CASE REPORT

Stroke or side effect? dofetilide associated facial paralysis after direct current cardioversion for atrial fibrillation

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Accepted 13 January 2019

SUMMARY

Dofetilide is a class III antiarrhythmic drug that has proven efficacious in maintaining sinus rhythm in up to 60% of patients with persistent atrial fibrillation. Dofetilide's most concerning adverse effect is QT prolongation and polymorphic VT, but providers should be aware of other rare significant side effects. We report a case of dofetilide associated Bell's palsy masquerading as stroke that developed shortly after a cardioversion. The patient's facial weakness, a side effect of dofetilide, resolved relatively quickly after discontinuation of the medication and a short course of oral corticosteroids.

BACKGROUND

Dofetilide is a class III antiarrhythmic drug that has proven efficacious in maintaining sinus rhythm in up to 60% of patients with persistent atrial fibrillation (AF) and can be used in conjunction with direct current cardioversion (DCCV) to increase the likelihood of maintaining sinus rhythm.¹ The major rare but serious side effects of dofetilide are torsades de pointes, nonsustained VT or sudden death.^{2,3} Other more common side effects ($\geq 5\%$) include headache, chest pain, dizziness and dyspnoea.⁴

There are no published reports on facial paralysis in association with dofetilide use, although it is listed as a potential side effect in $\leq 2\%$ cases.⁴ Given the increased incidence of stroke in the persistent AF population, the overlap between Bell's palsy secondary to dofetilide use and stroke-associated facial paralysis may be a source of confusion for clinicians. We describe the symptoms, duration of illness and potential treatment for patients who suffer from this rare side effect.

Figure 1 Drooping at the corner of the mouth (arrow). Loss of forehead wrinkle (arrowhead).

Figure 2 Resolution at 3 weeks.

CASE PRESENTATION

A 65-year-old man with a history of long-standing persistent AF was admitted to the inpatient cardiology service for initiation of oral dofetilide and DCCV. The patient had undergone a recent catheter ablation with recurrence of AF. Dofetilide was chosen over amiodarone for its lesser side effect profile and patient preference.

The patient's other medical history included obstructive sleep apnea treated with continuous positive airway pressure, hyperlipidaemia, gastro-oesophageal reflux and generalised anxiety. His outpatient oral medications included aspirin 81 mg once per day, rivaroxaban 20 mg once per day, carvedilol 20 mg two times per day, colchicine 0.6 mg two times per day, citalopram 10 mg once per day, atorvastatin 10 mg once per day and pantoprazole 40 mg once per day. His social history included no prior tobacco or alcohol use. His vital signs on admission: temperature = 36.3°C (97.3°F), blood pressure = 151/92 mm Hg, heart rate = 95 beats/min, respiratory rate = 12 breaths/min, oxygen saturation = 97% on room air. Complete blood cell count, creatinine and electrolytes on day of admission were within normal reference range.

On hospital day 1, the baseline ECG demonstrated a corrected QT-interval (QTc) = 438 ms. The patient's CHA₂DS₂-VASc score was 2; he had maintained uninterrupted anticoagulation therapy with rivaroxaban for more than 4 weeks. He received the first of five planned doses of dofetilide 500 mcg given every 12 hours. He underwent DCCV with a 360 Joule external synced shock 2 hours after initiation of dofetilide, resulting in conversion to sinus rhythm.

On hospital day 2, after receiving his second and third 500 mcg doses of dofetilide—36 hours after his first dose, the patient developed right facial

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To cite: Zhang L, Steckman D. *BMJ Case Rep* 2019;**12**:e227705. doi:10.1136/bcr-2018-227705

weakness and drooping of his mouth (figure 1). A neurological examination revealed no slurred speech, alerted consciousness, no dysarthria, aphasia, limb weakness or dysmetria. The calculated National Institute of Health stroke score was 2. Given his recent cardioversion, the primary diagnostic concern was for embolic stroke. An emergent head CT and CT angiogram, as well as a brain MRI were performed; all imaging studies showed no abnormalities.

On hospital day 3, the patient's facial weakness progressed to the forehead and upper half of the face. A diagnosis of Bell's palsy was made, and treatment with oral corticosteroids was started. The patient denied any recent illnesses, skin rashes, known tick bites or other sequelae of viral illnesses or Lyme's disease. Lyme serologies and PCR were negative. A review of the listed side effects for dofetilide showed a <2% frequency of facial paralysis.⁴ After a washout period, dofetilide was changed to oral amiodarone for maintenance of sinus rhythm. He was discharged home 24 hours later with 7 days of oral prednisone for treatment of Bell's palsy.⁵

On subsequent follow-up, the patient showed almost complete resolution of facial paralysis (figure 2).

INVESTIGATIONS

MRI brain.

CT head.

Lyme serology and PCR.

DIFFERENTIAL DIAGNOSIS

Cerebral vascular accident.

Transient ischaemic attack.

Herpes zoster infection.

Guillain-Barré syndrome.

Otitis media.

Lyme's disease.

HIV infection.

TREATMENT

Dofetilide, the presumptive cause of the patient's facial weakness was discontinued and a 7-day course of oral prednisone was started.

OUTCOME AND FOLLOW-UP

A follow-up visit 3 weeks postdischarge showed almost complete resolution of facial paralysis (figure 2).

DISCUSSION

In the above case, we describe a rare side effect associated with the use of dofetilide. This report is the first to describe the onset, timing, symptom severity, duration and potential treatment of dofetilide associated Bell's palsy.⁴

Bell's palsy, used to describe an acute peripheral facial palsy of unknown cause, is distinct from facial nerve palsy, which can be caused by a variety of conditions including herpes zoster

infection, Guillain-Barré syndrome, otitis media, Lyme's disease and HIV infection.⁶ Bell's palsy is typically associated with an isolated seventh cranial nerve neuropathy, as seen in our patient. Traditional pharmacological treatment of this condition is with early short-term oral glucocorticoids, typically 60–80 mg/day prednisone for 1 week.⁵ Most patients with Bell's palsy show some recovery within 3 weeks of initial symptoms, and >70% have full recovery even without treatment. In the case above, dofetilide administration was the only risk factor identified associated with the patient's Bell's palsy. Given the drug's temporal proximity to the patient's symptoms, we felt it prudent to discontinue the medication and begin corticosteroid treatment. Applying the Naranjo adverse drug reaction scale resulted in a score of 5, indicating a probable adverse reaction to dofetilide.⁷

Learning points

- ▶ Facial paralysis is a rare side effect of dofetilide. This side effect should be considered when initiating the drug to treat atrial fibrillation (AF).
- ▶ Ischaemic stroke is a well-known consequence of AF; sudden development of facial paralysis should appropriately raise the possibility of new stroke in patients with AF.
- ▶ Distinguishing Bell's palsy from ischaemic stroke in patients taking dofetilide is paramount as an incorrect diagnosis of acute ischaemic stroke may lead to the use of thrombolytics, which could result in major bleeding.

Contributors LZ is responsible for writing the manuscript, obtaining patient consent and providing initial patient care and follow-up. DS is responsible for a supervisory role, revisions of the manuscript and providing initial and follow-up care to the patient.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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