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Case Report

Grey Cases in Cardiology and Maneuvering in a Grey Zone, Where a Grey Attitude May Yield a Black Outcome

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Abstract: Grey zone in medicine and namely, in cardiology, represents a perplex area that clinicians have to navigate through and deal with. Grey cases in medicine represent intricate situations and the great challenge is to maneuver appropriately in order to narrow the grey zone and/or to move grey cases out of it. This may be achieved every so often by a comprehensive clinical approach, along with an extension of paraclinical tests. However, there are situations where grey cases remain in the grey zone, despite all efforts, and this may be related to the current medical progress. In cardiology, dealing with grey cases is critical given the risk of sudden cardiac event. Herein, we present two cases that illustrate grey zone in cardiology: a case of Brugada pattern in a 9-year-old-female patient and a case of acute heart failure with indeterminate brain natriuretic peptide levels. Discussion is made in the light of the relevant data from the medical literature.
Keywords: Grey zone, Grey case, Cardiology, Sudden cardiac event.

INTRODUCTION

The concept of the grey zone (GZ) in medicine is a fact, and it may represent controversies in daily medical practice. In this view, clinicians must implement all necessary clinical and paraclinical tools to try to narrow the GZ and to move grey cases (GC) out of it, whenever this is feasible [1, 2]. Moreover, clinical awareness and caution are essential in order to elucidate the condition to the patient, so the physician can develop a better perception of this confusing and bothersome situation called GZ [3].

GC and GZ in cardiology may represent a wide range of situations, for instance: the diagnosis and management of nonbacterial thrombotic endocarditis [4]; the prognostic value of peak oxygen consumption between 10 mL/kg/minute and 14 mL/kg/minute in chronic heart failure patients [5]; the origin of left ventricular hypertrophy in athletes (hypertrophic cardiomyopathy or athletic heart syndrome) [6]; the management of asymptomatic family members of patients with cardiac channelopathies [7].

Of note, management of GC in cardiology is particularly challenging given that navigating in a GZ while adopting a grey attitude may expose to the risk of sudden cardiac event, which may be potentially fatal. Herein, we present two cases to illustrate these situations: a case of Brugada pattern; a case of acute heart failure..

CASE REPORT

Case 1

A 9-year-old female patient presented in 2006 for syncope of unknown origin. Though the clinical settings were in favor of neurocardiogenic origin, tilt testing was negative. Importantly, electrocardiogram (EKG) findings were in favor of type 2 Brugada pattern (Fig. 1); in addition, other noninvasive paraclinical tests (Holter monitor, echocardiogram) revealed normal findings. Of note, there was a history of unexplained sudden cardiac death of the patient's paternal uncle. In view of that, an electrophysiological study was performed, which was negative at baseline. Also, a drug challenge (Flecainide 2 mg/kg over 10 minutes) did not result in any ST/T changes in V1/V2, and there was no inducible arrhythmia. When trying to explain this GC to the parents, a reflection came straight from the patient father: "Doctor, this is a situation of uncertainty and anxiety and could you guarantee that my child won't have a sudden cardiac death?" In view of that, an implantable cardioverter defibrillator (ICD) was implanted; however, 8 years later, the patient did not experience any arrhythmic event. She continues to have occasional fainting episodes in favor of neurocardiogenic origin, which decreased in intensity and frequency following treatment with beta-blocker.

Case 2

A 50-year-old-male obese patient, with a body mass index of 33 kg/m^2, had a history of a myocardial infarction. He also had a single chamber ICD implanted for an inducible ventricular tachycardia during an electrophysiological study. He presented in the afternoon to the emergency room for nocturnal paroxysmal dyspnea that occurred for the last 3 days. He was treated with beta-blockers, aspirin, angiotensin converting enzymes inhibitors and statins; also, he did not manifest any previous episode of heart failure. A previous echocardiogram (dating from one year ago) showed mild diastolic dysfunction and moderate systolic dysfunction with an ejection fraction of 45%. Physical examination showed a blood pressure of 150/90 mm hg, a heart rate of 75 bpm, no pulmonary crackles, and no lower legs edema. Laboratory tests showed cardiac troponin (cTn) T (cTnT) levels at 0.02 ng/mL and B-type natriuretic peptide (BNP) at 390 pg/mL, which was assessed as "normal" according to the facility norms. Chest X-ray (Fig. 2A) revealed mild cardiomegaly without parenchymal congestion, and the patient was discharged without further evaluation and with an appointment with his cardiologist on an outpatient basis. He came back at midnight with acute pulmonary edema; a comprehensive echocardiogram showed severe diastolic dysfunction with increased filling pressures and moderate systolic dysfunction. Also, a device check showed no arrhythmic events; however, there was excessive and "unnecessary" ventricular stimulation yielding ventricular pacing in over than 80%; BNP level was at 750 pg/mL at 24 hours post-admission; Fig. 2B shows parenchymal congestion and pulmonary edema.

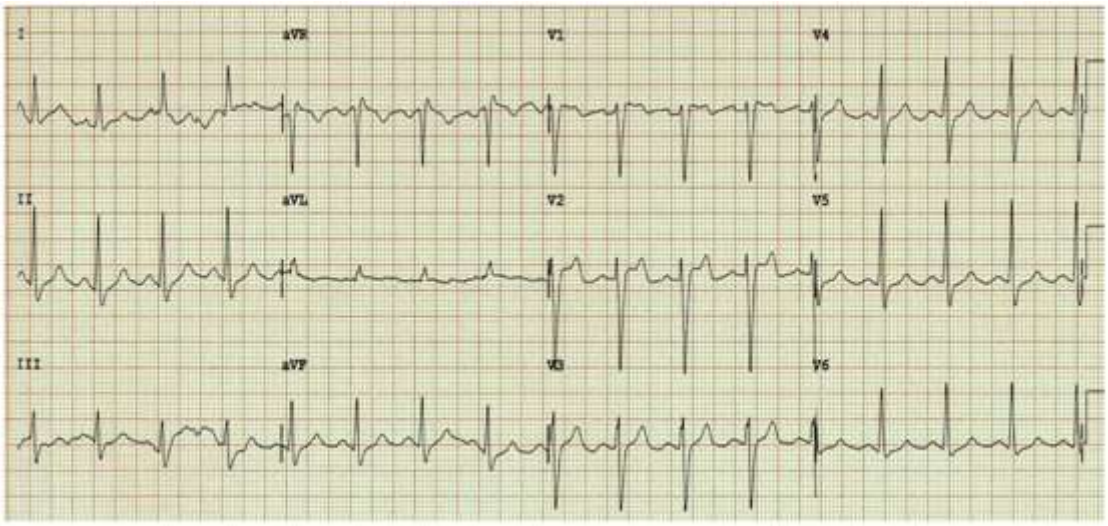

Fig. 1: Electrocardiogram showing an atypical right bundle branch pattern with saddle back ST elevation in V1/V2 compatible with type 2 Brugada pattern.

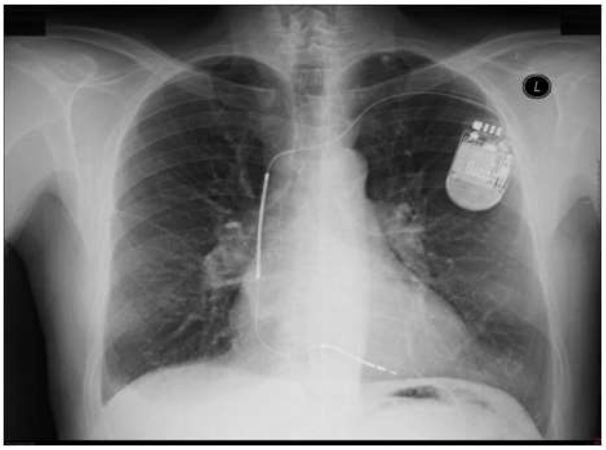

Fig. 2A: Chest X-ray showing the ICD box and lead; hilar congestion is also shown.

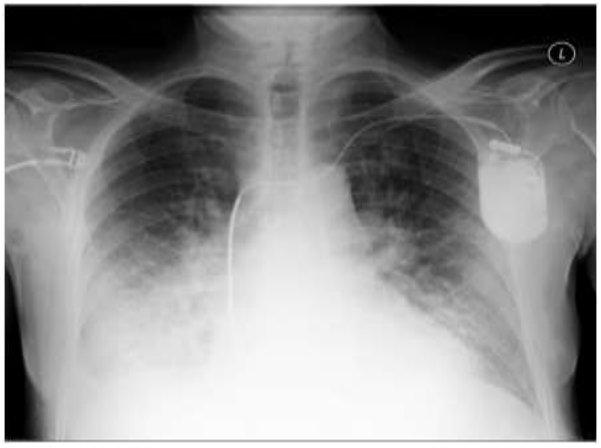

Fig. 2B: Chest X-ray showing parenchymal congestion related to acute pulmonary edema.

DISCUSSION

The patients presented above illustrate GC in cardiology. In each case, the great challenge was to displace a GC out of the GZ whenever this was possible. From this perspective, the physician must have a systematic algorithm in his mind, along with a clear clinical approach given that a GZ in the physician's mind will not help in this context [2, 8].

Namely in cardiology, we estimate that it is better to "do more rather than less", and although this approach may seem abusive, it is better to adopt this attitude rather than to count up one more sudden cardiac death.

Case 1 was a typical GC that was almost impossible to move out of the GZ, and this is related to the current perception in the management of Brugada pattern in a patient whose symptoms are supposed to be related to paroxysmal ventricular arrhythmia [9,10]. In the presented case, genetic testing was not available; of note, a mutation in the SCN5A gene, which encodes the cardiac sodium channel, is found in only about 20% of the subjects with Brugada pattern [9]. Moreover, the majority of these diseases have incomplete penetrance and variable expression, and thus genetic testing is not always helpful in formulating the initial diagnosis in this context; it is rather useful to extend testing to first-degree relatives [9, 10]. The prevalence of fluctuations between diagnostic and nondiagnostic EKG in patients with Brugada pattern is high, and this may have implications in correct phenotyping and risk stratification [11]. In the presented case, the initial ICD indication was "grey" (class IIA, level of evidence (C) [12] and the decision to "do more" was made, however, the lack of dysrhythmic events requiring ICD intervention 8 years later raises the question of appropriateness of the initial ICD indication.

Cases 2 represents a GC that could have eventually been displaced outside the GZ if a better diagnostic approach was adopted; in addition to the clinical settings, the key issue in this case is the BNP values, which presents a clue for judicious management. In fact, these values were labeled as "normal" according to the facility norms (based on a qualitative interpretation), whereas in these settings, these values could have been analyzed quantitatively and, accordingly, these values simply fit into a GZ [13, 14].

The REDHOT Investigators [14] reported that BNP levels from 100–500 pg/mL are GZ values; the GZ concept applied to BNP for the diagnosis of heart failure allows for a more rational approach in clinical practice, especially when adapted to relevant subgroups of patients (based on age and a history of heart failure) [15]. In the presented case, the patient had severe diastolic dysfunction, increased filling pressure with moderate systolic dysfunction, also he had excessive ventricular pacing resulting in atrioventricular and inter/intraventricular dyssynchrony, and these conditions combined may explain the hemodynamic dysfunction. A patient with a BNP value in a GZ should be well evaluated, especially when there are key issues predisposing to or explaining the hemodynamic compromise (obesity, severe diastolic dysfunction, moderate systolic dysfunction, previous myocardial infarction, mechanical dyssynchrony). In this view, we estimate that this patient should have been admitted initially, given the clinical context and the value of BNP in a GZ.

The assessment of any medical condition is based on a multitude of criteria, including the basic clinical settings and paraclinical tests. Though clinical settings are critical for an appropriate initial diagnostic approach, paraclinical tests represent, in most cases, an inevitable step for a definite diagnosis. Paraclinical tests are generally divided in two categories: qualitative and quantitative tests. Qualitative tests provide a binary (yes/no) information, and this yields a categorical information with an accuracy that is highly dependent on the test's discriminatory performance [13, 16]. Quantitative tests provide a numerical value, with a threshold set as the upper-normal limit based on a consensus derived from the results of trials that define normality; however, this upper-normal limit may vary according to the laboratory methods used, as well as according to the adopted coefficient of physiological variation [15]. The width of the GZ in a paraclinical test – whether qualitative or quantitative – depends on the clinical context, and on the discriminatory performance of the diagnostic test [15, 16]. In all cases that belong to a GZ, clinicians have to navigate with caution in order to handle the clinical situation and to narrow the width of the GZ [16].

CONCLUSION

Many conditions in medicine, and namely in cardiology, are not white or black; there are still many GC where an accurate diagnosis and/or best management is still indeterminate. In this context, clinicians cannot anticipate every complication that patients in the GZ may ever encounter, even if they are "covered" by protocols and guidelines that are mostly delineated in black and white lines. Accordingly, clinicians must be capable of navigating "safely" in the GZ when they are dealing with GC and, importantly, they must adopt a clear attitude given that grey management may yield a black outcome in cardiology, such as sudden cardiac death.

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