CLINICAL VIGNETTE

A Case of Myocardial Infarction Following Induction Chemotherapy for Acute Myelogenous Leukemia

Jennifer Jones, M.D., and Roswell Quinn, M.D., Ph.D.

Case Report

A 52-year-old man with hypertension, hyperlipidemia, obesity, glucose intolerance, and recent diagnosis of acute myelogenous leukemia (AML) was admitted for inpatient 7+3 induction chemotherapy. He completed induction on hospital day 9. His hospitalization was complicated by pancytopenia, new onset atrial fibrillation, and neutropenic fever. On hospital day 31, the patient complained of chest pain during morning rounds. He described the pain as a left-sided, squeezing pain that lasted an hour during his sleep the prior night.

At that time, his vitals were temperature 97.4, heart rate 71, blood pressure132/75, oxygen saturations 100% on room air with a respiratory rate of 16. His pain score was a 5. Physical exam was notable for normal heart sounds with regular rhythm, trace-pitting edema of the bilateral lower extremities, and a soft, non-tender abdomen. Labs that morning included white blood cells 1.36, hemoglobin 8.4, platelets of 116, sodium 136, potassium 4.7, chloride 102, bicarbonate 25, BUN 18 creatinine 0.82, and an INR 1.5. A lipid panel from two months prior included an LDL of 96 and an HDL of 28. Bedside EKG revealed ST elevations in leads II, III, and aVF with ST depression, t-wave inversion in aVL and Q waves in II and aVF. Right-sided EKG was remarkable for ST segment elevations in leads II, III, and aVF with ST depression in lead aVL.

The patient received aspirin, sublingual nitroglycerine, and urgent cardiac catheterization. He received bivalirudin shortly before catheterization. Angiography revealed a 100% occlusion of the distal RCA from an acute thrombus. There was also a 50% lesion to the mid LAD not requiring intervention. He underwent balloon angioplasty of his obstructing lesion and placement of a bare metal stent. He received a loading dose of 180 mg of ticagrelor and thereafter continued dual anti-platelet therapy with aspirin 81 mg indefinitely and ticagrelor 90 mg BID for at least one month. Further laboratory studies showed a troponin on 3.644, which subsequently peaked at 39.84.

AML and Coagulopathy

As a derangement of the myeloid cell linage, AML frequently confers both thrombocytopenia and coagulopathy. Thrombocytopenia can be both a component of the primary process, most often seen on initial presentation, and secondary to subsequent chemotherapy. Additional coagulopathies such as disseminated intravascular coagulopathy (DIC) and hyperfibrinolysis also occur, most commonly with the variant known as acute promyelocytic leukemia (APL).

Although seen less commonly, other hematological derangements occur in AML. The condition is also associated with arterial and venous thrombosis. In one study of 359 patients with acute leukemia, 9.6% of those with APL and 3.2% of non-APL patients presented with a thrombotic event.[1] Another cohort series of 5,349 Californians with AML demonstrated a 5.2% risk of venous thromboembolism over two years with 64% of those occurring within the first three months of diagnosis.[2] In contrast to the bleeding diathesis clinicians commonly associate with AML, hypercoagulability can be present. The hypercoagulable state conferred by AML is not negligible and may be comparable to that associated with solid organ malignancies.

The mechanisms of hypercoagulability in AML are complex and poorly understood. Microthrombotic phenomena are part of the spectrum of DIC and may cause thromboembolic disease in those patients with APL. Studies have demonstrated that AML blast cells themselves may display increased expression of tissue factor (TF) and cancer pro-coagulant (CP), which can cause aberrant activation of the coagulation cascade.[3,4] A study of 94 cases of thrombosis in AML found that 41% of thrombosis occurred after the initiation of chemotherapy. This suggests either the chemotherapy itself or the breakdown products of AML blast cells are prothrombotic. Additionally, all-transretinoic acid and anthracycline derived chemotherapy induce cellular breakdown which can contribute to endothelial expression of TF or release of TF from AML blasts. Doxorubicin has been shown to increase pro-coagulant properties of platelets.[5] Not all patients with AML become pro-thrombotic, however, suggesting possible genetic or environmental (e.g., immobility) contributions to hypercoagulability in this context.

AML and Myocardial Infarction

Data on the relationship between acute leukemia and myocardial infarction are limited to case reports. The overwhelming majority of these publications report MI as a presenting symptom for APL.[6-8] In these instances coronary blockage was likely related to DIC. However, hematological derangements in AML create multiple pathways that put patients at risk for coronary damage, including leukemic infiltration of the myocardium, circulatory compromise by leukostasis, leukemic thrombus, and coagulopathies.[9-11] Of all leukemias, AML may be the condition most commonly associated with leukemic thrombi or aggregates in the coronary

system.[12] However, such blockages can vary in terms of their pathophysiology. Post-mortem data has revealed MI in the context of APL related to tumor thrombus, red cell thrombus, and fibrin platelet thrombus.[13-15]

Less frequently reported in the literature are MI associated with variants of AML other than APL. As with APL, MI in these instances most often serves as the presenting symptom unlike our patient,[16] who had already received induction chemotherapy for his leukemia. Although clinicians typically think of cardiomyopathies as the primary cardiotoxic effect of chemotherapies, several agents are known to cause ischemic cardiac disease. These include fluorouracil, cisplatin, vinca alkaloids, interferon-alpha, IL-2, and capecitabine. A single care report also raised the questions as to the role of hyperhomocysteinemia in relation to an occurrence of MI in the context of AML.[17]

Given the thrombocytopenia that commonly accompanies AML, the use of dual anti-platelets agents post infarction often comes into question. Use of anti-platelet therapy is typically case by case, based upon the degree and predicted duration of thrombocytopenia.[18] The above case reports of AML patients with MI predominantly describe management with percutaneous coronary intervention and placement of drug eluting or bare metal stents. Given the risk of hemorrhage, cardiologists avoid the use of thrombolytics in these patients. One case report of an AML patient who underwent PCI followed by DES placement and dual antiplatelet therapy subsequently developed in-stent thrombosis and left atrial thrombus three days later, highlighting the need for continued vigilance in the context of this prothrombotic state.[19]

Conclusion

Despite pancytopenia, individuals with AML can develop thromboembolic phenomena. As a result, clinicians should have a high index of suspicion for both bleeding and clotting disorders in patients with AML. Many case reports detail MI as the presenting symptoms of AML. However, we describe a patient with AML who developed an MI following induction chemotherapy and in the context of thrombocytopenia. The treatment of MI in patients with AML is not standardized, but dual anti-platelet therapy is still considered the cornerstone of therapy. Optimal therapy for patients with AML who present with MI should be decided upon as an interdisciplinary discussion between hematology and cardiology.

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