Neurology, Psychiatry and Brain Research 32 (2019) 8–13

Contents lists available at ScienceDirect

Neurology, Psychiatry and Brain Research

journal homepage: www.elsevier.com/locate/npbr

Interdisciplinary safety precautions protocol for electroconvulsive therapy (ECT) in a patient with treatment-resistant major depression and Brugada ECG

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ARTICLE INFO

Keywords:
Brugada-like ECG changes
Treatment-resistant major depression
ECT
Anaesthesia

ABSTRACT

Introduction: Brugada syndrome (BrS) is a rare cause of sudden cardiac death in young, otherwise healthy individuals with a structurally normal heart. The diagnosis of BrS is made by typical ECG changes (so-called "coved" type 1-ECG) that may be transient and can be unmasked by sodium-channel-blocking medications. Once the pathognomonic ECG pattern is identified, potentially aggravating drugs have to be discontinued. Since many drugs in psychiatric indications have the potential to induce Brugada-like ECG changes, therapy in such patients is challenging and a rapid worsening of depressive or psychotic symptoms can be the consequence. The limited remaining psychopharmacological treatment options may lead to the consideration of electroconvulsive therapy (ECT).

Methods: In a patient with treatment-resistant major depression and high risk of suicide, a Brugada type 1-ECG has been recorded during routine control under antidepressant pharmacotherapy. We report on the successful treatment using ECT after establishing an interdisciplinary safety precautions protocol for patients with suspected BrS, involving cardiologists, anesthesiologists and psychiatrists.

Results: Specific considerations of the safety precautions protocol include choice of anesthetic agents, advanced cardiac monitoring, specific emergency prearrangements and the ECT procedure itself. The type of muscle relaxant chosen and the autonomic response on the seizure stimulation were considered most important to avoid ECT-related adverse events.

Conclusion: ECT might be a promising option in the treatment of severe depressive episodes in patients presenting with a Brugada ECG, if an interdisciplinary risk assessment and safety precautions are carefully considered.

1. Background

Brugada syndrome (BrS) is characterized by typical electrocardiogram (ECG) changes in the precordial leads and ventricular arrhythmia. It may lead from syncope to sudden cardiac death (SCD) in otherwise healthy young people. (Sheikh & Ranjan, 2014) The pathognomonic ECG pattern partially mimics an incomplete right bundle branch block along with a J-point elevation (> 2 mm in chest leads) and characteristic, but often transient ST-segment elevations followed by a negative T-wave in leads V1-V3 (so-called "coved type" or Brugada type 1-EEG).(Bayés de Luna et al., 2012) Only the spontaneous occurrence of the type 1-ECG, or the unmasking after drug challenge (see Table 1) are indicative for BrS.(Brugada, Campuzano, Arbelo, Sarquella-Brugada, & Brugada, 2018) As BrS was first described quite recently in the early 90 s, knowledge about this potentially life-threatening condition is still comparably low in clinical practice The prevalence of BrS is estimated at approximately 5-20/10,000 persons. It typically affects males (8–10 times more frequent than females) under the age of 40 years and is reported to be one of the most frequent causes of sudden cardiac or nocturnal death in the setting of a structurally normal heart. (Brugada et al., 2018) In one-fourth of BrS patients a causative gene mutation, in particular in the *SCN5A* gene encoding the cardiac sodium channel subunit, can be identified and thereby clarifies its pathogenesis. So far, more than 15 causative genes have been

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https://doi.org/10.1016/j.npbr.2019.03.004
Received 6 October 2018; Accepted 12 March 2019
Available online 20 March 2019
0941-9500/

Table 1
List of drugs and conditions that have been associated with arrhythmias and the typical Brugada type 1-ECG (selected list of drugs from http://www.BrugadaDrugs.org).

Antiarrhythmic Drugs	• Natrium Channel Blocker (Class IA): (Lidocaine), *Ajmaline*[§], *Procainamide*[§] • Natrium Channel Blocker (Class IC): *Flecainide*[§], *Pilsicainide*, *Propafenone*[§], *Allapinin*, *Ethacizin* • β-receptor Blocker (Class II): (*Propanolol–high dosage*) • Potassium Channel Blocker (Class III): (*Amiodarone*) • Calcium Channel Blocker (Class IV): (*Verapamil*)
Anesthetical Drugs	• Local Agents: *Procaine, Bupivacaine* • General Agents: *Propofol, (Ketamine)*
Psychotropic Drugs	• Tricyclic Antidepressants: *Amitriptyline, Clomipramine, Desipramine, Nortriptyline, (Doxepin)* • Tetracyclic Antidepressants: *Maprotiline* • Phenothiazines: *(Perphenazine), Loxapine, (Thioridazine), Trifluoperazine* • Selective Serotonin Re-uptake Inhibitors (SSRI): (e.g. *Fluoxetine, Paroxetine, Fluvoxamine)* • Mood-Stabilizer: *Lithium, (Lamotrigine), Oxcarbazepine, (Carbamazepine)* • Selective Noradrenaline and Dopamine Reuptake Inhibitor (SNDR): *(Bupropion)*
Other Drugs	• H1-Receptor Antagonists: *(Dimenhydrinate Diphenhydramine, Terfenadine)* • *(Metoclopramide, Tramadol)* • *Acetylcholine*
Other Predisposing Conditions	• Alcohol (high intake), Cocaine, Cannabis • Febrile state, combination of glucose and insulin, hyperkalemia, hypokalemia, hypercalcemia • Hypothermia, vagotonia

"Drugs to avoid", i.e. contraindicated drugs for Brugada syndrome; "Drugs preferably avoided" in parenthesis; § indicative for "Diagnostic drugs" to unmask hidden Brugada syndrome; (date of selection at BrugadaDrugs.org: January 18th, 2019)

described; however, loss-of-function mutations in the cardiac sodium channel gene *SCN5A* remain the most frequent genetic finding. Incomplete penetrance and variable expressivity further contribute to the fact that a negative genetic test does not rule out BrS.(Dendramis et al., 2015) The implantation of a cardioverter-defibrillator (ICD) is recommended by international guidelines and consensus statements in symptomatic patientens (i.e. syncopes, ventricular arrhythmias or resuscitated SCD), while asymptomatic patients with a spontaneous Brugada type 1-ECG should be assessed for the need of an ICD by means of electrophyiological studies (EPS). (Priori & Blomström-Lundqvist, 2015)

Beside inherited forms of BrS, the typical ECG alterations in the precordial leads can also be triggered by other conditions, e.g. ischemia or right ventricular compression (so-called Brugada ECG phenocopy (Baranchuk et al., 2012)) or may be unmasked by modulating factors like various drugs acting on cardiac ion channels in genetically predisposed patients (so-called drug-induced or acquired form of BrS) (Table 1). As opposed to mortality rates of up to 13% in BrS, the prognosis of drug-induced (and thereby potentially reversible) BrS is considered substantially better with rates of SCD in 4%. (Sieira et al., 2017) Known risk factors for drug-induced BrS and BrS-related cardiac events are typically antiarrhythmic and anesthetic drugs.(Staikou, Chondrogiannis, & Mani, 2012) Furthermore, a wide range of psychiatric drugs, especially antidepressants but also phenothiazine-type antipsychotics and mood-stabilizer have been associated with the induction of a Brugada type 1 ECG (see Table 1).(Postema et al., 2009) In addition, bradycardia and a higher vagal state or febrile episodes may predispose for higher cardiac events and unmask the typical ECG alterations.

It is conceivable that awareness and vigilance of Brugada ECGs will perceptively rise in the field of psychiatry, considering the high prevalence of mental disorders in the general population and the increasing prescription rates of psychotropic drugs. (Ilyas & Moncrieff, 2012) Only some decades ago, insights from drug-induced (acquired) and genetically related long-QT syndromes had a major impact on the psychopharmacological treatment regimens in psychiatry and reached high clinical pharmacovigilance in the psychiatric setting ever since. (Girardin et al., 2013)

Patients with treatment resistant major depression (TRD) or psychosis present a special challenge if a Brugada ECG pattern is revealed during antidepressant therapy and the current drug regimen therefore has to be discontinued. While further psychopharmaceutical treatment might be of additional risk for potentially lethal arrhythmias, life-threatening deterioration of depression or psychotic symptoms may arise (e.g. acute suicidality). Thereforemedical therapy warrants a meticulous balance between vital needs and risks. Electroconvulsive therapy (ECT), on the other hand, is a guideline-based and highly effective non-pharmacological treatment option for severe depressive and psychotic episodes, particularly for instances when rapid symptom alleviation is required. (Abrams, 2002) To date there is only a paucity of literature on ECT in the setting of BrS, restricted to reports of individual cases and a lack of prospective studies. (Konishi, Suzuki, Kondo, Baba, & Ogawa, 2012; Luckhaus et al., 2008; Tsutsumi et al., 2011)

Only recently a consensus-based guideline for anesthetic and perioperative management in patients with BrS during surgery has been published. (Dendramis et al., 2017) However, to the best of our knowledge neither criteria for a specific risk stratification nor appropriate recommendations for the anesthetic and interventional management in the context of ECT has been provided so far.

2. Case description

We report on a 41-year old male patient with a history of recurrent major depression. He was referred to our clinic for ECT from a community hospital because of a severe treatment-resistant depressive episode. His personal history was unremarkable for cardiac symptoms as well as his family history for BrS, SCD or others with a pacemaker or an implantable cardioverter device (ICD). In his current episode he was treated initially by venlafaxine 300 mg and risperidone 2 mg per day. After non-response, the treatment regimen was changed to amitriptyline 150 mg and quetiapine 150 mg, augmented by lithium 900 mg per day. During a routine ECG a newly occurred complete right bundle branch block (QRS width 128 ms) with a "coved" shaped ST-segment elevation of approximately 3 mV in lead V2 was detected. The pathognomonic repolarization pattern was diagnosed as drug-induced ECG-type I BrS (see Fig. 1a) and the pharmacotherapy therefore was discontinued. The ECG alteration in lead V2 resolved in subsequent controls which corroborates the suspected drug-induced BrS (see Fig. 1b). During Holter ECG recordings short episodes of second-degree atrioventricular block type Mobitz I (Wenckebach) were found during night´s sleep but remained clinical inapparent.

Since three drugs with Na-channel blocking properties

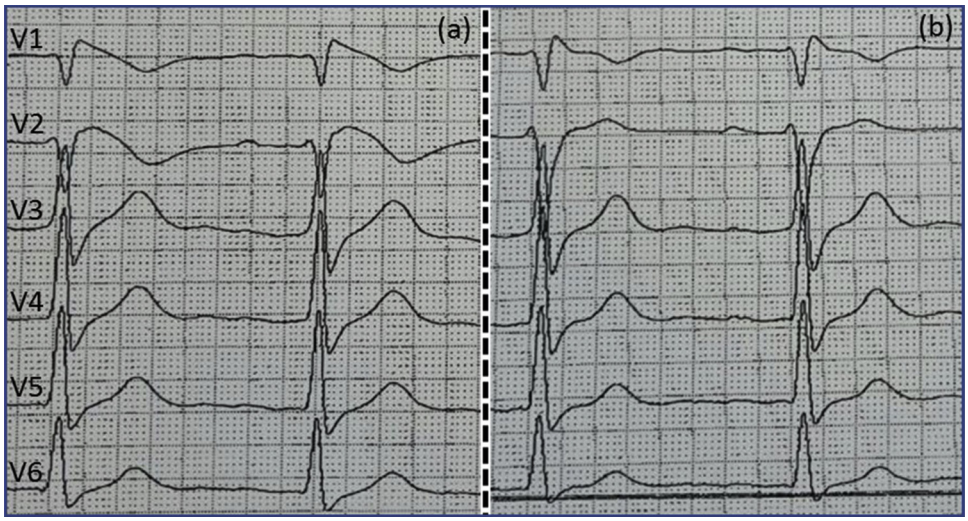

Fig. 1. (a) Routine ECG (speed: 50 mm/sec) during antidepressant pharmacotherapy with lithium, amitriptyline and quetiapine (all drugs with Na channel blocking properties): Chest leads showed a newly occurred right precordial ST-segment elevation followed by a negative T-wave (in lead V2), J-point elevation in V1 and V2, and right bundle branch block (S-wave in V6). The ECG is consistent with a Brugada type 1-ECG pattern ("coved type").
(b) After 10 days of discontinuation of pharmacotherapy the Brugada type 1-ECG resolved; the persistence of the first-degree atrioventricular block (PQ interval 243 ms) was found to be unrelated to the psychopharmacological treatment.

(amitriptyline, quetiapine and lithium) had been administered concomitantly at the time when the Brugada ECG was detected, the diagnostic classification as drug-induced ("true") BrS or acquired ST-elevation due to overdosing ("Brugada phenocopy") was not straightforward. However, we considered the presence ("overlap") of more cardiac conduction disturbances as indicative for the BrS condition (persistent first- and transient second-degree atrioventricular block). (Maury et al., 2013)

We did not see any indication for implantation of an ICD device since the patient showed only transient ECG changes that had been drug-induced and the medical history was unremarkable for clinical BrS.

On admission we saw a highly-distressed patient with mainly fearful and agitated depressive syndromes and life-threatening suicidal thoughts. Based on the individual patients' history of prior depressive or psychotic episodes, the assessment of urgency and the degree of treatment-resistance in the current episode, an interdisciplinary consultation round attended by experts in the departments of anesthesiology, cardiology and psychiatry was conducted. The patient and his close relatives were informed about the different treatment options at hand comprising the reconstitution of an alternative antidepressant pharmacotherapy, a treatment course of repetitive transcranial magnetic stimulation (rTMS), a trial with intravenous ketamine, and ECT treatment. The risk-benefit balance was considered for all treatment alternatives, e.g. the risk of either non-response due to the extended TRD status or hazardous cardiac events related to the BrS condition. With respect to the ketamine therapy, some recent randomized controlled studies showed a rapid onset of antidepressive and antisuicidal effect within 24 h in patients with TRD. (Singh et al., 2016; Zarate et al., 2006) However, ketamine is considered a "drug preferably to avoid" in patients with BrS due to reports of unmasking the ECG-pattern of BrS in ketamine intoxication [see BrugadaDrugs.org (Postema et al., 2009)].

The patient eventually consented to the initiation of an intravenous ketamine trial (0.5 mg/kg body weight administered intravenously during 40 min every second day), which was conducted under intensified cardiac monitoring by means of continuous 12-lead ECG and supervision of an anesthesiologist in the post-anesthesia care unit (PACU). Neither signs of any ECG alterations nor a significant increase in heart rate or blood pressure occurred. But in the absence of any effect on depressive symptoms, ketamine therapy was terminated after 4 treatment sessions. Subsequently, the patient gave his informed consent for ECT.

In addition to the standard anesthesia management for ECT, a 12-channel ECG, an external defibrillator and a temporary external pacemaker were placed as safety precautions. During the initial ECT sessions a cardiologist was supervising at bedside for an instant interpretation of ECG alterations. Anesthesia was carried out by the intravenous application of methohexital 150 mg (1.5–2 mg/kg body weight). Concomitantly atropine 1 mg was administered to reduce the ECT-related susceptibility of parasympathetic bradycardia or asystole during the initial seizure induction. For the same reason mivacurium 20 mg (0.25 mg/kg body weight) was chosen for muscle relaxation instead of the standard relaxation agent suxamethonium, as it is known to carry the risk of bradyarrhythmic events. The degree of relaxation was monitored via repeated Train-Of-Four (TOF)-stimulations. ECT was conducted following standard protocol (Waite & Easton, 2013) by means of a right unilateral electrical stimulus (Thymatron-IV® system, Somatics Inc.). For initial stimulus dosing the age-based method had been applied and the energy delivered was subsequently increased based on seizure quality parameters (maximum 504 mC). No asystole or bradycardia was observed immediately after the stimulus, but a slight broadening of the chamber complex was detectable during the post-stimulus tachycardia with a maximum heart rate of 120 beats per minute. Due to an insufficient muscle relaxation effect of mivacurium and the absence of bradycardia or asystole, the following ECT treatment sessions were conducted with suxamethonium 80 mg (1 mg/kg body weight). The dosage of atropine was tapered to 0.5 mg and finally stopped during further treatment sessions. The patient's condition improved remarkably after the 4th ECT session and the depressive syndrome remitted after a total of 12 sessions.

For maintaining the ECT effect on improvement, the patient was started on the MAO-inhibitor tranylcypromine. After reaching a dosage of 40 mg daily the patient experienced a feeling of dizziness and palpitations. The ECG revealed a symptomatic second-degree atrioventricular block type Mobitz I (Wenckebach), with heart rate slowing down to 30 beats per minute **(see** Fig. 2**)**. The treatment regimen was changed to venlafaxine (max. 225 mg) and mirtazapine (max. 45 mg) under which depressive episodes had remitted in the past. Concomitantly, a treatment course of rTMS (MagPro R100®, MagVenture Inc.) in the left dorsolateral prefrontal cortex was started as an augmentation strategy. After conducting 20 sessions of rTMS the patient experienced a severe relapse of depressive symptoms approximately 10 weeks after cessation of the initial ECT series.

We reinitiated a second course of ECT utilizing the identical safety protocol with the exception of mivacurium, which was replaced by suxamethonium as initial choice for muscle relaxation, since no cardiac side effects had occurred and the relaxation effect had reliably sustained throughout the first ECT series. Again, the patient showed a good response after the 3rd and remitted after the 8th treatment sessions. It is noteworthy that during the second ECT series short episodes of

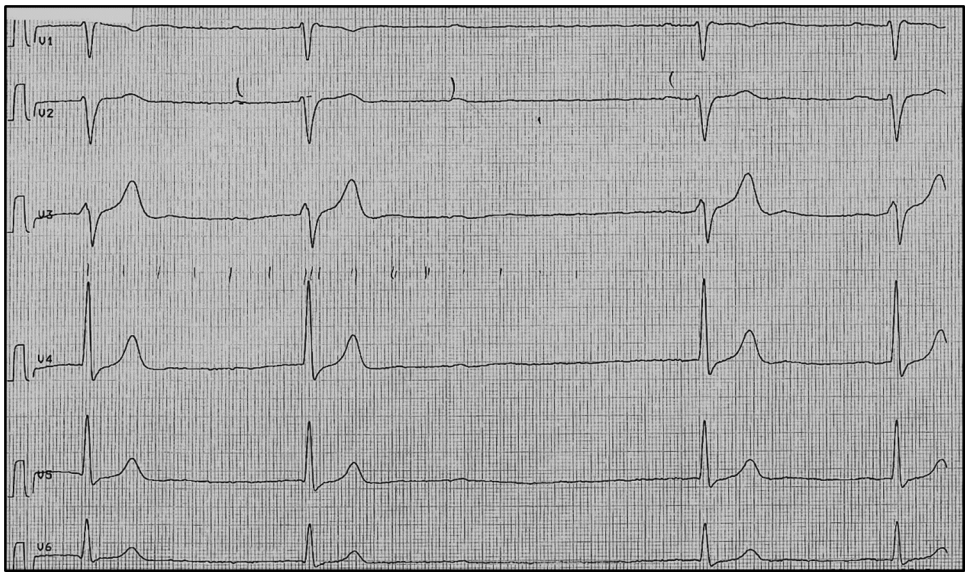

Fig. 2. Follow-up ECG (speed: 50 mm/sec) during treatment with tranylcypromine (40 mg/d) showing a second-degree atrioventricular block type Mobitz I (Wenckebach) with irregular atrioventricular conduction and heart rate, slowing down to 30 bpm. No Brugada-like ECG pattern in the regular right precordial leads. Of note, tranylcypromine is not contraindicated for use in patients with BrS.

bradycardia and asystole were present in some treatment sessions after seizure initiation without further arrhythmogenic complications and no need of intervention. After remission, a continuation ECT was started with increasing treatment intervals from 1 up to 4 weeks. The patient was finally discharged after 4 months and remained in remission on 1-year follow-up.

A genetic basis for the transient type 1-ECG changes for BrS was negative, since a comprehensive DNA analysis by Sanger sequencing showed no causal mutation in major and rare genes for BrS (i.e., *SCN5A, SCN1B, SCN2B, SCN3B and GPD1L*).

3. Discussion

The aim of this report is not only to describe another successful ECT in a patient with drug-induced BrS but to summarize the interdisciplinary safety considerations, which had comprehensively been undertaken preceding the commencement of the ECT treatment.

The clinical predicament as described in our report might be paradigmatic for selective psychiatric patients, in whom an inherited cardiac conduction disease is newly identified or at least strongly suspected due to characteristic ECG alterations as in the case described here (Brugada type 1-ECG). Due to its potentially life-threatening proarrhythmogenic effects the current psychopharmaceutical treatment needs to be abruptly discontinued in most cases. The remaining pharmacological treatment options might become scarce and even switching to a potentially less harmful drug could turn out to be ineffective. As a consequence, the patient's depressive or psychotic psychopathology can deteriorate severely and potentially culminate in an equivalent danger to life, if a suicidal crisis emerges. This full-blown clinical picture requires to quickly decide on alternative treatments with rapid effectiveness, which usually gives rise to the consideration of ECT as non-pharmacological and guideline-based treatment option.

To the best of our knowledge, only three cases have been reported about ECT in patients with BrS so far.(Konishi et al., 2012; Luckhaus et al., 2008; Tsutsumi et al., 2011) Luckhaus et al. (2008) reported about a patient with a prolonged asystole during ECT, who was subsequently diagnosed to have BrS. The ECT inherited risk for bradycardia and asystole and respective properties of the anesthetic agent propofol were discussed and weighted against the BrS itself as main reason for the arrhythmogenic event. The authors considered BrS as a potential cardiac risk factor during ECT. In another report by Tsutsumi et al. (2011) sugammadex was uneventfully utilized for the reversal of rocuronium-induced neuromuscular blockade in a patient with BrS under propofol anesthesia. In a third case reported by Konishi et al. (2012) the avoidance of suxamethonium was pointed out for safety reasons in a patient who underwent ECT for bipolar disorder, since its vagotonic effect might precipitate ventricular arrhythmia during anesthesia. However, none of these reports provided comprehensive information about the specifics of safety precautions that should be taken into account before ECT is commenced in patients with BrS.

The main contributing aspects in the risk assessment of ECT in patients with BrS are the possible cardiac side effects of the commonly applied anesthetic or concomitant medication, as well as the ECT procedure itself: the electrical stimulation required to generate the seizure activity is often associated with parasympathetic mediated bradyarrhythmia or asystole, followed by sympathetic mediated tachycardia and rise in arterial blood pressure. These episodes typically do not necessitate any interventional measures in routine ECT due to its brief and self-limited character. In patients with BrS the incidence of bradycardic events or any unbalances of the parasympathetic and sympathetic effects may precipitate ST segment elevation and subsequently hazardous ventricular arrhythmias. (Mizumaki et al., 2004)

Only recently, Dendramis et al. (2017) published a consensus statement for anesthesia management in patients with BrS to undergo surgery. Though some of these recommendations may be applicable, no specific safety precautions have been established for ECT so far. Considerations for such precautions should include specific cardiologic monitoring and interventional preparations, the adaptation of some anesthetic procedures as well as psychiatric prearrangements and drug restrictions (see Table 2). Therefore, the standard ECT protocol as described elsewhere (e.g. Waite & Easton, 2013) should be adapted for safety reasons in the BrS condition.

3.1. Cardiological considerations

In addition to routine circulatory and oxygen monitoring, a 12-channel ECG should be derived for continuous observation of conduction parameters and ST-segment changes in the right precordial leads. External defibrillator pads should be applied and an external pacemaker should be kept available. (Hayashida & Miyauchi, 2006) If an ICD or an internal pacemaker is already implanted, the device should be turned off or switched to a non-sensing mode, respectively. For rapid pharmaceutical intervention in case of malignant arrhythmias and electrical storm the beta receptor agonist isoproterenol should be kept ready as first choice. Quinidine and dobutamine have also been related to reduce ST segment elevation and suppress arrhythmic events.

Table 2
Safety precautions for electroconvulsive therapy (ECT) in patients with suspected or confirmed Brugada syndrome (modified from Dendramis et al., Am J Cardiology 2017).

Cardiologic considerations	• Continuous 12-lead ECG monitoring during the full intervention: observe for changes in conduction (QRS width, PR interval), ST-segment changes in the right precordial leads, premature ventricular beats or ventricular arrhythmias • External defibrillation pads should be applied before starting anesthesia and external defibrillator should be hold on "stand-by" • In addition, an external pacemaker device should be hold „stand-by "for potential bradyarrhythmia • Provide the supervision of a cardiologist/electrophysiologist at bedside • Keep isoproterenol and quinidine ready for use in case of ventricular arrhythmias or electrical storm
Anesthesiologic considerations	• Prefer methohexital, thiopental or etomidate as narcotic agent instead of propofol and ketamine (albeit may be used with caution) • Monitor anesthetic depth to prevent unnecessary deep anesthesia (e.g. bispectral index monitoring) • Avoid unintentional changes of the autonomic tone, especially parasympathetic stimulation • Prefer non-depolarizing agents as muscle relaxant, e.g. mivacurium or rocuronium, in order to avoid bradycardia e.g. due to suxamethonium („train of four "(TOF)-measurement required) and prefer sugammadex as reversal agent instead of neostigmine • Use atropine or glycopyrrolate (e.g., 0.5 – 1.0 mg) as premedication to reduce the likelihood of bradyarrhythmic events • Check for serum levels of electrolytes (potassium and calcium) and lactate as well as for renal and hepatic enzymes
Psychiatric considerations	• Review the current medication and update for each routinely prescribed or interventional-related drug for a status of 'drugs to avoid' or 'drugs preferably avoided' (see web reference at BrugadaDrugs.org) • Obtain an informed consent based on a thorough risk-benefit balance of the treatment options at hand (e.g. continuing an alternative pharmacotherapy, repetitive transcranial magnetic stimulation (rTMS), psychotherapy or natural course of disease) • Consider bifrontal stimulation (BF) over right unilateral (RUL) or bilateral stimulation (BL) for its lower incidence of bradycardia and asystole

(Dendramis et al., 2017) The impaired sodium channel status and associated limited conduction reserve is known to increase the probable pro-arrhythmic risks from all drugs that have sodium channel blocking properties. This has been verified particularly in BrS patients carrying the *SCN5A* mutation. (Sheikh & Ranjan, 2014) Furthermore, if the patient currently exhibits a spontaneous ECG-pattern of type I BrS this adds up to the interventional pro-arrhythmic risk. (Postema et al., 2009)

3.2. Anesthesiological considerations

According to the aforementioned consensus statement by Dendramis et al. (2017), general anesthesia in patients with BrS can be performed safely with the narcotic drugs propofol, thiopental and etomidate. These are anesthetics that are also commonly used in ECT. (Waite & Easton, 2013) However, propofol carries a theoretical risk of arrhythmogenic potential in patients with BrS and has been associated with ST segment elevations after bolus injection. (Dendramis et al., 2015) Therefore propofol is categorized as "drug to be avoided" at BrugadaDrugs.org, although considered safe when appropriate precautions are taken (see below). While at least some studies described unproblematic anesthesia with thiopental and etomidate in BrS (Jindai, Tanaki, Ohmura, Yamamoto, & Kobayashi, 2000) no reports have been published for methohexital yet. The latter is considered "gold standard" for anesthesia in ECT (Miller, Eriksson, Fleisher, Wiener-Kronish, & Young, 2009) and was administered uneventfully in our case reported here.

Close attention should be paid for selection of the neuromuscular-blocking agents in ECT. There is broad evidence that the application of the depolarizing agent suxamethonium is safe in the context of routine ECT. (Waite & Easton, 2013) As opposed to this, non-depolarizing agents like mivacurium or rocuronium should be favored in the BrS condition due to their lower risk of vagotonic mediated bradycardia and asystole. (Dendramis et al., 2017) Suggamadex has been used successfully as reversal agent for the non-depolarizing muscle relaxant in BrS, while neostigmine is not recommended due to its parasympathetic properties.(Dendramis et al., 2017; Konishi et al., 2012) In our case, we decided to switch to suxamethonium after the first ECT session as the relaxation effect of mivacurium was insufficient and no bradyarrhythmic events occurred under the premedication with 0.5–1 mg atropine. Equally important, a spontaneous ECG-Pattern of Typ I BrS did not apply. Atropine and glycopyrrolate have already been proven beneficial to prevent ST-segment changes in patients with BrS due to its anticholinergic properties. (Miyazaki et al., 1996) The premedication with atropine is also generally recommended to diminish the ECT related short-term bradycardia or asystole during electrical stimulation and the following seizure generalization. (Nagler, 2010) Further appropriate precautions for anesthesia in BrS are listed in Table 2 (for more specific details see Dendramis et al. (2017)).

It is important to mention that all recommendations are limited in their validity since they are based only on consensus statements for anesthesia during surgery which implies that adaptation for ECT might not be straightforward in every respect.

3.3. Psychiatrical considerations

As opposed to routine ECT, a discontinuation of the psychopharmacotherapy seems to be advisable before starting a first-time ECT in the BrS condition as not all cardiac risk factors have been fully elucidated for every drug so far. If the patient's individual condition does not allow discontinuing the current treatment, it is strongly recommended that the decision of using each drug is made after careful consideration. It is noteworthy that the patient reported here, experienced a symptomatic second-degree atrioventricular block type Mobitz I after starting treatment with an irreversible MAO-inhibitor which has been unsuspicious for carrying any pro-arrhythmic effects in BrS so far. Interestingly, some authors reported about distinctive phenotypes, in which other cardiac conduction disturbances were found to overlap with the typical BrS patterns. (Maury et al., 2013; Remme & Wilde, 2008)

For initiation of the ECT treatment, we decided to stimulate on the standard right unilateral (RUL) electrode placement which is the common treatment method in depression.(Waite & Easton, 2013) Although it is well known that RUL stimulation can evoke acute but transient cardiac effects, including bradycardia and even prolonged asystole in up to 40% of cases, these effects commonly do not warrant any intervention. (Nagler, 2010) In another study the change in heart rate by means of RUL, bitemporal (BT) or bifrontal (BF) stimulation has been investigated and BF stimulation was associated with the lowest incidence of asystole. Furthermore, for a mean pre-ECT heart rate of 85 beats per minute (bpm) the expected heart rate during stimulus was found to be 78 bpm in BF, 46 bpm in BT and 35 bpm in RUL treatment method. (Stewart, Loo, MacPherson, & Hadzi-Pavlovic, 2011) Dunne and McLoughlin (2012) conducted a meta-analysis, which found preliminary evidence that the BF method might be equally effective as BT or RUL stimulation in treating depression by means of ECT. Therefore, in case of a high susceptibility for BrS related ECG changes or even spontaneous patterns on the precordial leads, the decision about the

electrode placement should be carefully balanced and the BF stimulation seem to be the best choice with respect to safety reasons.

3.4. Limitations

It must be emphasized that this is only a preliminary version of a safety precautions protocol. More studies are needed to verify and refine the here presented recommendations.

3.5. Conclusion

In conclusion, we consider ECT as a promising treatment option for patients with suspected or confirmed BrS, if the current progression of depressive or psychotic disease warrants a reliable and effective treatment option with rapid onset of response. The close consultation of anesthesiologists, cardiologists, and psychiatrists is of utmost importance as an essential prerequisite before the commencement of ECT in the BrS condition.

Contributors

TH and FL were responsible for the conceptualization and writing of the article. JH, ESB and DM contributed to the writing and review of the drafts of the article.

Role of the funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

All authors declare that they have no conflicts of interest.

Ethical statement

Informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects have always been observed.

Acknowledgements

The authors wish to thank the clinical colleagues from anesthesia, cardiology and psychiatry who have contributed to the successful treatment of the patient.

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