Neurogenic atrial fibrillation

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Introduction

Atrial fibrillation (AF) is the commonest sustained arrhythmia encountered in clinical practice. Depending upon its time course, AF can be classified into three categories: paroxysmal, persistent and permanent.[1] Paroxysmal AF is characterised by recurrent episodes of AF alternating with sinus rhythm. The hallmark of paroxysmal AF is that most of the episodes of AF terminate spontaneously.[1] This condition is sporadic and the duration of episodes, severity of symptoms and intervals between attacks are highly unpredictable.[2]

The term 'neurogenic AF' can be used to define a type of paroxysmal AF in which two opposite mechanisms (vagal and sympathetic, which often interact) can be identified and in which autonomic nervous system (ANS)-induced heart rate changes in the sinus node have important influences on the arrhythmogenesis.

Both myocardium and conduction tissue in the heart are well innervated by nerve fibres from the ANS. The sinoatrial (SA) node, atrium and atrio-ventricular (AV) node are significantly influenced by autonomic tone. Vagal influences depress the automaticity of the sinus node, depress conduction and prolong refractoriness in the tissue surrounding the sinus node.[3] Vagal influences also shorten the atrial effective refractory period and decrease conduction velocity in a non-uniform manner.[4] Sympathetic influences exert the opposite effect. Sympathetic and parasympathetic terminals lie in close proximity to one another, and both are close to the target cells. Stimulation of the sympathetic system may affect vagal function, and *vice versa*. Acetylcholine release from the vagal nerve endings diminishes norepinephrine release from the surrounding nerve endings. Atrial vulnerability to vagal stimulation depends mainly on the shortening of the cycle length of the atrial impulse.[5] Vagal stimulation causes the formation of macro re-entry circuits such as flutter.[3] Sympathetic stimulation, on the other hand, provokes micro re-entry, automatic and triggered activity.[3] There is a predominance of vagal influences in normal atria; vagal withdrawal is an early characteristic of the diseased heart, preceding even the increase in sympathetic drive. The arrhythmogenic effects of the ANS are more likely to occur via the vagal limb in normal tissues and via the sympathetic arm in diseased tissue.[6]

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Vagally mediated paroxysmal atrial fibrillation

Vagally mediated paroxysmal AF occurs more commonly in men than in women (ratio 4:1).[7] The age of onset is usually 30–50 years. It hardly ever occurs in a structurally diseased heart, probably because any cardiac disease tends to shift the vagosympathetic balance towards a sympathetic predominance.[3]

The usual history is of weekly episodes. The heart rate is relatively slow during the episodes of AF and most patients complain of irregular heartbeats rather than dyspnoea, lightheadedness or syncope. A typical attack usually begins at night and lasts for a few hours. Attacks do not start in the morning: on the contrary, conversion to sinus rhythm frequently occurs in the morning, when the sympathetic drive is higher. Neither physical exertion nor emotional stress triggers the arrhythmia but a period of relaxation that follows may trigger it. Cough, nausea, rest, post-prandial states and alcohol are also precipitating factors.[8] Vagally mediated AF rarely, if ever, progresses to permanent AF.

A 24-hour ECG can confirm the role of the ANS by showing progressive slowing of the heart rate over a few hours, or even a few beats, before the onset of arrhythmia.[3] An increase in the respiration-related heart rate variation (which is vagally mediated) preceding the onset of AF also confirms the role of the ANS. As concerns the cause of vagally mediated AF, it is probably more appropriate to think in terms of heightened sensitivity of the cardiovascular system to the changes in autonomic function, rather than an intrinsic abnormality of the ANS.[9,10]

Published experience of the treatment of vagally mediated AF is limited. Beta blockers and digoxin are not only ineffective but are contraindicated, as they tend to precipitate the arrhythmia and prevent the traditional anti-arrhythmic treatment from being effective. Prophylaxis is not indicated unless AF occurs so frequently that the efficacy of any intervention can be assessed. Paroxysms that remain few and far between, and relatively asymptomatic may not warrant prophylaxis.

When episodes are more frequent or when symptoms become intolerable, long-term use of antiarrhythmics has been shown to maintain sinus rhythm at one year 50% to 60% of the time, but these medications carry proarrhythmic risks.[11] Flecainide and disopyramide both have significant vagolytic properties, and are useful drugs for this condition. Since this

arrhythmia occurs mainly in young people with normal myocardial function, the negative inotropic effects of these drugs can be ignored. Propafenone is perhaps not a good choice for this condition because of its beta-blocking properties.

Atrial pacing very consistently prevents vagally induced AF and can be used for patients with frequent recurrences.[12] Transvascular atrial parasympathetic nerve system modification by radiofrequency catheter ablation can also abolish vagally mediated AF.[12]

Adrenergically mediated paroxysmal atrial fibrillation

Adrenergically induced paroxysmal AF occurs much less frequently. It can occasionally result from disorders such as hyperthyroidism or phaeochromocytoma. More often, however, there is no evidence of a primary ANS disturbance. Sympathetic influences are suggested by the clinical history of attacks occurring during the daytime, with stress or exercise. This arrhythmia is characteristically associated with polyuria.[13] It occurs much less frequently than vagally mediated AF in the absence of heart disease. In patients with identified heart disease and paroxysmal AF, sympathetic influences play a predominant role.

A 24-hour ECG can confirm the diagnosis by showing an increase in sinus rate and ectopic supraventricular beats before the onset of AF. It may also show the diminution of respiration-related short-term heart rate variation, signifying the absence of vagal modulation.

There is no reason to suspect any disturbance of the ANS as the basic cause of this sympathetic mediated AF. Again it is appropriate to think in terms of heightened sensitivity to the heart rate acceleration and the loss of vagal influences that occur prior to the arrhythmia onset.[3]

As far as the treatment of adrenergic AF is concerned beta blockers are clearly the drug of choice. There is no role for atrial pacing in this condition.[3]

Conclusions

The autonomic nervous system plays a very important role in the pathogenesis of paroxysmal atrial fibrillation in some patients. A clear understanding of this point is necessary as it has important therapeutic implications. Although patients with pure vagal or adrenergic AF are uncommon, when the clinical history reveals a pattern of onset of AF that has features of one or other of these syndromes, the clinician may be able to select drugs to prevent further episodes. The published experience with neurogenic AF is very limited. Until cardiovascular pharmacologists and electrophysiologists develop awareness of, and interest in, neurogenic AF this treatable condition will be under-treated.

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