

Question 5 – September 4

A 34 year old woman undergoes a hematopoietic stem cell transplant (HSCT) for acute myeloid leukemia (AML). She receives myeloablative-conditioning therapy with busulfan and cyclophosphamide. On day 15 post-HSCT she develops jaundice, right upper quadrant pain, and ascites. She undergoes transjugular liver biopsy with normal hepatic vein venogram and hepatic venous pressure gradient of 18 mm Hg. Histology reveals congestion in zone 3 with associated hemorrhage and collagen deposition within the central vein. What is the best treatment for this patient?

- A. Anti-coagulation
- B. Thrombolysis
- C. Defibrotide
- D. Tranjugular intrahepatic portosystemic shunt (TIPS)
- E. Liver Transplantation

Answer: C

This patient presents with classic symptoms of sinusoidal obstruction syndrome (SOS) after high-intensity myeloablative conditioning therapy for HSCT. Busulfan and cyclophosphamide are both associated with higher risk of SOS compared with lower intensity, non-myeloablative conditioning regimens. SOS develops within the first month post-HSCT, and in the case of cyclophosphamide conditioning, typically within 20 days. This patient meets diagnostic clinical criteria based on Seattle Criteria (at least 2 of following criteria within 20 days of HSCT: total bilirubin > 2 mg/dL, hepatomegaly or right upper quadrant pain, > 2% weight gain). In addition, hepatic venous pressure gradient [HVPG] greater than 10 mm Hg is highly specific for SOS (91%), and histology is consistent showing classic early findings of zone 3 congestion and early collagen deposition that subsequently progresses to non-thrombotic occlusion of central veins and sinusoids. In addition to diuretic therapy, treatment options are limited. Anti-coagulation alone or in conjunction with thrombolysis has been studied with high rates of bleeding and little clinical benefit (29% survival) and is not recommended. Transjugular intrahepatic portosystemic shunt (TIPS) is effective for treating portal hypertension but does not improve survival (3-month mortality 87.5%) and is not recommended for severe SOS post-HSCT. There is limited evidence to support TIPS in SOS after solid organ transplantation. Liver transplantation for SOS can be considered in patients with benign conditions or malignancy with favorable prognosis but would not be considered in this patient having just undergone therapy for AML. Defibrotide is a single-stranded polydeoxyribonucleic acid with fibrinolytic, anti-thrombotic, and anti-ischemic properties. Defibrotide (6.25 mg/kg) given for at least 14 days led to complete remission in up to 55% of patients and survival past post-HSCT day 100 in 43% of patient, both significantly improved compared with historical controls. The US Food and Drug Administration approved defibrotide for the treatment of severe SOS in April 2016. There are also data to support defibrotide for prophylaxis of HSCT, although this is currently limited to the pediatric population.

References

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