Case Report

A Case of Paroxysmal Atrial Fibrillation Improved after the Administration of Proton Pump Inhibitor for Associated Reflux Esophagitis

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Abstract A 64-year-old man had demonstrated palpitations caused by paroxysmal atrial fibrillation (AF) documented by ambulatory electrocardiographic monitoring. Effectiveness of antiarrhythmic agent (disopyramide: 300 mg/day) was limited. Based on the gastrointestinal endoscopic findings, proton pump inhibitor (PPI: rabeprazole, 10 mg/day) was administered to eliminate heart burn due to reflux esophagitis. Symptoms of paroxysmal AF and reflux esophagitis were confusing due to the anatomical proximity of the diseased organs and concomitant occurrence in the evening and when in a supine position. After the additional PPI therapy, not only was reflux esophagitis improved subjectively and endoscopically but also paroxysms of AF markedly reduced. Because esophagus is attached to left atrial posterior wall and the role of inflammatory process on the development of AF is highlighted, amelioration of reflux esophagitis by PPI may have been followed by the remarkable reduction of paroxysms of AF.

Key words: atrial fibrillation, proton pump inhibitor, reflux esophagitis

Introduction

Atrial fibrillation (AF) is a common arrhythmia and the incidence of AF increases age-dependently1. However, the effectiveness of antiarrhythmic agents for AF is limited and nonpharmacologic therapy is currently expected as a curative treatment2. Radiofrequency (RF) catheter ablation is attempted mainly to isolate arrhythmogenic pulmonary veins (PVs) from the left atrium (LA), because AF is maintained in LA by fibrillatory stimulus originated from PVs. LA contacts the esophagus so closely that there is a potential risk of atrioesophageal fistula as a serious complication of isolation of PVs by RF ablation3.

On the other hand, gastroesophageal reflux disorder (GERD) is supposed to be increasing by the alterations in life-style occurring in this country. Proton pump inhibitor (PPI) is available as the first choice of therapy for GERD4,5. It is, therefore, likely not to be rare to encounter patients with AF associated with GERD in a clinical setting. The effects of PPI on AF remain unclear, because there have been
controversial reports, i.e., PPI increases compensatory secretion of gastrin\(^{97}\), which is suspected to be a vagal co-transmitter\(^{8}\) inducing AF\(^{90}\) versus reports that PPI is effective as an adjunctive therapy for AF associated with GERD\(^{90}\). Here, we report a case of paroxysmal AF treated successfully by PPI administered for associated GERD.

**Case Report**

A 64-year-old man demonstrated recurrence of palpitations caused by paroxysmal AF documented by ambulatory electrocardiographic (ECG) monitoring (Fig. 1). At the first visit to the outpatient clinic, blood pressure was 138/78 mmHg. Pulse was regular and its rate was 68 bpm. Physical examination showed no specific abnormalities. Serum chemistry suggested no sys-

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**Fig 1.** A: Electrocardiographic (ECG) recording of the onset (upper) and the termination (lower) of the paroxysmal atrial fibrillation (AF). B: Ambulatory ECG documenting a paroxysm of AF that occurred from 19:47 to 19:48 p.m.
Fig 2. Part of atrial fibrillation quality of life questionnaire (AFQLQ) in Japanese completed prior to (A) and again following (B) the administration of proton pump inhibitor (PPI). This questionnaire characterized postprandial and nocturnal occurrence of palpitation (A) and remarkable improvement of palpitation after the administration of PPI (B).

Fig 3. Endoscopic findings prior to the administration of proton pump inhibitor indicating esophagitis (A) and hiatus hernia (B). Esophageal mucosa demonstrated white coating (arrows in A) and ECJ was dislocated (arrow in B). There was no sign of Barrett's esophagus.

temic illness including electrolyte imbalance and thyroid dysfunction. Chest X-ray, pulmonary function test and transthoracic echocardiography demonstrated no structural abnormalities. AF had been treated by conventional antiarrhythmic agents such as disopyramide and cibenzoline. These agents were initially effective, but the effectiveness was diminished by continued administration, allowing the recurrence of the paroxysms of AF. The frequency of the paroxysmal episodes was several times a day. Palpitation was evident in the evening, especially after dinner and when the patient assumed a supine position (Fig. 2A). This patient also complained of postpran-
dial heart burn and epigastric discomfort, which were confusing to the precordial and epigastric feelings related to palpitation. Then he underwent gastrointestinal endoscopic examination, which demonstrated reflux esophagitis associated with hiatus hernia (Fig. 3).

After obtaining this diagnosis, administration of proton pump inhibitor (PPI: rabeprazole, MW = 381, 10 mg/day) was initiated. Helicobacter pylori were negative serologically and histopathologically. Rapid urease test was also negative. Under this treatment, symptoms of reflux esophagitis evaluated by Frequency Scale for the Symptoms of GERD (FSSG) were markedly relieved, i.e., the FSSG score was reduced from 26 to 15. Moreover, palpitation also disappeared several hours after starting PPI therapy unexpectedly. Symptomatic improvement was evident in atrial fibrillation quality of life questionnaire (AFQLQ) authorized by Japanese Society of Electrocardiology, as shown in Fig. 2B. The administration of PPI was continued for one month, thereafter discontinued under the guidelines of the Japanese medical insurance system. However, the patient did not complain of palpitation and AF was not documented by ambulatory ECG monitoring for several weeks. Amelioration of endoscopic finding was also confirmed. Throughout the entire clinical course, antiarrhythmic agent was not altered (disopyramide; 300 mg/day). Thereafter, PPI was administered intermittently and there was no relapse of frequent AF paroxysms, i.e., AF is currently documented about once a month by ambulatory monitoring.

Discussion

Although it remains unknown whether the incidence of GERD in patients with AF is greater than that in the general population, both AF and GERD are considered as common diseases that show a tendency to increase with prolonged life-span and alterations in life-style occurring in this country. In fact, this case of AF is also associated with GERD, and symptoms of AF and GERD are confusing and concomitant in this case. This seems to be due to physiological and anatomical reasons. Physiologically, AF and GERD may stem from an identical autonomic background. Although autonomic modulation of AF is complicated, concomitant occurrence of symptoms due to AF and GERD suggests that AF is vagally mediated in this case. Vagal tone augmentation shortens effective refractoriness in LA inhomogeneously, which leads to the paroxysms of AF and increases gastric juice secretion exacerbating GERD.

Anatomically, proximity of esophagus to LA is of unnoticed importance because recent investigations demonstrated that AF is promoted by inflammatory mechanisms. Reflux esophagitis sometimes causes esophageal bleeding and deformation, suggesting that inflammatory process penetrates the esophageal muscle layers. AF is easily supposed to be exacerbated, if such inflammatory process due to esophagitis extends to the neighboring posterior LA wall. PPI administered in this case was unexpectedly effective in suppressing paroxysms of AF (Fig. 2B), suggesting that endoscopic amelioration of esophagitis may have induced favorable effects of PPI on AF paroxysms. Actually, Gerson et al. also reported three cases of GERD in which antacidic therapy reduced paroxysms of associated AF. Their study emphasized close etiologic linkage of AF and GERD under simultaneous ambulatory ECG and
esophageal pH monitoring and is compatible with our case report.

In addition to the preventive role of PPI on inflammatory extension to LA, PPI may have direct or indirect cardiac actions. Although serum gastrin was not evaluated in this case, chronic PPI therapy or subsequent possible hypergastrinemia may augment cholinergic effects\(^{17}\) leading to the occurrence of vagally mediated AF\(^{14}\). On the other hand, our previous investigation demonstrated functional possibility of myocardial proton pump exerting K\(^+\)-H\(^+\) counter-transportation, which plays important roles in intracellular pH regulation and transmembrane K\(^+\) balance in myocardium\(^{18}\). This possible transport system may cause extracellular K\(^+\) uptake, and local hypokalemia predisposes toward AF paroxysms clinically\(^{19,20}\) and experimentally\(^{21}\). Therefore, PPI inhibiting this possible transporter is supposed to be antiarrhythmic. Further basic studies are required to identify the possible cardiac target of PPI.

In conclusion, we presented a case of paroxysmal AF treated successfully by PPI administered for associated GERD. General effects of PPI on AF remain unknown, being presumably counterbalanced with respect to the direct or indirect cardiac actions. However, PPI is concluded to be effective on AF at least when associated with GERD as in this case by ameliorating reflux esophagitis. We sometimes recognize various etiologies of AF such as pulmonary and thyroid diseases and limited effectiveness of conventional pharmacologic therapy on AF in such cases. Association of AF and GERD should be highlighted in this report and accumulation of such cases may lead to an established treatment protocol with PPI as adjunctive therapy for AF.

An observational study regarding the therapeutic effects of PPI on AF including this case was presented in the Second Asian-Pacific Atrial Fibrillation Symposium 2006 in Tokyo.

References


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逆流性食道炎に対して投与したプロトンポンプ阻害剤が奏功した
発作性心房細動の一例

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症例は64歳男性。動悸を主訴に来院した。ホルター心電図の結果より動悸は発作性心房細動によ
ると考えられた。動悸は胸やけと前後して起床時食後や臥位で多かったため、この症例の心房細
動は迷走神経依存型と考えられた。しかし従来の抗不整脈薬（ジャピラミド：300 mg/日）の心房細
動に対する抑制作用は十分ではなかった。内視鏡検査では逆流性食道炎も確認され胸やけはこれに
よると考えられたため、プロトンポンプ阻害剤（ラベプラゾール：10 mg/日）を投与したところ、
胸やけの改善とともに動悸も著減した。これは内視鏡所見の改善から考えると、逆流性食道炎によ
る炎症機転が食道と隣接する左房へ波及していた可能性と、これがプロトンポンプ阻害剤によって
抑制された可能性が考えられた。プロトンポンプ阻害剤自体の心臓迷走神経や心房筋への作用はな
お不明であるが、少なくとも逆流性食道炎をともなう発作性心房細動に対して、プロトンポンプ
阻害剤は補助的な治療効果を有すると考えられる。