A 79 yo woman with chronic atrial fibrillation, renal insufficiency, and depression who was status post MV repair, TV repair, and bi-atrial maze procedure in 2004 presented in 2010 with biventricular dysfunction (LVEF 30%), severe MR, and severe TR. She was deemed a poor surgical candidate and managed medically, with multiple subsequent admissions for CHF exacerbations. Left heart catheterization revealed LAD disease, and she was eventually scheduled for CABG and MV replacement. Induction and dissection were uneventful. Prior to CPB, she was started on vasopressin and milrinone infusions. In addition, methylene blue was bolused 2mg/kg over 30 minutes, followed by an infusion at 1mg/kg/hr. CPB was initiated without incident, and the patient was weaned from CPB on milrinone, epinephrine, norepinephrine, vasopressin, and methylene blue. She was taken to the ICU intubated with adequate hemodynamics and a temperature of 36.6 C.

Over the next few hours, she developed rigors and required increased minute ventilation for progressively worsening respiratory acidosis. Five hours after arrival, her temperature reached 40 C. In addition, her hemodynamics worsened and she developed oliguria. CK and myoglobin levels were elevated at 502 u/L and 3221 ng/mL, respectively. With a working diagnosis of malignant hyperthermia, one dose of dantrolene 1mg/kg was given, after which her symptoms improved dramatically. She had two episodes of recurrence requiring repeat dosing.

While this certainly may have been the result of MH, other possibilities remain. One such possibility is serotonin syndrome secondary to an interaction between methylene blue and serotonergic drugs (such as SSRIs and SNRIs). Methylene blue has been thought of as relatively benign, but with its increasing use and the increasing prescription of antidepressants, it is now recognized that the combination of methylene blue and serotonergic drugs may trigger serotonin syndrome. The USFDA has issued a warning advising against using the combination.

The difficulty in determining the diagnosis in this case lies in the fact that both malignant hyperthermia and serotonin syndrome are clinical diagnoses which look very similar to one another and may be confounded by the opioids received during a typical cardiac anesthetic. The gold standard test for MH is only performed at five centers in North America and requires a fresh muscle biopsy, requiring the patient to travel for testing. In addition, getting insurance to cover these expenses may be a challenge. With all of these hurdles, many do not pursue testing.

With the increasing use of methylene blue, providers should be aware of the interaction between methylene blue and serotonergic medications.

7. Ng BKW, Cameron AJD. Psychosomatics 2010;51:194-200