50 - 195
Urea (mmol/L)	17.6	3.3	2.3 - 7.5
Creatinine (umol/L)	145	68	50 - 115
Platelets (x10^9/L)	88	374	150 - 450
International normalized ratio	1.8	1.0	0.8 - 1.2

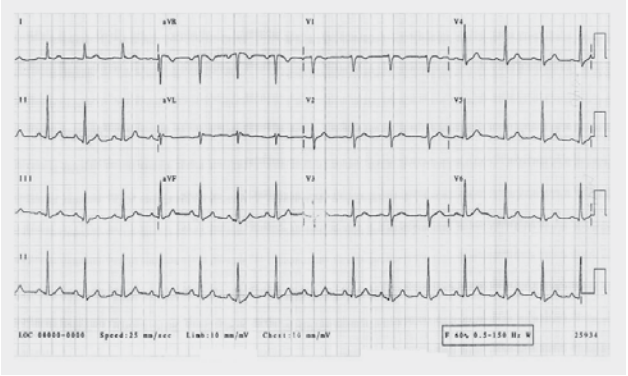

Figure 3 - Twelve-lead electrocardiogram shows normal sinus rhythm at rate of 90/minute.

rhythm at the rate of 90/minute (**Figure 3**). There were no arrhythmia recorded in Holter monitoring at 3 and 6 months follow, and he denied any further episodes of palpitation or pre-syncope.

Discussion. A retrospective analysis of the ECG of 20 patients out of 46 with acute hepatitis in one of Italian studies shows that, the most commonly associated manifestations were clinically non significant and very unlikely to be associated with hemodynamic instability. Fifty percent of these changes were seen mainly in P waves, and ST-segments followed by conduction disorders in the form of right bundle branch block, and left bundle branch block in 35% of cases. Junctional rhythm was seen only in one case. In review of the literature, one case report of complete heart-block associated with amoebic hepatitis. The heart block disappeared and the Stokes-Adams attacks ceased shortly after the start of therapy with emetine[5] In another case reported by Kontaxis et al,[6] of a complete heart block in a child following infectious hepatitis required permanent pacing pacemaker implantation. Significant bradycardia and hypotension were reported in a patient with hepatitis A, and progressive cholestasis improved with corticosteroid therapy.[7] A pacemaker was required in another case as of severe and unresponsive bradycardia associated with viral hepatitis.[8] In our case acute hepatitis of unknown aetiology without significant hyperbilirubinemia has been associated with transient dysrhythmia in the form of tachy-bradyarrhythmia in the absence of cardiac ischemia. Recovered completely without sequelae after resolution of acute hepatitis. Although the exact etiology usually is not identified, most cases are believed to be attributable to a combination of intrinsic and extrinsic influences. The most common intrinsic causes are idiopathic degenerative disease, coronary artery disease, and age-related down-regulation of calcium channel expression in the sinus node.[4] The most common extrinsic causes are medications and autonomic hyperactivity.[9] Cardiomyopathy, myocarditis/pericarditis and autoimmune disease also may cause intrinsic SND. Medications that depress sinus nodal function often are implicated as the cause of SND including Beta-

blockers, calcium channel blockers, cardiac glycosides, and membrane-active antiarrhythmics (amiodarone, sotalol, bretylium), less commonly, phenytoin, amitriptyline, lithium, and phenothiazine. Autonomic dysfunction may be caused by vagal stimulation slowing the sinus rate and lengthening the refractory period of the sinus node. Carotid sinus syndrome has been associated with increased vagal tone that infrequently leads to symptomatic bradyarrhythmia, electrolyte imbalance (for example, hypokalemia or hypocarbia), hypothyroidism or hyperthyroidism, hypothermia, and sepsis.

In conclusion, multiple mechanisms might be involved in acute hepatitis that can affect the cardiac conduction system, including autoimmune mechanisms, medication, and electrolyte disturbance, especially in older age. We were not able to identify a specific cause during the acute hepatic derangement for SND. Idiopathic degenerative disease of the atrium and sino-atrial junction could explain the situation, but complete recovery of the node associated with complete resolution of the illness suggests that other mechanisms are attributing to the aging heart.

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