Transplants Prolong AL Amyloidosis Survival Rates

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BOSTON — High-dose intravenous chemotherapy and autologous stem cell transplantation significantly improve the survival and organ response of some patients with primary amyloidosis, a longitudinal analysis has shown.

Until recently, the prognosis for patients with primary amyloidosis has been poor, with median survival rates of just 1-2 years, said Martha Skinner, M.D., at a meeting on advances in rheumatology sponsored by Harvard Medical School.

Primary amyloidosis, also called AL amyloidosis, involves an overproduction of amyloid light (AL) chain proteins caused by an underlying plasma cell abnormality. The excess proteins build up in tissues and organs, disrupting the structure and function of the heart, liver, kidneys, spleen, intestines, skin, and nervous system. Amyloid cardiomyopathy is a particularly fatal complication of the disease.

Conventional treatment with low-dose oral melphalan has been associated with a very low response rate, said Dr. Skinner, director of the amyloid program at Boston University Medical Center. Recently, however, aggressive treatment with high-dose intravenous melphalan followed by stem cell replacement or rescue has proven to be a more effective therapy, she said. In selected patients, this regimen has resulted in hematologic remission, improved survival rates, and reversal of amyloid-related disease, according to a review of outcome data.

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Dr. Skinner and her colleagues analyzed data for 701 consecutive patients with AL amyloidosis who participated in six separate trials over a period of 8 years. They looked for evidence of persistent disease after treatment, and they assessed duration of survival and organ function.

Of the combined study populations, 394 patients were eligible for high-dose melphalan (100-200 mg/m^2) and stem cell transplantation based on organ involvement and clinical status. Of these, 312 patients initiated treatment. The remaining 82 eligible patients did not proceed with treatment by choice or because of disease progression.

Among the treated patients, 40% had a complete hematologic response, defined as no evidence of an underlying plasma cell dyscrasia 1 year after treatment. Of those who remained in complete remission 1 year after treatment, 8% had relapses within 2 years, but none had relapses after 2 years, said Dr. Skinner.

Patients with a complete hematologic response had greater statistically significant improvements in end-organ disease, compared with treated patients who had evidence of persistent plasma cell dyscrasia, she said.

The hematologic and end-organ responses to treatment were accompanied by measurable and sustained quality of life improvements based on Short-Form Health Survey (SF-36) scores, said Dr. Skinner. At baseline, the scores were significantly lower on all eight SF-36 scales, compared with age-matched population norms. At 1 year, all of the scores had improved, with the mental component summary scores reaching the population norm. The physical component summary scores, which were lower than the population norm but still improved, were higher in the subgroup of patients who achieved a complete hematologic response, she said.

Mortality within 100 days of treatment was 13%, said Dr. Skinner, noting that patients in the treatment group who had cardiomyopathy had the highest mortality, compared with the other patients in the treatment group. The median survival of the treatment group was 4.6 years, Dr. Skinner said. Of 137 treated patients with heart involvement, approximately half were alive after 1.5 years, compared with 6.5 years for those treated patients without heart involvement. Half of the patients who were not eligible for the aggressive treatment died within 4 months.

The results should be taken in context, Dr. Skinner advised. "Patients were collected from multiple studies." ■