Ginkgo biloba-induced frequent ventricular arrhythmia

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The use of herbal medications is becoming ever more widespread, but data for them are not yet as robust as for conventional drugs. The available safety information indicates that potential side effects of such use can be due to allergic reactions and bleeding.

In this report, a case of frequent ventricular arrhythmias probably due to Ginkgo biloba is presented. The patient complained of palpitations twice in a month and on both occasions symptoms and electrocardiographic evidence of ventricular arrhythmias resolved with discontinuation of Ginkgo biloba.

This case underlines that continuing research is needed to elucidate the pharmacological activities of the many herbal remedies now being used.

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Introduction

The growing use of herbal remedies in industrialized countries has far exceeded the increase in available information on their benefits, adverse effects and drug interactions[1].

Preliminary safety information indicated that potential side effects of such therapy are mainly due to allergic reactions and bleeding, but lately it has been recognized that herbal remedies may have sympathomimetic activity, thus promoting hypertension and arrhythmias[2]. Rhythm abnormalities, however, have been reported with herbs such as hellebore, Ma huang, oleander and yohimbine[3], but not with Ginkgo biloba, which nowadays is the most widespread herbal remedy in the United States[4].

The present case report involves a patient presenting with frequent ventricular arrhythmias possibly associated with the use of Ginkgo biloba.

Case report

A 49-year-old man (a physician) had been undergoing herbal therapy with Ginkgo biloba (40 mg, 3 times daily) for 2 weeks in an attempt to increase his cognition. He had a family history of hypertension, had been a smoker until the age of 30 and had been in good health in the past. He came to our observation complaining of palpitations. At the time of presentation, he was not an alcohol drinker and was on a low dietary salt intake diet as a measure to neutralize the familial tendency to develop hypertension. No drug was used for any reason. Physical examination revealed a blood pressure of 130/85 mmHg and normal heart sounds with no murmur at auscultation. The 12-lead ECG had a normal morphology but showed sinus rhythm with frequent ventricular premature beats (Fig. 1). All ectopic beats were isolated and monomorphic, with the appearance of left bundle branch block. For this reason, a noninvasive evaluation was programmed for the following days and the patient decided to suspend the use of any potential arrhythmogenic factors, including coffee (he usually drank two cups daily) and tea (he used to drink one cup daily). He also suspended treatment with Ginkgo biloba. Symptoms of palpitations disappeared within 2 days. Laboratory examination did not show any abnormalities. Of note, the blood concentration of electrolytes as well as the levels of FT3, FT4 and TSH were within normal limits. At Doppler echocardiography, there was no evidence of any structural or functional abnormality of the heart and its valves. The patient underwent maximal exercise stress which was stopped at a workload of 150 W because of exhaustion. At peak exercise, his heart rate was 105 b/min and the blood pressure was 160/100 mmHg (rate-pressure product 24 000

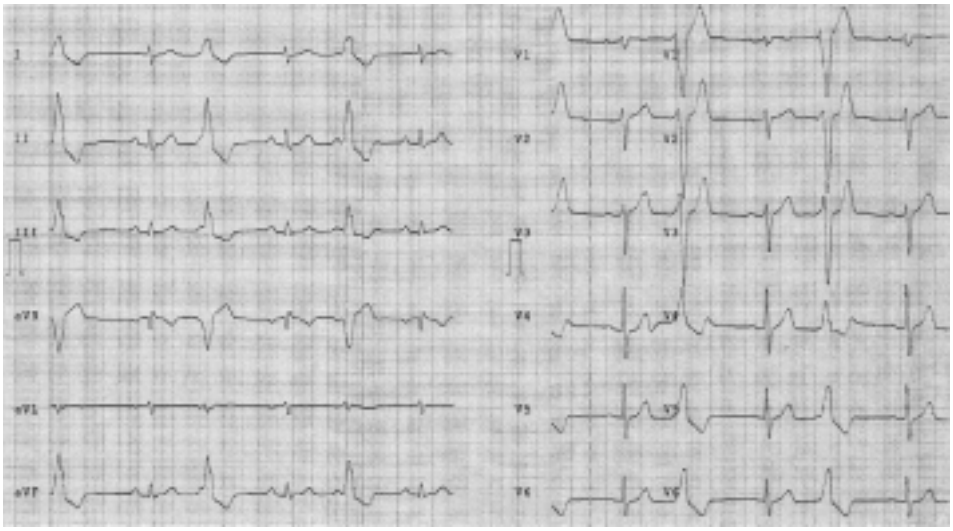

Figure 1. *Resting 12-lead ECG showing a left bundle branch block premature ventricular depolarization pattern. Otherwise, the ECG pattern is normal.*

b/min∗mmHg). Throughout the test, no changes in the ST segment or arrhythmias were observed. At Holter ECG monitoring, his heart rate averaged 70 b/min, ranging from a minimum of 40 b/min at 3:05 a.m. (while asleep) to a maximum of 145 b/min at 1:30 p.m. (while climbing the staircase at hospital).

The patient remained symptom-free for 2 weeks. He continued to abstain from coffee and tea, but he decided to resume with the Ginkgo biloba therapy. Two days later he again presented with palpitations and came to our observation. The patient immediately underwent repeat Holter ECG monitoring which showed a slight increase in the average heart rate (82 b/min) as well as the presence of frequent, isolated ventricular ectopic beats (total 2150) which were unevenly distributed throughout the 24-hour period. All premature beats had a left bundle branch block morphology and resembled those recorded at the initial Holter ECG. Since a possible association between Ginkgo biloba and the arrhythmia was hypothesized, the patient again stopped taking the drug. Symptoms ended the following day and no further ECG evidence of arrhythmias was detectable. After 3 months, the patient underwent follow-up Holter ECG which did not show any arrhythmia.

Discussion

Herbs have been used as medical treatments since the beginning of human pharmacotherapy, and are generally supposed to be effective in multiple conditions[1].

Several herbs also have a potential for cardiovascular diseases, including venous insufficiency, intermittent claudication, hyperlipidemia, hypertension, and congestive heart failure. Various mechanisms, including antioxidant, antiplatelet, fibrinolytic, antiatherosclerotic, antihyperlipidemic, antiarrhythmic and vasodilatory functions, have been advocated to explain the favorable effects of herbs[2]. Many herbal remedies used today, however, have not had to face the test of careful scientific assessment, and some may cause serious toxic effects and major drug-to-drug interactions.

A recent review has summarized the adverse effects of herbal therapies that impact on the cardiovascular system[3]. Herbal remedies may induce adverse cardiac effects including sympathomimetic activity, hypertension, and arrhythmias. Rhythm abnormalities have been reported with herbs such as hellebore, Ma huang, oleander and yohimbine, but not with Ginkgo biloba[3].

Ginkgo biloba is the most widespread herbal remedy in Western countries and is used for improving cognition and memory as well as for cerebrovascular disease, peripheral vascular disease, sexual dysfunction, affective disorders, multiple sclerosis, retinal disorders and hearing loss[4].

The mechanisms by which Ginkgo and its constituent compounds improve vascular health include free radical scavenging, antiplatelet actions, anti-inflammatory actions, vasodilation, and decreased blood viscosity. Ginkgo may benefit cerebrovascular disease by improving blood flow, reducing ischemia-reperfusion injury or inhibiting platelets[3]. Therapeutically full doses of Ginkgo biloba extract have been shown to provide cardioprotective effects in the rat mainly due to the inhibition of free radical formation[5].

Common side effects include nausea, dyspepsia, headache and allergic skin reactions, while more serious adverse effects such as subdural hematomas, intracerebral hemorrhage and hyphema have been occasionally reported[6].

To our knowledge, this case report is the first to suggest that the use of Ginkgo biloba might trigger ventricular arrhythmias even in otherwise normal individ-

uals. The possibility that Ginkgo biloba might favor rhythm abnormalities has been raised only by a previous laboratory investigation. Kubota et al.[7] have lately shown that dietary supplements (including Ginkgo biloba extract) can significantly increase the electrical activity, thus raising the beat rate and the contractile force in atria isolated from rats.

In conclusion, along with raising concern on a previously unrecognized potential side effect of Ginkgo biloba, this case report calls attention to the safety profile of herbal products. With the high prevalence of their use in Europe and the United States today, the clinician must inquire about the potential for benefit and harm. Tailored recommendations for each active ingredient are crucial, rather than lumping all herbal medications into one category. In addition, a mechanism for the more accurate reporting of the adverse events related to herbal medications is mandatory.

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