PERSPECTIVE

LESS IS MORE

An Adverse Reaction to a Medication Given to Treat an Adverse Reaction
A Teachable Moment

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Story From the Front Lines

A woman in her 70s with a history of well-controlled chronic obstructive pulmonary disease (COPD) and paroxysmal nonvalvular atrial fibrillation without underlying structural heart disease was transferred to an academic medical center for management of febrile neutropenia. Her initial atrial fibrillation event occurred many years before and resolved spontaneously without treatment.

In 2011 she was admitted at another hospital for bronchitis. During this hospitalization, she experienced return of her atrial fibrillation with a rapid ventricular rate. An initial attempt to control her rhythm with sotalol hydrochloride failed as a result of unspecified medication intolerance. She was subsequently given amiodarone hydrochloride and converted to normal sinus rhythm, in which she remained for almost 2 years.

In 2013, the patient began to experience increasing fatigue and weight loss. She was admitted with recurrent atrial fibrillation and found to be severely hyperthyroid with serum levels of thyrotropin of less than 0.01 mIU/L (reference range, 0.3-5.7 mIU/L) and free thyroxine of 29 ng/dL (reference range, 0.5-1.2 ng/dL [to convert to picomoles per liter, multiply by 12.871]). She had no history of thyroid disease, and her thyrotoxicosis was attributed to toxic effects of amiodarone of unspecified type. Although amiodarone therapy is usually continued in thyrotoxicosis because cessation may increase severity, it was discontinued because of recurrent atrial fibrillation. She began receiving methimazole 30 mg daily for presumed type I hyperthyroidism, and rhythm control was attempted with dofetilide. She converted to sinus rhythm while receiving dofetilide but continued to have intermittent episodes of atrial fibrillation. Approximately 1 month later, she visited an endocrinologist complaining of fatigue. At that visit, laboratory testing revealed persistent hyperthyroidism and her methimazole dose was increased to 60 mg daily. She continued receiving that dose without symptomatic improvement and 2 months later presented to an outside institution with fever and sore throat. Transfer to our hospital was requested when routine laboratory tests revealed pancytopenia in addition to fever and thyrotoxicosis. On admission, her blood hemoglobin level was 8.1 g/dL (reference range, 12.0-15.5 g/dL [to convert to grams per liter, multiply by 10]), hematocrit was 25% (reference range, 35%-45% [to convert to proportion of 1.0, multiply by 0.01]), platelet count was 12×10^3 cells/μL (reference range, 150-450 × 10^3 cells/μL [to convert to ×10^9 cells per liter, multiply by 1.0]), and white blood cell count was 800 cells/μL (reference range, 3200-9800 cells/μL [to convert to ×10^9 cells per liter, multiply by 0.001]). A manual differential identified no neutrophils.

Teachable Moment

Unfortunately, the patient experienced a life-threatening adverse reaction (febrile neutropenia) to a medication (methimazole) prescribed to treat a severe adverse reaction (thyrotoxicosis) to another medication (amiodarone). Atrial fibrillation is the most common cardiac arrhythmia, and multiple treatment strategies exist. In this case, a rhythm control strategy with amiodarone was pursued. Rhythm control does not offer a survival advantage compared with rate control,[1] and there are several potential advantages to the rate control strategy, including decreased risk of adverse drug effects.[2] An early rhythm control strategy may be preferable in individual patients with diastolic dysfunction or excessive symptom burden because of effects on quality of life. One study using the Short Form Health Survey (SF-36) found that both rate and rhythm control strategies were associated with an equivalent improvement in quality of life, which means that rhythm control decisions for quality of life may need to be individualized.[3]

Concern for acute bronchospasm with β-blockade in patients with COPD may cause hesitation in pursuing a rate control strategy in some patients. However, the patient tolerated sotalol, which has β-blocking properties, without known exacerbation of her COPD. Also, a Cochrane Review[4] of 22 studies suggests that cardioselective β-blocker treatment has no adverse effects in patients with reversible airway disease. In addition, the patient had a structurally normal heart and normal ejection fraction at the time of diagnosis and could have been treated with calcium channel blockers for rate control.

Agranulocytosis is the most dangerous adverse effect of antithyroid drugs. The risk of agranulocytosis with methimazole treatment is age and dose dependent. Agranulocytosis with neutropenia occurs more frequently in patients receiving a dose of 60 mg/d compared with 30 mg/d (1.6% vs 0.5%).[5]

Acute onset of atrial fibrillation with rapid ventricular rate in an inpatient can be alarming. The initial desire to return the patient to normal sinus rhythm is augmented by our nomenclature: the default is called normal. In this acute setting, many inpatients are given antiarrhythmic medications with potential long-term

consequences. A rate control strategy may have prevented 2 future hospitalizations and the costs and burdens of additional medications and physician visits and preserved an equivalent duration and quality of life. The potential consequences of medication use are often difficult to weigh in the acute care setting, a phenomenon inadvertently yet elegantly described by the team's medical student at the conclusion of the presentation: "Isn't everyone on amiodarone?" she asked.

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