CASE REPORT

Ventricular tachycardia after initiation of fingolimod

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SUMMARY

Fingolimod, a sphingosine-1-phosphate receptor modulator, is used for the treatment of relapsing-remitting multiple sclerosis. It is well known to cause bradyarrhythmias. We present a 63-year-old woman who was admitted to the hospital with sustained monomorphic ventricular tachycardia 2 weeks after fingolimod initiation. Further evaluation showed that the patient's ventricular tachycardia was most likely secondary to her medication. Medical practitioners need to be aware of such possible life-threatening side effects while using fingolimod.

BACKGROUND

The use of fingolimod to treat multiple sclerosis has grown/is growing. The most common side effects are headache, liver transaminase elevation, diarrhoea, back pain, cough, influenza, sinusitis, abdominal pain and extremity pain.¹ Serious side effects, including bradycardia and atrioventricular block, have previously been reported.² Our patient was diagnosed with ventricular tachycardia secondary to fingolimod. This association has only been reported once previously.³ Ventricular tachycardia should be considered when fingolimod is used to treat multiple sclerosis.

CASE PRESENTATION

A 63-year-old Caucasian woman with a previous medical history of relapsing-remitting multiple sclerosis and hypertension presented to the emergency room after being called by her cardiologist because an abnormal heart rhythm had been detected by her surface-mounted Holter monitor. The patient's neurologist referred her to cardiology to be cleared prior to starting fingolimod. She underwent basal ECG, which showed sinus bradycardia (figure 1). The patient reported no previous history of palpitations, syncope or chest pain. She received her first dose of fingolimod at the cardiology office and was monitored for 6 hours with no abnormalities noted. Her cardiologist decided to put her on a surface-mounted Holter monitor, given her sinus bradycardia. Thyroid stimulating hormone was checked and was normal. Echocardiogram was normal. Previous medical history was significant for relapsing-remitting multiple sclerosis for 14 years. Prior to starting fingolimod, she had been on interferon beta-1b since her diagnosis.

Two weeks later the patient was instructed to go to the emergency room because of ventricular tachycardia captured by the Holter monitor. In the emergency room, the patient reported palpitations

and chest discomfort at home in concordance with the monomorphic ventricular tachycardia that was noted on the monitor (figure 2). She denied chest pain, shortness of breath, loss of consciousness or other symptoms. Physical examination was normal. The patient's only other medication is amlodipine.

In the hospital, fingolimod (Gilenya) was held. Laboratory investigations, including complete blood count, basic metabolic panel, thyroid function, liver function and renal function, were normal. The echocardiogram was checked in the hospital and was normal. Cardiac monitoring showed no other evidence of cardiac arrhythmias. Cardiac catheterisation showed normal coronary arteries. The electrophysiological study was normal with no inducible ventricular arrhythmia.

DIFFERENTIAL DIAGNOSIS

- ▶ Structural heart disease.
- ▶ Ischaemic heart disease with arrhythmia.
- ▶ Electrolyte imbalance.
- ▶ Thyroid disease.
- ▶ Drug-induced ventricular tachycardia.

TREATMENT

Management included medication cessation. The patient was observed in the hospital for 4 days with no evidence of further arrhythmias.

Outcome and follow-up

The patient was discharged home in a stable condition. She was followed for 2 months with no evidence of arrhythmias.

Discussion

Fingolimod inhibits lymphocyte egress from lymph nodes, through interaction with the sphingosine-1-phosphate receptor, thereby inducing lymphopenia.⁴ Sphingosine-1-phosphate receptors are expressed on different types of cells, including atrial, ventricular and septal myocytes.⁴ Side effects including bradycardia and atrioventricular block can occur, given that sphingosine-1-phosphate receptors are expressed on cardiac cells.⁴

Fingolimod is frequently used in cases of relapsing-remitting multiple sclerosis after it was found to be effective in randomised controlled trials.⁵ Multiple side effects have been reported in the literature, the most common being headache, liver transaminase elevation, diarrhoea, back pain, cough, influenza, sinusitis, abdominal pain and extremity pain.¹ It has been associated with the development of tumefactive demyelinating lesions.⁶ Other side effects include varicella zoster virus infections,⁷

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Figure 1 Patient's ECG showing sinus bradycardia.

progressive multifocal leucoencephalopathy,⁸ cryptococcal meningoencephalitis⁹ and macular oedema.¹⁰

Previous reports of death secondary to fingolimod raised more concern about potential cardiac causes of mortality.¹¹ One report of ventricular tachycardia was reported in a young patient with no previous cardiac history who presented with dizziness and headache, after which she was found to have monomorphic ventricular tachycardia.³ Premature ventricular complexes were noted to increase in frequency in another patient.¹² The possible arrhythmogenic effects of fingolimod were described in a further patient who developed paroxysmal atrial fibrillation after receiving the medication.¹³ Given the unexplained nature of sudden death in previous reports, underlying ventricular tachycardia secondary to fingolimod could be the potential cause of death.

Our patient was discharged with no complications, although serious outcomes could occur. Medical practitioners should

Figure 2 Patient's ECG showing monomorphic ventricular tachycardia.

be aware of this potential side effect and discuss it with their patients.

Learning points

- ▶ Fingolimod can cause ventricular tachycardia that may lead to death.
- ▶ Follow-up is warranted when starting fingolimod, even for asymptomatic patients.
- ▶ Patients should be warned about the association between fingolimod and ventricular tachycardia. Symptoms such as palpitations should be reported to medical practitioners immediately.

Contributors FE and AA took care of the patient in the hospital. Both drafted the manuscript. MLA took care of the patient in the hospital. SAH edited the manuscript, reviewed related literature and agreed the final manuscript.

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