ELECTROCARDIOGRAPHIC ALTERATIONS DURING EXERCISE STRESS TESTING IN THE "BRUGADA SYNDROME"

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INTRODUCTION

Some years ago the Right Bundle Branch Block (RBBB) pattern did not represent any malignancy if it was not associated to structural heart disease. Nonetheless the recognition of some symptoms as syncope, palpitations, sudden death and/or sudden death family background associated to an electrocardiographic pattern of RBBB with ST segment elevation in right precordial leads turned out to be an electrocardiographic marker of sudden death risk in a group of patients with no proven structural heart disease [1-4]. This is now recognized and observed almost everywhere around the world for it has a medical and social impact that is important for its high association with malignant ventricular tachyarrhythmias. This relatively new syndrome is known as *"Brugada Syndrome"* named after the people who first described it *(Pedro and Josep Brugada).* These same authors have advocated it since their first publication in 1991 and almost a decade after; it has had a unique relevance with multiple publications. The possible pathophysiology that involves the ionic channels genesis has been proven and its genetic association as well[5].

GENERAL CONSIDERATIONS

Evidently it can be recognized as a clinical electrocardiographic entity in a 12 lead electrocardiogram, the concealed form being difficult to suspect. An exercise stress testing can be useful to unmask certain cases, and with these electrocardiographic alterations making it more evident[6]. The *"Brugada Syndrome"* is easy to be identified with a typical electrocardiogram.(Figure.1)

The electrocardiographic alterations can be due to the autonomic tone, playing an important role in its presentation (concealed or intermittent)[7]. With the administration of antiarrhythmic drugs sodium channels blockers, some cases can be increasingly unmasked rising this syndrome presentation[8-11]

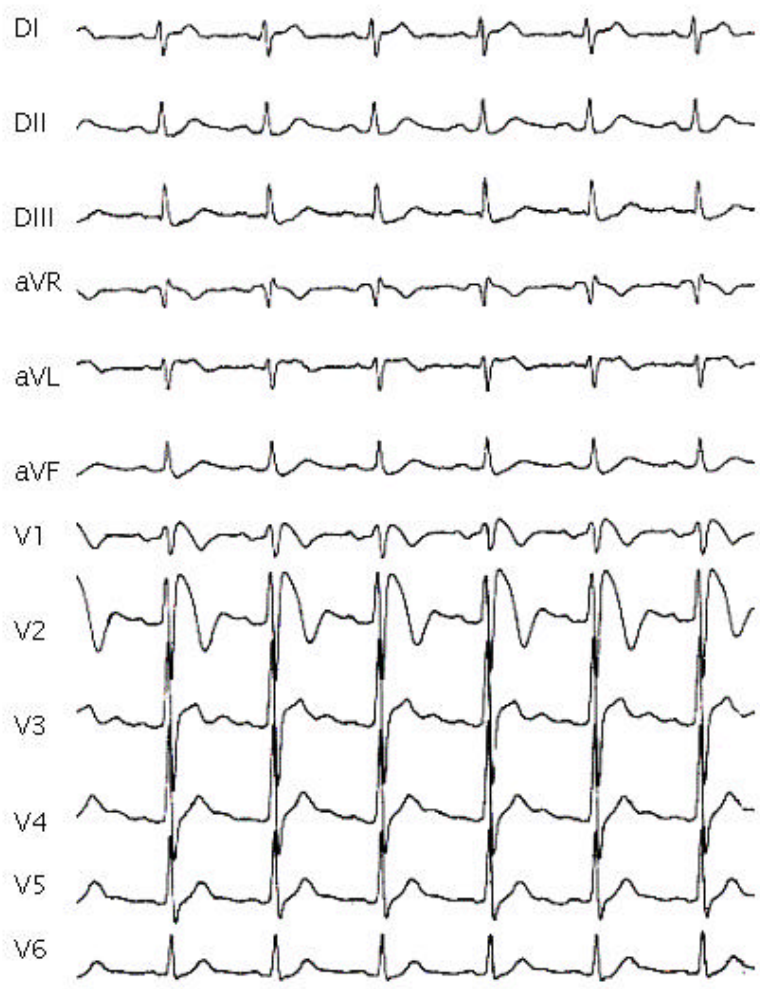

Figure 1: Typical ECG of the syndrome. In this case convex ST segment elevation in V_1 a $V_3$was observed.

EXERCISE STRESS TESTING

Electrocardiographic changes in the exercise stress testing have not been carefully studied in patients carrying the *"Brugada syndrome"*.

Few reports referring to this diagnostic method exist[6,12].It is important to consider the changes that exist during effort that are dynamic and that have as outcome a ventricular rate acceleration by vagal suppression, increase of alveolar ventilation and increase of venous return as a result of sympathetic vasoconstriction. In a healthy subject the net effect is a cardiac output increase in rest before the effort is started. The magnitude of the hemodynamic response during effort depends on the degree and volume of the muscular mass used. During first phases of exercise in the upright position, cardiac output increases when beat volume is elevated, mediated by the Frank-Starling mechanism and cardiac rate; cardiac output increase in last exercises phases is due to an acceleration in ventricular rate.

During exhausting exercise, sympathetic discharge is in the upper limit and parasympathetic stimulation is suppressed resulting in vasoconstriction in most circulatory systems except active muscles and in cerebral and coronary circulation. When exercise is at a maximum, venous and arterial noradrenalin release starting in sympathetic nerve endings is increased improving ventricular contractility. During recovery phase hemodynamics takes its basal condition for a few minutes.

In the *"Brugada Syndrome"* electrocardiographic alterations are unavoidable when influence of autonomous tone as mediator in the genesis of this alteration[13-15]. As a matter of fact an increase in heart rate causes a lowering in the elevation of ST segment, where while decreasing heart rate this ST segment elevation is increased [7]. These data are again in agreement with the loss of the dome of the action potential at epicardial level as the cause of ST segment elevation. I_{to} becomes more prominent at slow rates, increases heterogeneity and produces an ST segment elevation. These data are also in agreement with the clinical observation in the Asian area documenting a bradycardia dependency and a higher incidence of sudden death during sleep in patients with this syndrome[7]

Most authors coincide there is a ST segment normalization in exercise, this being facilitated by a heart rate increase and an increase in adrenergic stimulation what decreases ST segment elevation.

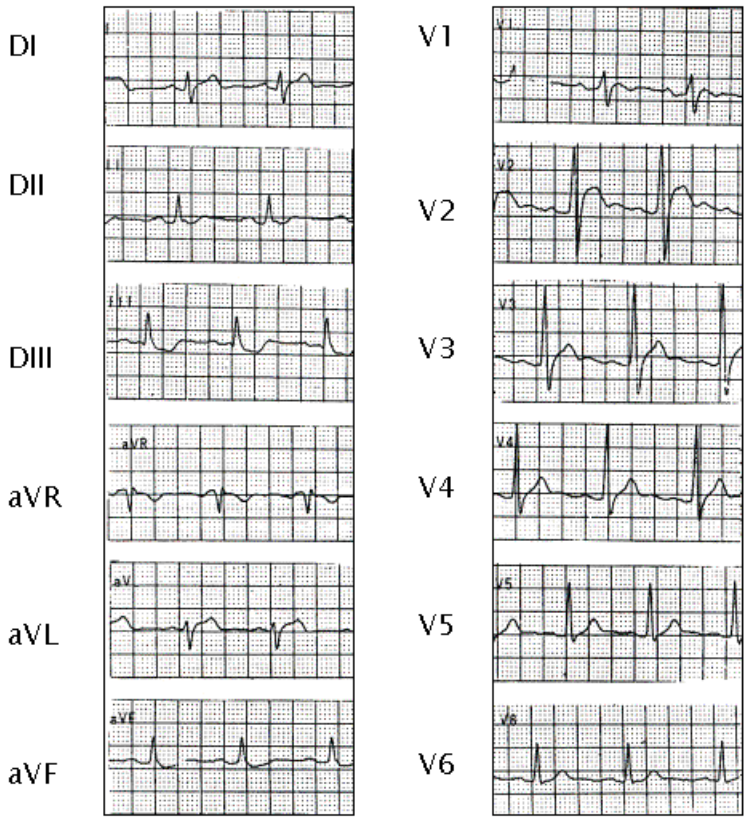

Figure 2: After a syncopal episode. A positive segment RS-T elevation from V_1 to V_3 was observed

We show these alterations in an asymptomatic 28 year old subject with no important background until an only syncope occur with no prodromes, attending to hospital assistance where an alteration during physical exploration was detected. One electrocadiogram taken during that time (Figure 2) showed sinus rhythm with a heart rate of 75 bpm, with AQRS at +70º, a 200 msec PR interval, S>R complexes in V_1 with a convex ST segment elevation (2mm) from V_1 to V_3 and a U wave present. It had a concave downsloping ST segment (mirror image) of DIII and aVF. an intermediate degree RBBB: start time of intrinsecoid deflection (STID) = 80 msec in aVR and 40 msec in V_1. After in a routine test an electrocardiogram was taken. (Figure 1) That evidenced an intermediate degree RBBB image; STID = 75 msec in aVR and 35 msec in V_2 and a convex ST segment elevation of V_1 to V_3 of more than 3 mm. A thorax X rays film and a transthoracic echocardiogram

mode M, bidimensional and color coded Doppler did not detect structural heart diseases. A 24 hour Holter monitoring showed 2,400 msec sinus pauses and a second degree sinus atrial block (Mobitz II) at night. An exercise stress testing with Bruce protocol showed a decrease in ST segment elevation in V_1 and V_2, more so in V_2, until normalization. (Figure 3) After, during early phase of recovery patient started to have a positive ST segment elevation in V_2 (at first minute) that progressively augmented until 10 mm, more evident at 3 and 6 minutes. A 13 mm positive ST segment elevation was reached. (Figure 4) Patient never showed any kind of tachyarrhythmias during exercise test.

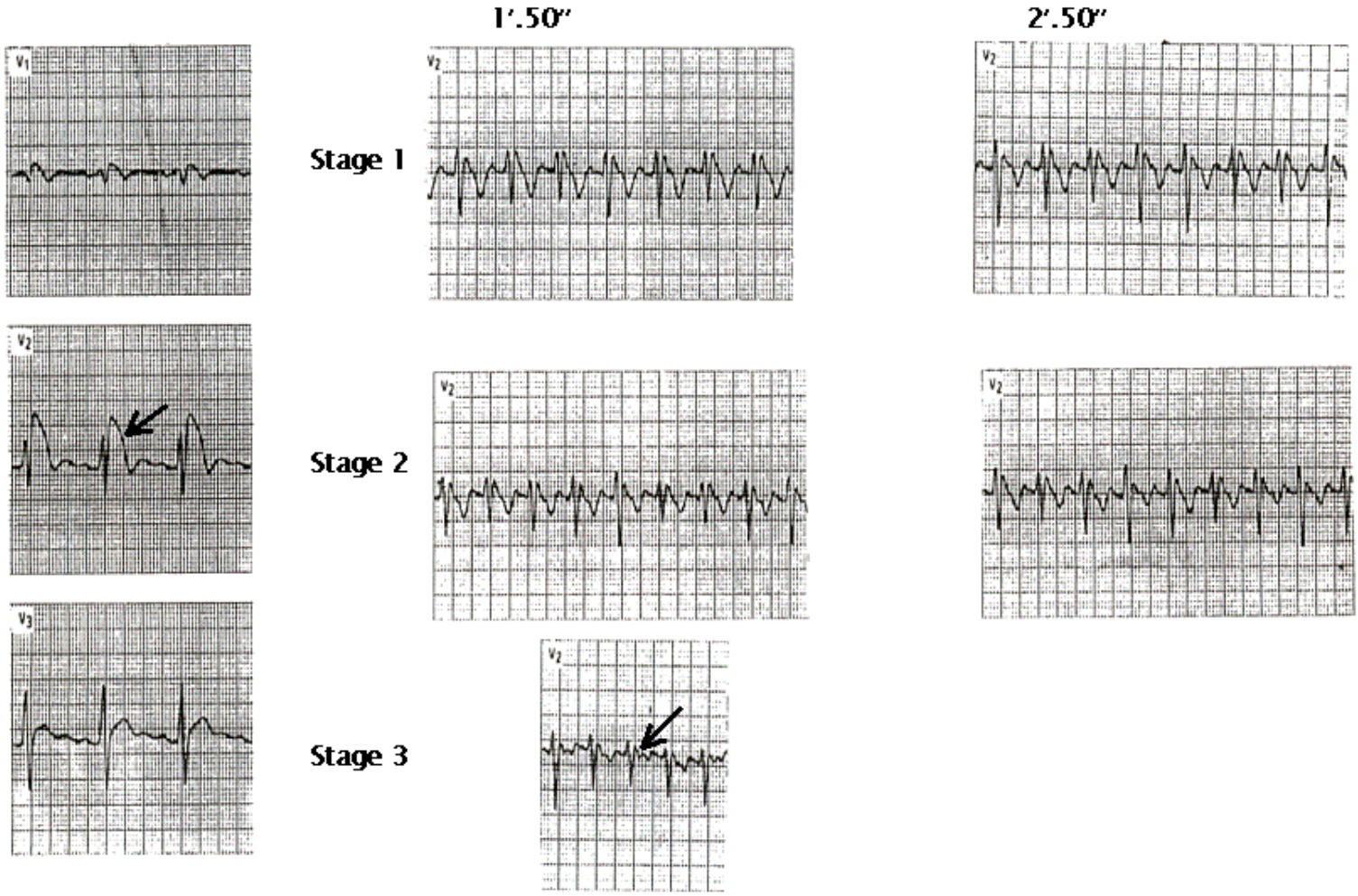

Figure 3: Three surface leads before exercise stress testing showing ST segment elevation, more evident in V_2 (arrows) are presented in the left panel. In the right panel, at the beginning of exercise test, normalization of ST segment is observed in stage I, II and III. More evident in stage III.(arrows)

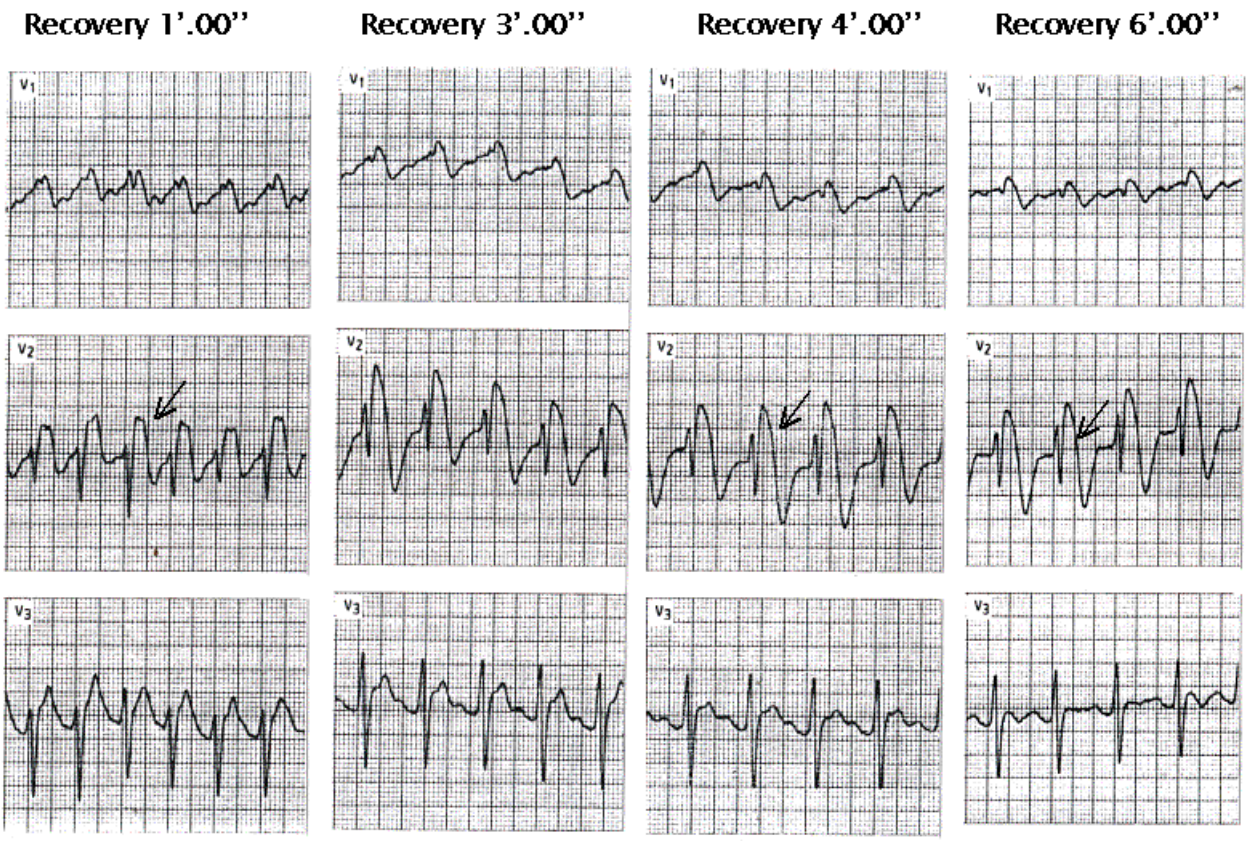

Figure 4: During the recovery phase progressive increase of positive ST segment levation was observed in minutes 1,3,4 and 6. (arrows)

Nonetheless another 33 year old patient with a syncope history and family background of sudden death had an electrocardiogram compatible with the *"Brugada Syndrome"*. (Figure 5) When an exercise stress testing with Bruce protocol was done we found that during the effort phase and at maximum effort contrary to a ST segment normalization, a discreet increase of the ST segment elevation of 2 mm in V_1 and V_2 occurred, (Figure 6) and when looking closer to this lead and comparing stage I to IV it is observed with more detail.(Figure 7) During recovery phase a decrease in the ST segment elevation was observed, at a normal level as before the test. (Figure8)

These electrocardiographic changes in this patient are interesting for one would expect ST segment changes to decrease at exercise, nonetheless they did not occur.This could be interpreted as a paradoxical response. Besides this same patient presented monomorphic ventricular extrasystoles, self-limited with a RBBB image.

It is important to comment that this was the only patient with the electrocadiographic *"saddleback"* variety, different to the other patient that had the convex variety also called *"coved"*. Electrocardiographic changes *"saddleback"* like are frequent in patients with exaggerated bradycardia and these could be due to a vagal tone increase.

We systematically studied a family with the *"Brugada Syndrome"* with 7 affected individuals and during the exercise stress testing 5 showed normalization of ST segment during exercise and during recovery phase an ST segment elevation increased, was observed.

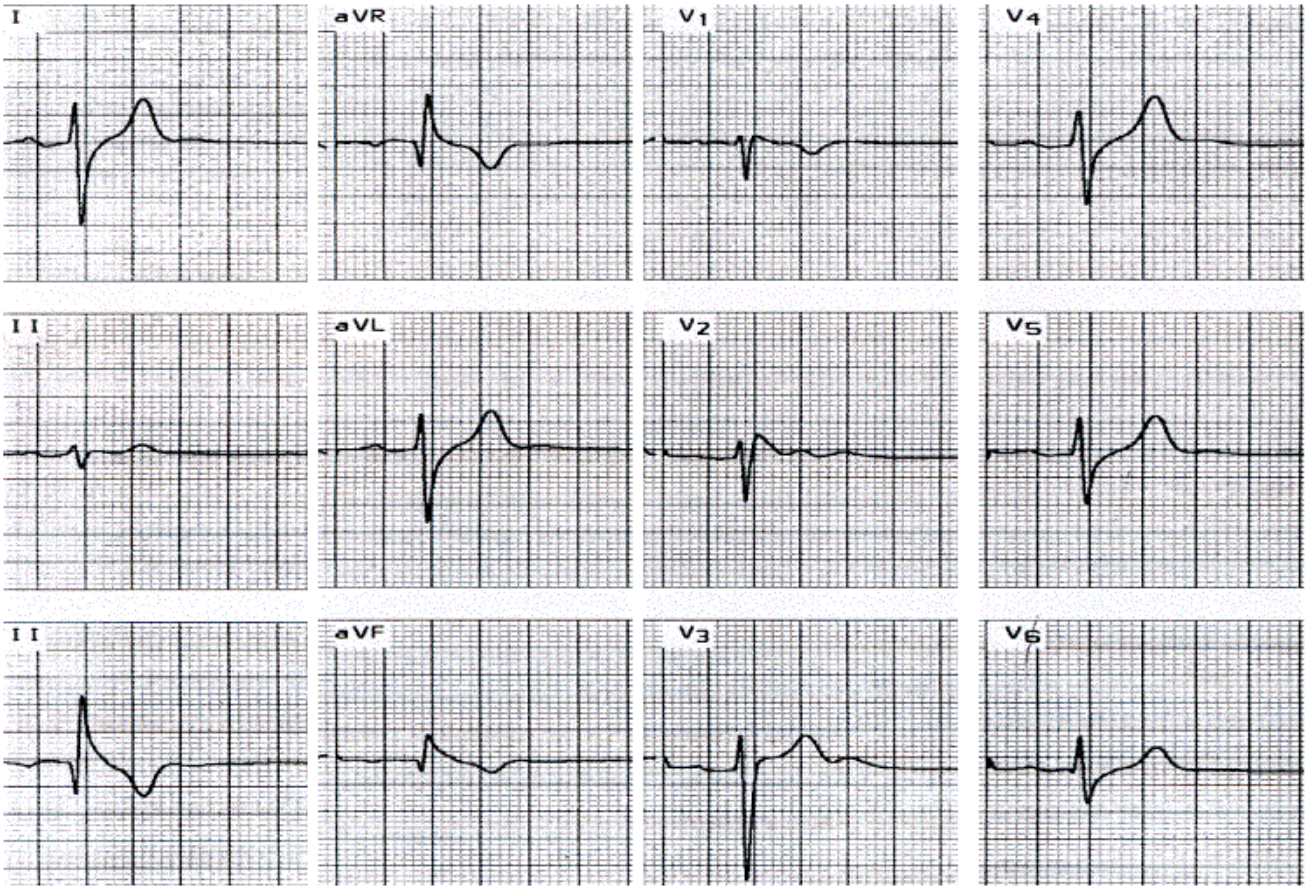

Figure 5: 12 lead electrocardiogram where a *"Brugada Syndrome"* with *"saddleback"* variety.

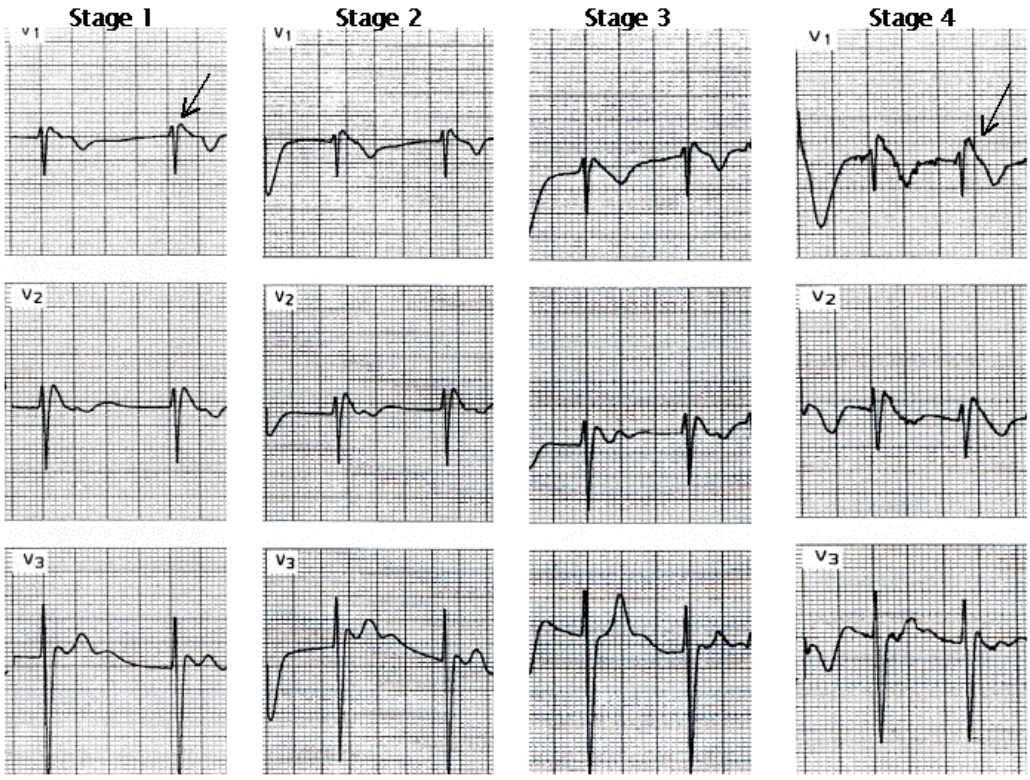

Figure 6: During the effort phase in stages I, II, III and IV it is observed how discreetly ST segment elevation in V_1 (arrows).

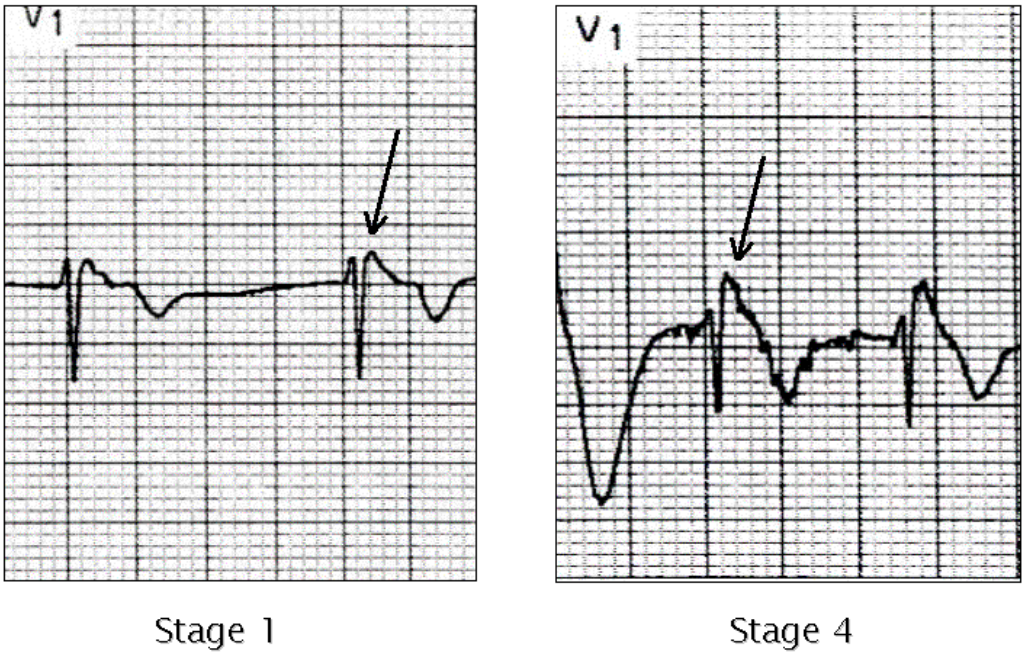

Figura 7: When getting closer to V_1 leads in stages I and IV we can better see the increase of ST segment elevation (arrows)

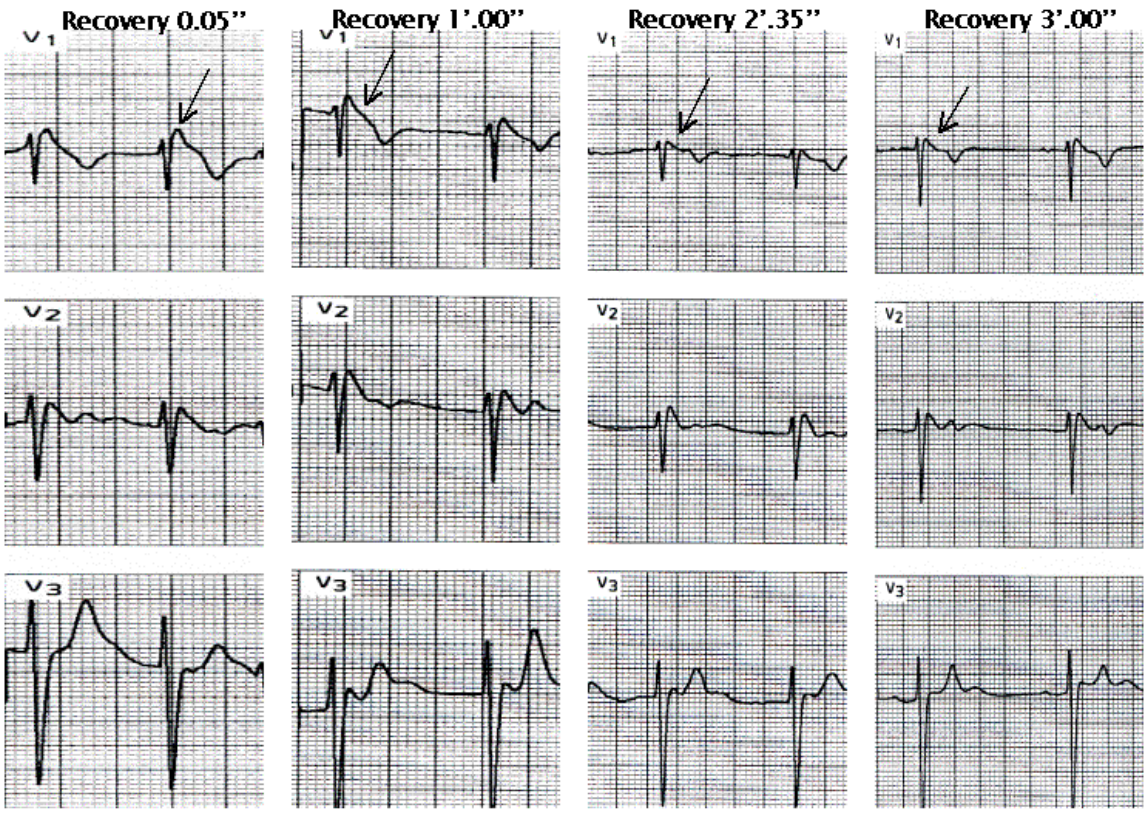

Figura 8: During the recovery phase we can see how the positive ST Segment elevation is normalized after minute three.(arrows)

CONCLUSIONS

As we have seen the electrographic changes in patients with the *"Brugada Syndrome"* are dynamic. Normalization of ST segment is certainly more frequent during exercise but the paradoxical form where ST segment increases during exercise can be present. And even though we have seen this in only one patient with a presentation of an electrocadiographic "saddleback" variety, it must be considered that the changes can be exacerbated when vagal tone effect is more predominant (recovery phase) where these changes are more easily observed and could simulate acute myocardial lesion for the so prominent positive of ST segment elevation. These alterations exist by themselves but do not exclude the co-existence of other concomitant diseases as has been documented before.

Everything seems to indicate that the spontaneous changes of the electrocardiogram have a relation with the autonomic tone, but will be necessary to demonstrate it with prospectives studies later.

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