Multiple and Concurrent Arrhythmia

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Given the unique interventional emphasis in our specialty, Teaching Rounds in Cardiac Electrophysiology has frequently centered on the pearls and pitfalls associated with electrogram analysis and complications of lead implant extraction or ablation and in mapping complex arrhythmia circuits. In this issue of Circulation: Arrhythmia and Electrophysiology, Fabrizio et al., in a refreshing departure from this norm, take us to a more classic medical teaching rounds relevant to rhythm management. They present a patient with multiple changing malignant rhythm disorders resulting from caffeine toxicity. Their submission is replete with clinical diagnostic dilemmas, treatment difficulties, and also a succinct but comprehensive discussion of caffeine toxicity and the heart.

Sinus Tachycardia

Prominent sinus tachycardia with drug overdose may be from an agent that is primarily vagolytic, sympathomimetic, or both. Agents that produce vagolysis at toxic levels include first-generation antihistamines and tricyclic antidepressants, whereas common proadrenergic drug toxicity is seen with cocaine, nicotine, pseudoephedrine, and caffeine.1,2

Distinguishing between these groups is aided by the coexisting loss of secretions (saliva), dry skin, and urinary retention with vagolytic agents and prominent vasomotor effects that accompany the sinus tachycardia with sympathomimetic drugs.

Sinus Tachycardia and Malignant Ventricular Arrhythmia

The combination of sinus tachycardia and VT or ventricular fibrillation occurs with certain drugs at toxic levels.

Sympathomimetic Agents

Amphetamine-Like Drugs

The clinical scenario may be a patient on medication for attention-deficit disorder or weight loss, as well as possible recreational drug use. Specific drugs include dextroamphetamine, methamphetamine, and methylphenidate. MDMA (3,4-methylenedioxymethamphetamine; Ecstasy) is a recreational drug that has a similar rhythm toxic profile. Patients may intentionally consume an overdose, or anti–attention deficit disorder drugs may be taken too frequently by students during examinations, and so on. Most agents cause elevated blood pressure when hypotensive VT is not present, and patients may quickly exhibit changing triggered rhythms along with sinus tachycardia, including atrial tachycardia and triggered ventricular fibrillation.4-6

Monamide Oxidase Inhibitors

Less commonly used antidepressants, such as phenelzine, unlike the tricyclics, have prominent sympathomimetic effects, including markedly elevated blood pressure, sinus tachycardia, and VT. These effects are caused by reduced metabolism of circulatory catecholamines with monamide oxidase inhibitor use. Drug interactions with serotonin uptake inhibitors, tricyclic antidepressants, and tyramine-containing foods may precipitate arrhythmias.
Cocaine
Cocaine abuse and overdose present with a strikingly hyperadrenergic state. Marked sinus tachycardia, severe hypertension, and ventricular arrhythmias may occur together or closely follow one another. Ventricular fibrillation may also occur as a result of myocardial infarction occurring from coronary vasospasm or thrombosis.2,4

Herbal Agents
Herbal weight loss agents, such as ephedra, found in the popular agent ma Huang at toxic levels may precipitate simultaneous sinus tachycardia and triggered VT. Hypertension is usually present. A similar syndrome also is found with licorice root and oleander poisoning. The latter produces a very similar arrhythmia profile to digitalis toxicity, including the occurrence of AV block but with somewhat more prominent pro sympathetic effects, including sinus tachycardia.2,5

Anticholinergic Agents
Tricyclic antidepressants in an overdose scenario may exhibit monomorphic VT and sinus tachycardia. VT typically occurs in the context of prominent QRS duration increase and possible AV block. First-generation antihistamines may produce a similar syndrome but with normal or enhanced AV conduction because histamine is a weak AV nodal–blocking drug.3

Sinus Tachycardia With Malignant Ventricular Arrhythmia but Without Significant Hypertension
Nicotine poisoning as part of intentional insecticide or nicotine substitute overdose or with green tobacco sickness seen in plantation workers may present with sinus tachycardia and VT. The blood pressure responses, however, follow a temporal profile with initial hypertension along with tachycardia followed by significant hypotension usually with the heart rate returning to normal or with sinus bradycardia.5

Theophylline toxicity most closely parallels the patterns of arrhythmogenesis seen with caffeine intoxication. Adenosine receptor antagonism and phosphodiesterase inhibition with coexisting increase catecholamine release produce multiple arrhythmias but without hypertension. Sinus tachycardia, atrial tachycardia, atrial fibrillation, triggered VT, and ventricular fibrillation, similar to what was seen in the patient described by Fabrizio et al with caffeine, may be present. Indeed, as noted by the authors, some of caffeine cardiac toxicity from relatively small amounts of theophylline, a metabolic product of caffeine. A unique arrhythmia seen rarely with other agents but not uncommon with theophylline toxicity is multifocal atrial tachycardia.7

Caffeine toxicity because of peripheral vasodilation, as seen in the described patient, produces hypotension, despite the otherwise overall picture of sympathetic stimulation. The hypotension is seen with or without ventricular arrhythmia and may be a clue when multiple and concurrent arrhythmias are present that point to the specific etiology. Although decreased peripheral vascular resistance is the hallmark, the coronary circulation may show an opposite pattern with coronary vasospasm (similar to cocaine in this regard but without the hypertension). The management plan and pertinent pharmacology of caffeine is excellently described by Fabrizio et al.1

Treatment Difficulties With Drug Overdose–Related Arrhythmias
Because of the multiple pharmacological actions of both antiarrhythmic agents, as well as noncardiac drugs that present with arrhythmia, treatment is challenging and may require aggressive supportive care as was required in this patient. Although hyperadrenergic features are present, the use of β-blockers in some cases may result in unopposed α-agonist and precipitous hypertension. Similarly, alkalization, a mainstay of tricyclic overdose, may interfere with the metabolism or action of other drugs, including antiarrhythmic agents, and result in a secondary toxic profile.2,3 The authors also importantly point out the need for long-term planning and care in the intentional overdose patient, which in their case meant transfer to an inpatient psychiatric facility.1 One of the present authors had the misfortune of caring for a patient with oleander toxicity who after aggressive and eventually successful management of multiple arrhythmias and circulatory support sadly died in a later suicide.

Summary
Fabrizio et al take us back to the original, general, medical grand rounds but use an unusual arrhythmia syndrome with multiple and concurrent tachycardias and take us through the differential diagnosis which provides a useful reference for managing caffeine toxicity.

Disclosures
S.J. Asirvatham receives no significant honoraria and is a consultant with Abiomed, Ativio, Biosense Webster, Biotronik, Boston Scientific, Medtronic, Spectranetics, St. Jude, Sanofi-Aventis, Wolters Kluwer, Elsevier, and Zoll. W.G. Stevenson is co-holder of a patent on needle ablation that is consigned to Brigham and Women’s Hospital.

References

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