

Contribution of autonomic nervous system exploration in the diagnosis of symptomatic sinus bradycardia - A report of two cases

Lalla Fatima Ezzahra El-Hassani¹, Amine Ahmindach¹, Ilyas El-Kassimi^{2*}, Salwa Cheraou¹, Halima Benjelloun³, Fellat Roukia³, Mohamed Cherti¹

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A symptomatic sinus bradycardia is a very common situation in cardiology for which the diagnostic and therapeutic management are far from being well codified. After ruling out the obvious and reversible causes, the differential diagnosis between sinus bradycardia caused by vagal hypertonia and sinus

dysfunction is often not easy subjecting the patient to electrophysiological exploration. We report 2 cases of permanent sinus bradycardia for which a non-invasive exploration of the autonomic nervous system (ANS) has led to the diagnosis of vagal hypertone bradycardia, in the first case after electrophysiological exploration, whereas in the second case the electrophysiological study was not performed.

Key Words: Nervous system; Symptomatic sinus; Bradycardia; Electrophysiological

INTRODUCTION

Symptomatic sinus bradycardia (SB) is a special entity whose prognosis depends strongly on etiology. Even after ruling out the obvious and reversible causes, in its etiological diagnosis approach, it is often difficult to differentiate a SB caused by benign vagal hypertonia from an organic sinus dysfunction requiring the implantation of a Pace maker. In order to cope with this dilemma, it is often necessary to resort to invasive complementary explorations which may in some cases fail to reveal a specific etiology; while a simple detailed study of the autonomic nervous system (ANS) could contribute to the diagnosis and put the patient on the right therapeutic path.

CASE REPORTS

Case 1

A 51-year-old woman started complaining of extreme fatigue associated with migraine six months before her visit to our department for which she was prescribed vitamins and paracetamol by her family physician. She has no medical history and did not take any bradycardic medication. She denies chest pain, breathlessness or syncope. The physical examination was normal except for a regular heart rate (HR) of 40 beat per minute (bpm). Her blood pressure was 110/60 mmHg, with a heart rate of 40 bpm. Cardiovascular and pulmonary auscultation were normal, thyroid palpation showed no node or thyroid enlargement, abdominal and neurological examinations were normal Her ECG showed a sinus bradycardia of 45 bpm, heart axis at -19°, PR of 140 ms, thin QRS and normal QTc (Figure 1).

Chest x-ray was normal, blood tests including troponin, renal function, hepatic function, TSH, electrolytes, calcium and phosphore were normal. Echocardiography showed a normal heart structure and function. Holter ECG showed a sinus bradycardia during most of the nyctemer (daytime average HR of 47 bpm and nocturnal average HR of 35 bpm) interspersed by few episodes of sinus tachycardia with a maximum HR of 130 bpm, it showed no atrial or ventricular arrhythmias nor conduction abnormalities, the QT was normal. Exercise testing showed an increase in HR from 45 bpm at rest to 110 bpm at the first level, the test was stopped at the third level of Bruce protocol at 85% of the theoretical maximal heart rate for shortness of breath with no ischemic or rhythmic events.

The electrophysiological study (EP study) in Figures 2 to 5 does not find any evidence for an intrinsic impairment of sinus function or atrioventricular conduction, namely: the conduction intervals in the basic state are normal

with AH=116 ms, HV=55 ms, the corrected sinus node recovery time is normal (CSRT) at 134 ms, eliminating sinus dysfunction. The anterograde refractory period of the atrioventricular node or Wenckebach point is 680 ms with a suprahisian block. The administration of atropine leads to an acceleration of heart rate from 47 to 73 bpm. The carotid massage on the right and the left does not trigger any abnormality.

Exploration of the autonomous nervous system (ANS) was requested to establish a diagnosis, and showed the following autonomic profile: Vagal hyperactivity, central and peripheral alpha sympathetic hyperactivity, weak central and peripheral beta sympathetic activity and a mild baroreceptor abnormality. The patient was prescribed hygienic and dietary measures including high liquid intake, salt-enriched diet, compression stockings and pharmacological therapy phenobarbital 10 mg bid which allowed relieving the symptoms and raising the HR to 55 bpm. The follow-up at 9 months is satisfactory.

Case 2

A 48-year-old former smoker male was referred for symptomatic bradycardia. He complained of headaches followed in neurology for 7 years. His headaches are associated with sweating, vomiting and vertigo that worsen in times of

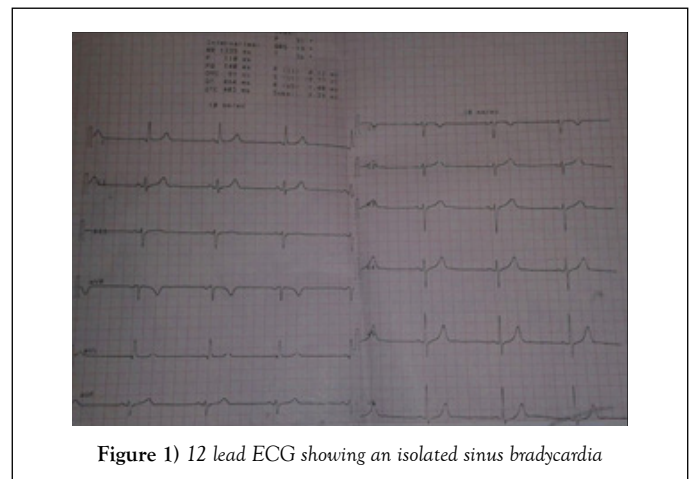


Figure 1) 12 lead ECG showing an isolated sinus bradycardia

¹Department of Cardiology "B", Ibn Sina University Hospital Center, Rabat, Morocco, ²Department of Internal Medicine, Mohammed V Military teaching Hospital, Rabat, Morocco, ³Department of Cardiology "A", Ibn Sina University Hospital Center, Rabat, Morocco.

Correspondence: Ilyas El-Kassimi, M.D., Department of Internal Medicine, Mohammed V Military Teaching Hospital, Rabat, Morocco, Tel: +212614742828, email: dr.elkassimiiyas@gmail.com.

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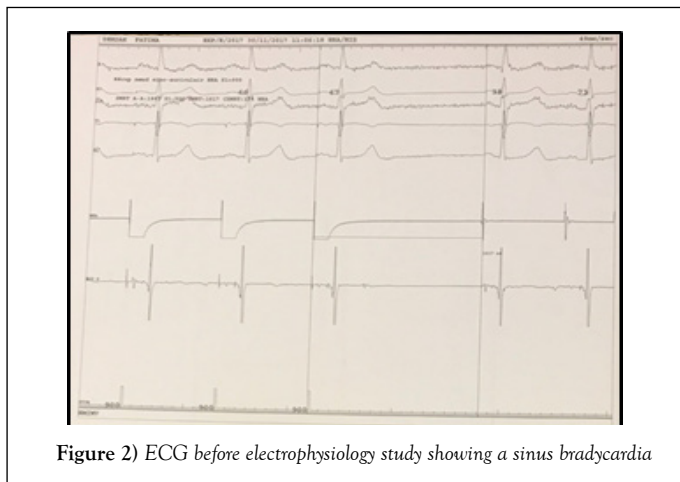


Figure 2) ECG before electrophysiology study showing a sinus bradycardia

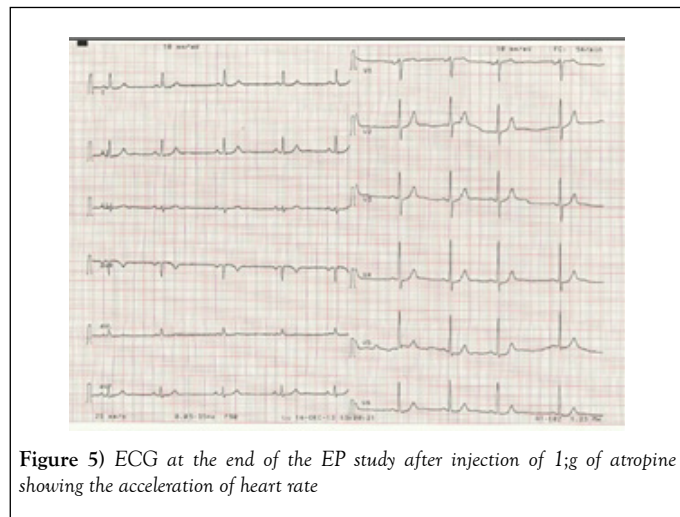


Figure 5) ECG at the end of the EP study after injection of 1g of atropine showing the acceleration of heart rate

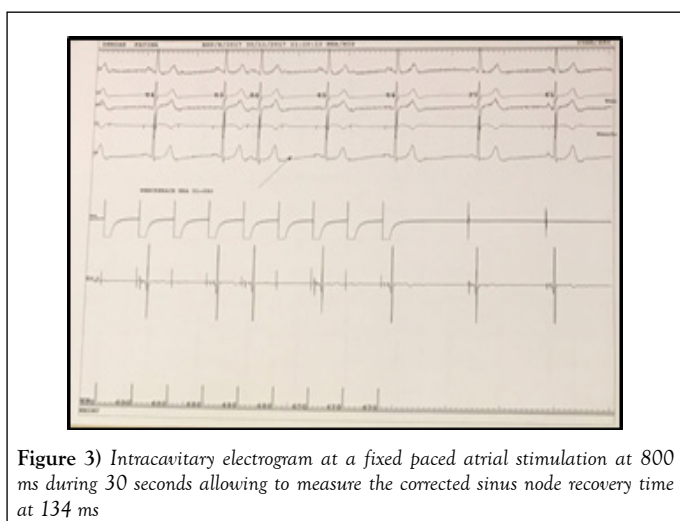


Figure 3) Intracavitary electrogram at a fixed paced atrial stimulation at 800 ms during 30 seconds allowing to measure the corrected sinus node recovery time at 134 ms

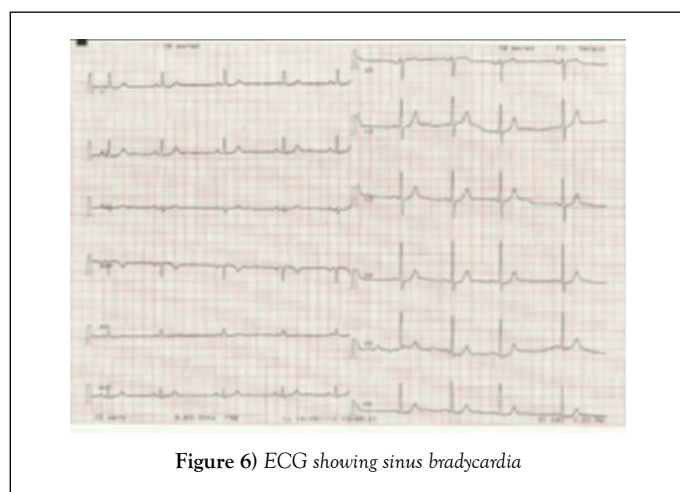


Figure 6) ECG showing sinus bradycardia

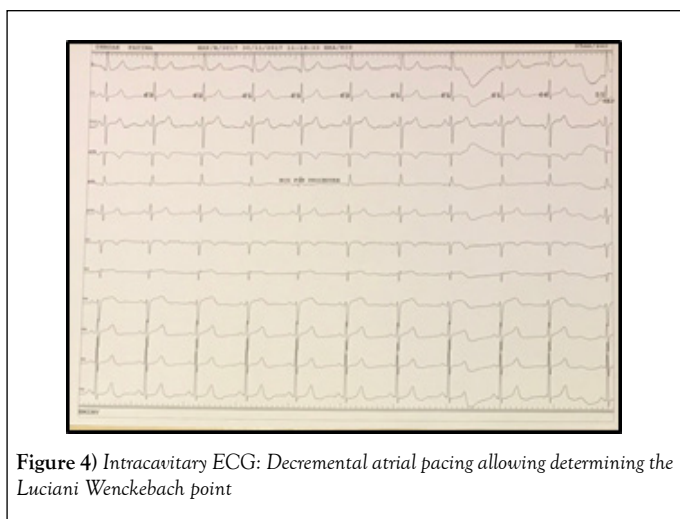


Figure 4) Intracavitary ECG: Decremental atrial pacing allowing determining the Luciani Wenckebach point

stress and after insomnia. The presence of familial bradycardia (sister and son) was noted. Physical examination was normal, the ECG showed a sinus bradycardia at 48 bpm, cardiac ultrasound imaging was normal, Holter ECG showed daytime sinus bradycardia as low as 34 bpm associated with pauses of less than 2 seconds. Exercise test showed a good adaptation of heart rate and blood pressure to stress. The ANS exploration found an increased vagal tone associated to a central α and β sympathetic hyperactivity. A phenobarbital-based treatment was administered with good clinical evolution (Figure 6).

DISCUSSION

Sinus bradycardia (SB) is defined as an electrical impulse that originates in the sinus node but with a frequency of less than 60 cycles per minute. It is mild between 50 and 59 bpm, moderate between 40 and 49 bpm and severe below 40 bpm. It can be caused by either an organic sinus node involvement (degenerative, ischemic, infiltrative, and inflammatory), or a functional impairment: (drug intake, dyskalemia, hypothyroidism, hypothermia, hypoglycemia, peptic ulcer or vagal hypertension).

The sinus node (SN) is the heart's main pacemaker, its cells have the ability to automatically generate a spontaneous action potential at a frequency of 80 to 100 cycles per minute by means of the pacemaker current (I_f) responsible for a slow and spontaneous diastolic depolarization until reaching the activation threshold of an action potential that propagates in the rest of the cardiac conductive tissue. To adapt this intrinsic automatism of the heart to different physiological states, SN is regulated by the autonomous nervous system (ANS). The parasympathetic system permanently slows down the sinus node through the right vagus nerve acting through acetylcholine by slowing down the spontaneous diastolic depolarization slope resulting in a decrease in sinus node impulse frequency and therefore heart rate (HR). In contrast, the sympathetic system, which has as the main neurotransmitter norepinephrine, acts on the beta-adrenergic receptors of SN and accelerates the spontaneous diastolic depolarization slope, thus increasing the SN impulse frequency and the HR.

SB is not always pathological, it can be observed in physiological states as in the elderly and endurance athletes. Although pathological, it can remain, often, asymptomatic and is found only accidentally; its tolerance is variable clinically, a slow heart rate remains mostly of no consequence when it is moderate or settles progressively, if bradycardia is extreme or occurs suddenly, the clinical scene may be unambiguous. In this case, nonspecific and variable symptoms may appear: brief discomfort with lightheadedness, dizziness, presyncope and syncope. When an underlying cardiac disease is

present, SB can manifest as angina or congestive heart failure. Finally, in the pauci-symptomatic forms, the symptoms can be translated as asthenia, intolerance to the effort or an ideomotor slowing down (1). The SB represents a particular entity whose diagnosis can be suspected on clinical examination and confirmed with the ECG or the ECG Holter if intermittent.

The etiological assessment for a reversible cause includes a good history, a complete clinical examination, an ECG, a biological assessment (electrolytes, magnesium, calcium, glycose, thyroid status and troponin) and transthoracic echocardiography if structural heart disease is suspected.

In case of normal initial assessment and in the absence of an obvious cause for bradycardia, the differential diagnosis between sinus dysfunction and sinus bradycardia due to autonomic dysfunction gain a foothold. Other 2nd line investigations seek to confirm or refute the organic involvement of the SNS/impover. The ECG Holter is the test of choice for the diagnosis of sinus dysfunction with a 100% specificity when it demonstrates sinus pause/stop, sinoatrial block or alternating bradycardia-tachycardia. But it is not uncommon for the Holter ECG to remain inconclusive by finding only sinus bradycardia that can be permanent or intermittent. The stress test may be useful in the case of symptoms of stress in search of chronotropic insufficiency, but its diagnostic value is low for the diagnosis of other types of arrhythmias in sinus dysfunction (2,3).

The pharmacological test for the study of intrinsic sinus function after blocking autonomic nervous system influences by intravenous use of atropine and propranolol (4) has low sensitivity and specificity for the diagnosis of sinus dysfunction due to a large individual variability in the response to this test. The place of this test is very limited in case of intermittent sinus bradycardia.

Electrophysiological study explores sinus function mainly by measuring the corrected sinus node recovery time (CSRT) by the Mandel method (5). According to the 2018 syncope ESC recommendations, a CSRT greater than 525 ms supports organ dysfunction of the sinus node (6). The prognostic value of this method is poorly defined, especially since CSRT may be lengthened in case of vagal hypertonia (7). Several studies have shown that dysautonomia associated with organic involvement of the sinus node plays an important role in the onset of symptoms (8-10). Electrophysiological Investigation will be reserved for patients with SB who have experienced syncope under specific conditions (supine, exercise, or palpitations), patient with underlying heart disease, and patients with bifascicular block.

In the first case we report, electrophysiological study was in favor of sinus bradycardia by vagal hypertonia as it showed a 134 msCSRT and an elevation of the heart rate from 47 to 73 bpm after blockade of autonomic control by atropine. To confirm the involvement of the autonomic nervous system, we used an exploration of this system which confirmed the vagal hypertonia. However, in the second case, we preferred to perform a cardiovascular exploration of the autonomous nervous system before exploring the sinus node invasively which allowed us to make the diagnosis of a sinus bradycardia by vagal hypertonia with great certainty and exempt the patient from an invasive gesture.

Cardiovascular exploration of autonomous nervous system is based on the study of variability in heart rate and blood pressure during various ANS stimulation tests. Tests such as Hand grip, mental stress and orthostatic testing explore the sympathetic system while the variability of heart rate during deep breathing, Valsalva and the initial phase of the orthostatic test provide information on the functioning of the parasympathetic system.

A broad consensus places the deep breathing test as the pillar test for the exploration of parasympathetic function (11-14). This test explores the

variability of heart rate (HR) over 6 cycles of inspiration and deep expiration lasting 5 seconds each. During inspiration the vagal tone is lifted, and the heart rate rises causing a sinus arrhythmia. Measuring this variability allows a quantitative approach to vagal activity. The ratio HR at expiration/HR at inspiration of 30% is considered normal; variability above 30% refers to a vagal hypertone.

CONCLUSION

In the two present cases, the diagnosis of vagal hypertonia was made in the deep breathing test which showed an exaggerated sinus arrhythmia and in the orthostatic test which showed a significant increase in cardiac HR exceeding 20% by lifting the vagal brake during the first few seconds after standing up.

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