High-NR: an anticoagulation near miss.

Tyler Anstett, DO – PGY2

Story from the Front Lines:

It was a busy call day and I was called by the Emergency Department for a new admission. The patient was a 45 year-old man who was referred to the hospital by his primary care provider (PCP) for an INR that exceeded the outside laboratory test parameters – their equipment simply read greater than 8.0. Once the patient arrived at the Emergency Department, an INR was sent to the lab with a result of 13.4 with another sent two hours later returning a value of 15.8. The INR was checked by his PCP for routine monitoring of his warfarin dosing.

Despite having a significantly elevated INR, the patient was completely asymptomatic. He demonstrated no evidence of bleeding, bruising, headache, or GI upset. He had normal vital signs and all other laboratory testing was normal.

When asked why he was taking warfarin, the patient indicated he was placed on this medication after developing a blood clot that was associated with a central venous catheter during a hospitalization eight months prior. The catheter was removed at that time.

Despite rigorous investigation into medication administration, dosing, diet review, and pharmacy verification, it was never determined what caused this significant elevation in this patient’s level of anticoagulation.

Ultimately, the patient received 10mg of oral vitamin K, was admitted to the hospital for monitoring, discharged home with a down-trending INR, and advised to stop taking his warfarin without any adverse effects during the hospitalization.

Teachable Moment:

The above case demonstrates two things: 1) warfarin therapeutic levels can be erratic and can be difficult to predict, and 2) warfarin and other anticoagulant medications should be used with caution, for the shortest duration. In 2006, an evaluation of over 6000 patients taking warfarin showed that patients were outside the therapeutic range almost 50% of the time\(^1\). Further, according to a meta-analysis of 33 studies, major bleeding events (those involving a critical organ or body cavity, requiring transfusion of blood products, or hospitalization) occur with a rate of 7.2 per 100 patient-years. Additionally, fatal bleeding events occur with a rate of 1.3 per 100 patient-years\(^2\). As a result, adverse effects of warfarin ranked third highest amongst adverse drug effects causing hospital admissions in an evaluation of over 18000 patients\(^3\).

Though the risk of bleeding is always a consideration, warfarin can be life saving in the proper setting e.g. unprovoked venous thromboembolism or after mechanical heart valve placement. Unfortunately, as recently discussed in an editorial by Maynard\(^4\), upper extremity line associated thrombosis is not an indication with sufficiently robust data to confidently guide anticoagulant therapy. This issue
notwithstanding, both the American College of Chest Physicians and international clinical practice guidelines recommend treatment of line-associated upper-extremity thromboses with full anticoagulation (and catheter removal if able) for a period of three months.\textsuperscript{5,6} This patient had been maintained on warfarin for five months longer than necessary, placing him at undue risk for harm. It is not clear why he was maintained on extended anticoagulation and did not recall a discussion of benefits and risks of anticoagulation beyond the usual three months.

Of note, the risk of bleeding with an elevated INR has not been extensively studied. In one cohort study of 6761 patients taking warfarin, of 1104 patients with an INR greater than 5, major bleeding occurred at a low rate of 0.96% over 30 days.\textsuperscript{7} However, in this study all INR values were in the range of 5-9, and 80% of the elevated values were less than 7, making it difficult to extrapolate the risk of bleeding in the present case.

While this patient suffered no adverse effects from his dangerously elevated INR, he was at risk of serious bleeding and endured an avoidable hospitalization and all its accordant risks. Although near-misses are less dramatic than bad outcomes, they offer an opportunity for evaluation and intervention to prevent harm to our patients. The above case highlights how we should not only strive do no harm, also prevent harm before it occurs.

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