Case report

Brugada pattern masquerading as ST-segment elevation myocardial infarction in flecainide toxicity

Lovely Chhabra a,*, David H. Spodick b

a Department of Internal Medicine, Saint Vincent Hospital, University of Massachusetts Medical School, Worcester, MA 01608, USA
b Department of Cardiovascular Medicine, Saint Vincent Hospital, University of Massachusetts Medical School, Worcester, MA 01608, USA

Article info
Article history:
Received 16 February 2012
Received in revised form
27 April 2012
Accepted 15 June 2012
Available online 22 June 2012

Keywords:
Brugada pattern
STEMI
Flecainide toxicity
Electrocardiogram

Abstract
Flecainide (a class 1c antiarrhythmic) produces a dose-dependent decrease in intracardiac conduction. Its well known common electrocardiographic effects are prolongation of PR and QT intervals and the QRS complex duration. We report a case of flecainide toxicity in an elderly female who presented with a type 1 Brugada pattern who essentially had a previously normal ECG pattern on therapeutic dose of flecainide therapy. The case describes a rare electrocardiographic abnormality induced by flecainide toxicity which otherwise could be easily misinterpreted as a ST-segment elevation myocardial infarction (STEMI) without lack of expertise and high clinical suspicion.

Copyright © 2012, Cardiological Society of India. All rights reserved.

1. Case report

An 86-year old female was brought to the hospital with complaints of generalized weakness, decreased appetite and mild confusion of 5 days duration. She also reported nausea, mild epigastric and atypical chest discomfort relieved by belching. Her past medical history included hypertension, lower gastrointestinal bleeding and atrial fibrillation for which she was started on flecainide (150 mg twice daily) 2 months prior to the current presentation. Her echocardiogram done 2 months ago was unremarkable. Family history was noncontributory. Initial vital signs were stable and physical examination was essentially unremarkable except mild cognitive impairment. Her laboratory work-up including hemogram, basic metabolic panel, liver function tests, urinanalysis and cardiac enzymes were within reference range except mild elevation in her creatinine level (Cr = 1.4 mg/dl) compared to her baseline (Cr = 1.0 mg/dl). An ECG at the admission time demonstrated right bundle branch block (RBBB) like morphology, coved type 3.5 mm ST elevation with T-wave inversion in leads V1 and V2 consistent with a type 1 Brugada pattern and a prolonged QRS duration [Fig. 1]. Her previous ECG done a month prior on flecainide therapy was essentially normal [Fig. 2]. The emergency room (ER) physician activated the cardiac catheterization team for possible ST-elevation myocardial infarction (STEMI) without lack of expertise and high clinical suspicion.

Copyright © 2012, Cardiological Society of India. All rights reserved.

http://dx.doi.org/10.1016/j.ihj.2012.06.010
atypical clinical symptoms more likely consistent with anti-arrhythmic drug toxicity. IV fluids with bicarbonate supplementation were initiated and she was admitted to the cardiac care unit for closer monitoring. Repeat ECG 6 h later revealed a bifascicular block pattern, relative decrease in QRS duration and decreased ST elevation to 2.5 mm in leads V1 and V2 [Fig. 3]. Another ECG 12 h later showed an incomplete RBBB like morphology, normalization of the PR interval and QRS duration and decreased ST elevation at 2 mm in leads V1 and V2 consistent with a still persistent type 1 Brugada pattern [Fig. 4]. Results of serum flecainide level drawn in the ER returned the following day at 2350 μg/L (Therapeutic range: 200–1000 μg/L). On Day 2, she was asymptomatic and her mental status returned to her baseline. An electrocardiogram before discharge on Day 4 showed complete normalization [Fig. 5]. Flecainide was discontinued and she was discharged on diltiazem and aspirin as she had refused warfarin. An outpatient clinic follow-up 4 weeks post-discharge showed a normal ECG and also screening ECG’s obtained in five first-degree relatives revealed no obvious abnormality for Brugada pattern, including her 65 years old brother who had a normal ECG on flecainide therapy for AF.

2. Discussion

Flecainide is a class 1c antiarrhythmic drug (AAD) that blocks sodium channels. Flecainide produces a dose-dependent decrease in intracardiac conduction, but its effects on intra-atrial and AV nodal conduction are less pronounced than those on His-Purkinje conduction and ventricular activation. It prolongs the PR interval, the QRS complex duration and some QT prolongation may also be noticed due to a widening of the QRS complex, so that the JT interval and QTc remain unchanged or slightly increase. ST elevation is an under recognized electrophysiological abnormality induced by flecainide which can often mimic an acute myocardial infarction. Previous studies have suggested that flecainide can induce a new Brugada ECG pattern or can unmask a Brugada syndrome by inducing a type 1 Brugada pattern in patients with pre-existing type 2 or type 3 Brugada patterns. Drug-induced Brugada pattern can be generally seen at standard therapeutic dose of flecainide and such patients may have a possible underlying genetic predisposition (like SCN5A mutations) causing abnormality of native sodium channel activity. Interestingly, our patient didn’t have any self or family risk factors for Brugada syndrome and didn’t demonstrate any electrocardiographic abnormality at baseline or on therapeutic dose of flecainide but a type 1 Brugada pattern with cove shaped ST elevation was revealed at the toxic dose of flecainide which showed complete resolution after discontinuation of flecainide therapy. Thus, our case likely represents a complete iatrogenic induction of the type 1 Brugada phenotype due to flecainide toxicity in a patient without
any clinical suggestion of the congenital abnormality which would otherwise have had likely manifested at therapeutic flecainide dose. The most likely explanation for this would be that toxic dose of a sodium channel blocker like flecainide may induce an iatrogenic sodium channel defect in a normal individual similar to a patient with sodium channel genetic defect like with “loss of function” mutation. Thus, an ST-elevation related to Brugada pattern could occur selectively at toxic dosing in any patient receiving flecainide therapy. Because these drugs frequently are used to treat tachyarrhythmias in patients who may present with chest pain, this rare ECG manifestation of Class 1c drugs should be recognized to avoid misdiagnosis of acute myocardial infarction. ER physicians should maintain a high suspicion for flecainide toxicity especially in elderly and patients with poor renal function. With a good clinical history and high index of clinical suspicion, an unnecessary intervention could be avoided by the ER physicians as they form the foremost important part of STEMI care measure protocol. Reiffel recently reported an interesting case study where Brugada pattern was noted in a patient who consumed a single 600 mg oral dose of flecainide who otherwise had a normal ECG while not on flecainide therapy. This observation raised the question as to whether when administered as a diagnostic test, higher flecainide doses than have been commonly used should be used, or, alternatively, whether the response in his patient could be a “false-positive” that might be seen in some normal individuals if exposed to this much flecainide. The answer to this question however remained unclear probably because of three reasons: there was no available ECG to compare while the patient was on standard therapeutic flecainide dose, flecainide level on the patient was not obtained for objective confirmation and also genotype study was not performed. The patient in our case had several ECG’s in outpatient follow-up after she was started on the standard therapeutic dose of flecainide which were essentially normal, however Brugada pattern was present at the toxic drug level which occurred likely due to the drug-induced sodium channel defect (although patient remained on standard flecainide dose). There was gradual narrowing of the QRS complex which was accompanied by a parallel reduction of the ST-segment elevation with a delay of several hours. This finding suggests that global reduction of the fast inward sodium current is the primary electrophysiological defect and the repolarization abnormality is secondary with a drug-induced Brugada sign and confirms one of the previous observation reported by Hudson et al. The genotype study was not performed in our case for the reason that it would be extremely unlikely for a genetic Brugada syndrome to manifest for the first time at the age of 86 years especially when patient previously had all normal electrograms in her life including the ones obtained on the standard therapeutic flecainide level. Thus, Brugada pattern was specifically induced at a toxic level of flecainide (though on the standard therapeutic dose) in the setting of transient renal insufficiency in our patient who had no prior risk factors of Brugada syndrome and when no electrocardiographic abnormality was seen earlier at standard therapeutic flecainide dose. Also, the screening ECG’s obtained in first-degree relatives showed no abnormality including one of her brothers on flecainide therapy. This case finding suggests that a Brugada phenotype may serve as a standard electrocardiographic sign for the drug toxicity and a high suspicion for the same should be raised even in asymptomatic patients who are on standard therapeutic doses of such agents and have tolerated them well in the past.

3. Conclusion

ST-segment elevation can result from administration of class 1c drugs and should be considered as a differential in patients receiving such drug agents. ST elevation is often seen as a part of the drug-induced Brugada pattern in patients with underlying sodium channel defect but can occur de novo even in patients with no genetic defect receiving strong class 1c agents like flecainide. Brugada pattern can selectively result from a toxic dose of flecainide and in those patients who have tolerated the therapeutic dose of flecainide well in the past without any demonstrated electrocardiographic abnormality; this electrocardiographic sign may represent drug toxicity.

Conflicts of interest

All authors have none to declare.

REFERENCES