Autologous Hematopoietic Stem Cell Transplant for Systemic Sclerosis Improves Anemia from Gastric Antral Vascular Ectasia

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To the Editor:

Systemic sclerosis (SSc) is a severe autoimmune condition characterized by both fibrotic and vascular complications. This can progress to functionally devastating subcutaneous fibrosis, as well as death from pulmonary, cardiac, renal, or gastrointestinal (GI) involvement. High-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (HSCT) is the first therapy to show evidence of clinically significant improvement in skin and lung function as well as quality of life in SSc when compared to intravenous cyclophosphamide (CYC). The multicenter, phase III randomized trial, Autologous Stem Cell Transplantation International Scleroderma, also showed a significant benefit in long-term, event-free survival with autologous HSCT compared to CYC, despite a higher early treatment-related mortality. A publication from the European Group for Blood and Marrow transplantation (EBMT) has updated guidelines for autologous HSCT in autoimmune diseases, including SSc.

GI involvement is the presenting feature of the disease in 10% of patients with SSc. A recent case-control study of unselected patients with SSc, without routine endoscopy, showed a 1% prevalence of gastric antral vascular ectasia (GA VE) in SSc. This study also highlighted the significant morbidity of GA VE by showing its association with iron-deficiency anemia requiring transfusions, and scleroderma renal crisis. There are, however, no data on the effect of HSCT on GA VE.

Three patients (all women, median age 36 yrs) had persistent bleeding from GA VE in the 12–24 months prior to autologous HSCT at our institution. The diagnosis of GA VE was made by endoscopic assessment. All patients required regular transfusions and multiple endoscopic treatments with argon plasma coagulation (APC). They had significant skin and pulmonary involvement refractory to multiple disease-modifying agents including CYC. Patients 1 and 2 had each received a total of 3.75 g/m² in divided doses. Patient 3 had received a total of 2 g/m². This pre-HSCT CYC therapy did not alter the natural history of GA VE, with all patients remaining transfusion-dependent.

The red cell transfusion requirements in the period of 12–24 months pre-HSCT were 91, 24, and 14 units for patients 1, 2, and 3, respectively. After informed written consent, as part of a phase II trial in our institution, stem cells were mobilized with CYC (2 g/m²). Unmanipulated autologous stem cells were infused following CYC (200 mg/kg) and antithymocyte globulin (40 mg/kg) conditioning. The transplant protocol did not involve any graft manipulation because there is little evidence for any clinical benefit of this from the current literature of autologous HSCT for autoimmune diseases. This approach is also supported by the EBMT guidelines.

The combined median pretransfusion hemoglobin for our patients prior to HSCT was 76 g/l (range 47–88 g/l). This improved to 121 g/l post-HSCT (range 91–142 g/l, p < 0.0001; Figure 1). All patients achieved transfusion independence by Day 20 post-HSCT and maintained stable hemoglobin at median followup of 420 days. Surveillance endoscopy performed in 1 of the patients showed significant improvement in vascular ectasia, which had been detected prior to HSCT (Figure 2). SSc disease activity scores and functional status, including the Rodnan skin and the Health Assessment Questionnaire scores, also improved following transplant.

GA VE is associated with early diffuse cutaneous SSc and morbidity because of severe anemia. Current treatment for GA VE is repeated endoscopic coagulation, usually with APC. This does not address the underlying pathophysiology and requires multiple endoscopic procedures. The effect of autologous HSCT on GA VE is unknown. One case series reported resolution of GA VE post-intravenous CYC, suggesting a role for the immunomodulatory effect of this agent on the underlying pathophysiology of GA VE. However, those patients became transfusion-independent much later, at 6–8 months post-CYC. This may reflect the higher concentrated dose of CYC in HSCT that resulted in significant improvement in skin scores and function, raising the possibility that high-dose immunosuppression is required to reverse both the systemic skin fibrosis and gastric vascular dysfunction. Similarly, in our patient cohort, there was no major benefit from pulsed CYC, suggesting a different mechanism of action of HSCT.

Our case series suggests that autologous HSCT may be an effective disease-modifying therapy for GA VE as a complication of SSc. Prospective studies of autologous HSCT for SSc should analyze the endoscopic features of GA VE in response to HSCT, and correlate these with immunological and clinical variables to fully ascertain this welcome and unexpected benefit of HSCT in these patients.
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Figure 2. Endoscopic images before and after autologous HSCT. HSCT: hematopoietic stem cell transplantation.