The deadly duo: Spontaneous pericardial effusion with early tamponade due to concomitant Rivaroxaban and Amiodarone use.

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**Introduction:**
Direct oral anticoagulants, including Rivaroxaban, are widely used for non-valvular atrial fibrillation due to a better safety profile than Coumadin. Drug-drug interactions between Rivaroxaban and Amiodarone can lead to severe hemorrhagic complications.

**Case:**
A 77-year-old male with a history of DVT/PE on chronic Rivaroxaban presented to the emergency with weakness. On presentation, he was in new-onset atrial fibrillation with a rapid ventricular response. Cardiology recommended transesophageal echocardiography (TEE), DC cardioversion, and continuing Rivaroxaban for anticoagulation. His hemoglobin was 10.2 g/dl. Amiodarone was commenced for rate and rhythm control in preparation for cardioversion. TEE on the 4th day of admission showed a new significant moderate circumferential pericardial effusion measuring 2.3 cm without tamponade. After a successful cardioversion, normal sinus rhythm was restored.

The next day, he had a sudden hemoglobin drop from 7.7 g/dl to 6.4 g/dl in 24 hours with no overt bleeding. He became more dyspneic and hypotensive with systolic blood pressure in the 70s. Rivaroxaban was discontinued. A CT scan showed the development of a moderate pericardial effusion, with no evidence of active gastrointestinal bleeding or apparent malignancy. An echocardiogram showed an increased circumferential pericardial effusion, now measuring 2.6 cm, as shown in figures 1 and 2.

Observing early clinical signs of tamponade, Cardiology performed an urgent pericardiocentesis yielding 700 cc of serosanguinous fluid. Pericardial fluid analysis showed 441,000 RBCs, 1500 total nucleated cells, and negative cytology. Stool occult blood was negative, and the hemorrhagic pericardial effusion was deemed likely due to the drug-drug interaction between Amiodarone and Rivaroxaban, with Amiodarone enhancing the anticoagulant effects of Rivaroxaban. Follow-up serial echocardiograms did not show a recurrence of the effusion, and Rivaroxaban was safely resumed.

**Conclusion:**
Amiodarone increases Rivaroxaban drug levels by inhibiting the CYP3A4 hepatic pathway, predisposing to life-threatening bleeding complications. Vigilant monitoring is necessary whenever these are co-administered.

Figure 1: Parasternal long axis view.

Figure 2: 2.6 cm pericardial effusion