Stem Cells Offer Option For Refractory Vasculitis

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

S tem cell transplantation may be an option for patients whose lives are threatened by medically refractory vasculitis, Dr. Thomas Daikeler and his colleagues have reported. Up to 20% of vasculitis patients don’t respond to conventionally dosed immunosuppression, Dr. Daikeler said in an interview. Options for these patients are very limited, he said. However, his review of 20 patients who received the transplants showed that 93% responded positively, with 7 achieving sustained complete remission (Ann. Rheum. Dis. 2006 Sept. 1 [Epub doi:10.1136/ard.2006.056630]).

Dr. Daikeler, of the University of Basel, Switzerland, reviewed outcomes in 15 patients included in the European League Against Rheumatism (EULAR) database or the PROMISE international medical database, and 5 additional patients identified through a Medline search. The following is a summary of the details of the 15 EULAR/PROMISE patients. Their median age was 37 years (age range 10-57 years). Four had cryoglobulinemia, three had Becher’s syndrome, three had Wegener’s granulomatosis, and the others had Churg-Strauss angiitis, Takayasu’s arteritis, and a polyarteritis nodosa. All patients had active disease and had failed intensive immunosuppressive therapy, including cytotoxic drugs. Most of them (14) had an autologous stem cell transplant first; 1 had an allogeneic transplant first. At the time of the analysis, the median follow-up for all patients was 44 months (range 16-84 months). The response rate was 93%. Overall, seven responded partially and needed maintenance immunosuppression for minor disease, seven patients were in complete remission, and one patient showed stable disease.

Three patients died. One patient with partial response relapsed 24 months after allogeneic transplant and died of graft-versus-host disease; a second patient who achieved complete response of his underlying polyarteritis nodosa died of lung cancer 2 years after autologous transplant; the third patient showed no response to therapy and died of right ventricular failure due to severe preexisting pulmonary hypertension 26 months after the initial transplant. Among the 14 patients who received an autologous transplant, there were 2 relapses—one at 2 months and one at 24 months post transplant. One of these patients then received an allogeneic stem cell transplant and relapsed again 2 years later with headache and aphthous disease. In this patient, the transplant was successfully treated with four cycles of rituximab and cyclophosphamide.

The second relapsed patient received another autologous transplant 24 months after the first one. This was followed by another relapse 4 months later, and then an allogeneic transplant, which led to partial remission lasting for 24 months. Six patients in the group experienced neuropsychiatric complications, and two of them had reactivation of cytomegalovirus and Epstein-Barr virus. One patient experienced transient pancytopenia and transient cardiotoxicity. Among the five patients identified in the Medline search, the following outcomes occurred: complete remission 18 months after transplant in a patient with polyarteritis nodosa; cessation of all disease activity, no medication necessary, for a 4-year-old with intesinal Behçet’s syndrome; cessation of disease activity, no medication necessary, for a child with small-vessel vasculitis; complete remission 16 months after transplant for patient with Wegener’s granulomatosis. Since the graft-versus-host disease is an issue only with allogeneic transplants, Dr. Daikeler suggested that autologous transplants for these patients be evaluated in larger clinical trials.

Rituximab Targets Systemic Complications of Sjögren’s

BY DIANA MAHONEY
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R ituximab is a safe and effective treatment for the systemic complications of primary Sjögren’s syndrome, judging from the findings of a small retrospective study.

Recent investigations have linked high levels of B-cell autoreactivity with high levels of disease activity and the development of a range of systemic complications, including arthritits; vasculitis; lymph node enlargement; thyroid, lung, kidney, nerve, and muscle problems; and an increased risk of developing B-cell lymphoma.

To assess the safety and efficacy of rituximab (Rituxan), an anti-CD20 antibody that targets B cells, for treating the systemic manifestations of primary Sjögren’s syndrome (pSS), Dr. Raphaële Seror of Bicêtre Hospital, Paris, and colleagues obtained records from six referral centers in France for 16 female patients (median age 59 years) diagnosed with the condition who had been treated with rituximab for either lymphoma or other complications (Ann. Rheum. Dis. 2006 Sept. 1 [Epub doi:10.1136/ard.2006.057919]).

All of the patients included in the evaluation received a 100 mg pulse of methylprednisolone, and either 20 mg of oral cyclosporine or an intravenous pulse of 5 mg desclerohemarin before each rituximab infusion, and four of the patients received concomitant immunosuppressants.

Rituximab therapy induced complete remission in four of the five lymphoma patients but was not effective in one patient with salivary lymphoma. Among the 11 patients with systemic complications, rituximab was effective in 9, including 4 with cryoglobulinemia, 2 with pul-

monary involvement and polynosyvits, 2 with polynosyvits, and 1 with mononeureitis multiplex. Despite rituximab therapy, one patient with cryoglobulinemia experienced a worsening of peripheral nerve involvement, and the patient with thrombocytopenia remained below 10,000/mm³, the authors reported.

The investigators also assessed laboratory outcomes, including changes in erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, cryoglobulinemia, B-cell biomarkers, and, for some patients, serum B cell activating factor of the tumor necrosis factor family (BAFF) levels from retrospective ELISA assessment of frozen samples. B-cell depletion was achieved in 14 of the 15 patients. Median ESR and CRP levels decreased from 60 to 20 mm/h and from 11.4 to 4 mg/L, respectively.

Median rheumatoid factor decreased from 124 to 7.5 IU/mL, disappearing completely in five patients. Median gama- globulin, IgG, and beta-2 microglobulin levels also decreased, while median BAFF levels increased, possibly as a consequence of B-cell depletion, the authors hypothesized.

During the median 14.5-month follow-up, five patients relapsed, four experienced a flare of oral and lymphoma was diagnosed in one patient treated initially for cryoglobulinemia. Clinical relapse was associated with the reappearance within 3 months prior to relapse of peripheral blood B cells and an increase in B-cell biomarkers. Rituximab was effective in all but four of five patients treated for relapse. Only three of the patients experienced moderate adverse events, including delayed, infusion-related flulike reactions, the authors wrote.

Cutaneous Neonatal Lupus May Signal More Serious Outcomes

SAN ANTONIO — All cases of congenital heart block are caused by neonatal lupus, Dr. Bernice Krafchik said at a meeting sponsored by Skin Disease Education Foundation.

About half of neonatal lupus babies will have congenital heart block. Part of the challenge in diagnosis is that more than half of mothers are asymptomatic, added Dr. Krafchik, professor emeritus of pediatrics and medicine, the Hospital for Sick Children, University of Toronto.

The heart block is usually complete heart block: “These patients require a pacemaker—you have to really watch these kids closely, the pacemaker itself can cause a lot of stress.”

In general, babies with just cutaneous lesions of neonatal lupus may have skin lesions. There are four reasons for referral to pediatricians: produce a “raccoon” face, annular erythema with atrophy, central erythema with an edge, and telangiectasias.

The telangiectasias are less common but might persist into adulthood. Some telangiectasias respond to laser treatment, although scarring can be problematic, said Dr. Krafchik.

Neonatal lupus can cause thombocytopenia and hepatitis as well. Hepatitis occurs in approximately 10% of affected neonates and is usually mild with “excellent recovery,” she said at the meeting. SDEFF and this new organization are wholly owned subsidiaries of Elsevier.