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Case report

Allogeneic bone marrow transplant for chronic myelogenous leukemia in a patient with multiple sclerosis

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Summary:

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system in which immune mechanisms appear to be an important component of the pathophysiology. Although the clinical manifestations are variable, a subset of patients develops a progressive clinical course associated with marked neurologic impairment and significant morbidity. BMT has been proposed as a treatment for such patients based on preclinical data as well as clinical observations in other autoimmune diseases. We report clinical and MRI findings in an MS patient, later diagnosed with CML, and treated with an allogeneic BMT.
Keywords: multiple sclerosis; allogeneic BMT; autoimmune disease

Case report

A 46-year-old woman had a 29 year history of relapsing and remitting MS. Her symptoms included recurrent right optic neuritis, episodic vertigo, persistent left-sided sensory abnormalities, and progressive decline in motor skills, balance, and memory. She had comorbid migraines and chronic daily headaches. She was diagnosed with CML in chronic phase and underwent high-dose chemotherapy with busulfan and cyclophosphamide followed by allogeneic marrow stem cell rescue from her HLA-matched brother in April 1995. Graft-versus-host disease (GVHD) prophylaxis consisted of methotrexate given on days 1, 3, 6 and 11 post-transplant, and cyclosporine beginning the day before transplant and continuing for 4 months post-transplant. She had no complications related to GVHD, and thus received no other GVHD treatment other than the prophylaxis.

Pre-BMT neurological evaluation revealed tangential thought processes, poor concentration, pale right optic nerve, subtle bilateral intranuclear ophthalmoplegia, increased lower extremity tone, symmetrical hyper-reflexia, bilateral Babinski's signs, and diminished sensation in the left arm and leg (See Table 1). Paraclinical evaluation included a brain MRI showing multiple white matter lesions, one of which enhanced following gadolinium administration (Figures 1 and 2), and cerebrospinal fluid analysis showing oligoclonal bands; both findings characteristic of multiple sclerosis.[1]

She tolerated the acute phase of her BMT well with no clinical exacerbation of her MS, and no GVHD. Follow-up neurological evaluations were done at 4 and 12 months following BMT. During this time she had no clinical exacerbations of her MS. At four months post-BMT, the patient reported subjective improvement in conjugative eye movements and in her left-sided sensory deficit. Neurologic examination demonstrated improved sensory perception to pinprick on the left. At 12 months her memory is improved and thought processes are better organized. Her internuclear ophthalmoplegia, hyper-reflexia, Babinski's signs, and sensory deficits are resolved. Her MRI at 12 months revealed no remaining enhancing lesions, as well as no new lesions (Figures 3 and 4). She remains in hematologic remission with no signs of GVHD, and is off all immunosuppressive medications.

Discussion

This patient did not experience worsening of her MS symptoms during either the acute phase of BMT or through 14

Table 1 Neurologic findings before and after BMT

Neurologic findings pre-BMT	*Neurologic findings post-BMT*
Hyper-reflexia and bilateral Babinski's signs	Normal reflexes and plantar response
Bilateral internuclear ophthalmoplegia	Normal eye movements
Decreased sensation in left arm and leg	Normal sensation
Oligoclonal bands in CSF	Not yet re-tested
Tangential thought processes and poor concentration	Probably improved
Pale right optic nerve	Unchanged

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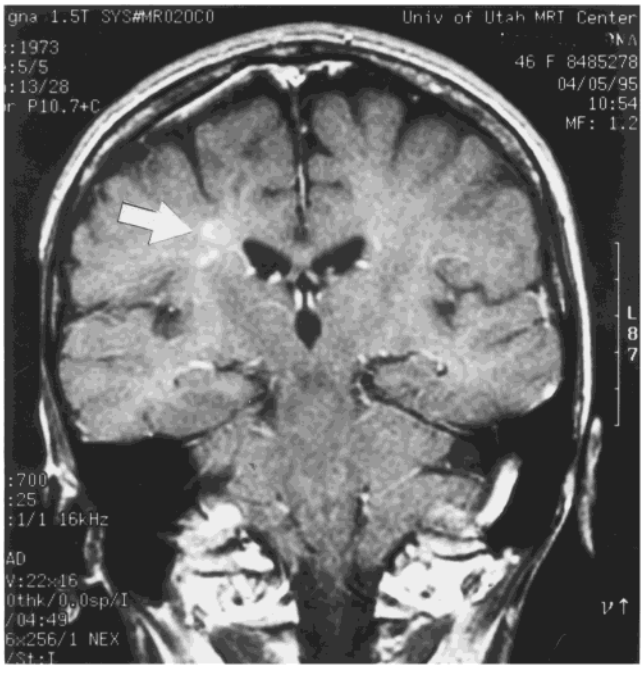

Figure 1 Coronal MRI prior to BMT showing gadolinium enhancing periventricular lesions (TR 700, TE 25). Gadolinium enhancement represents abnormally increased permeability of the blood–brain barrier and correlates with disease activity in multiple sclerosis.

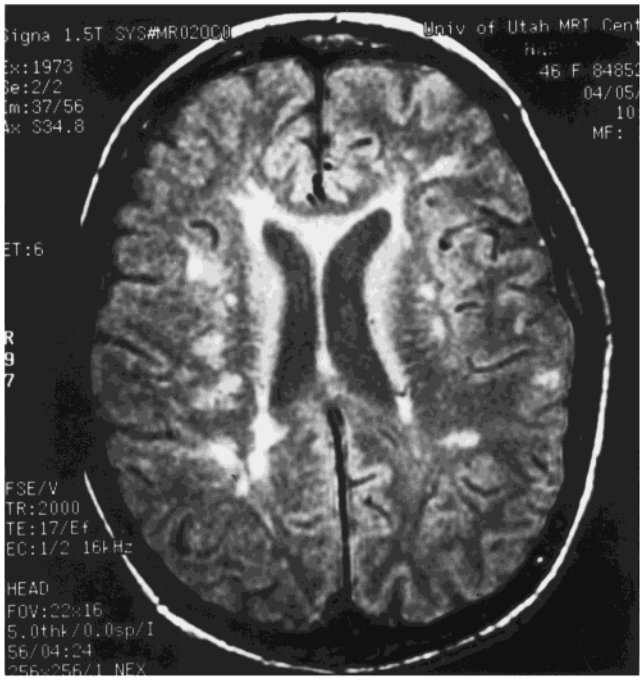

Figure 2 Axial T-2 weighted MRI prior to BMT showing multiple areas of increased signal in periventricular white matter (TR 2000, TE 17). These represent areas of active or chronic demyelination.

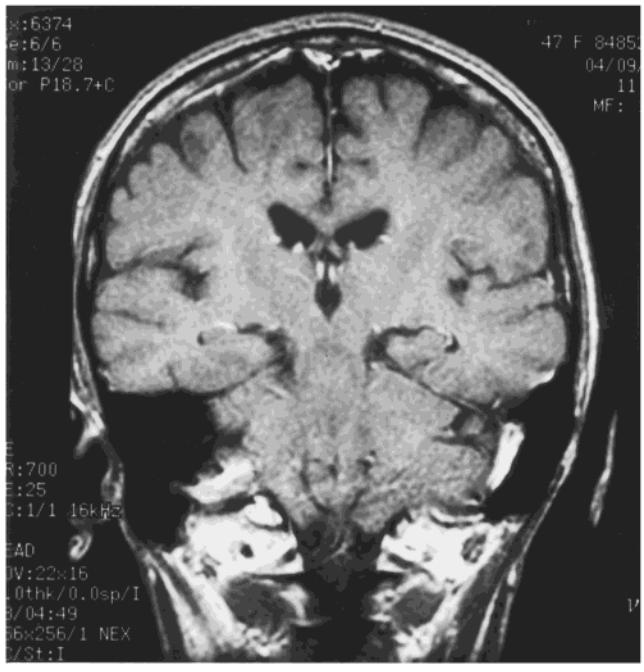

Figure 3 Coronal MRI 12 months following BMT showing resolution of gadolinium enhancing periventricular lesions (TR 700, TE 25).

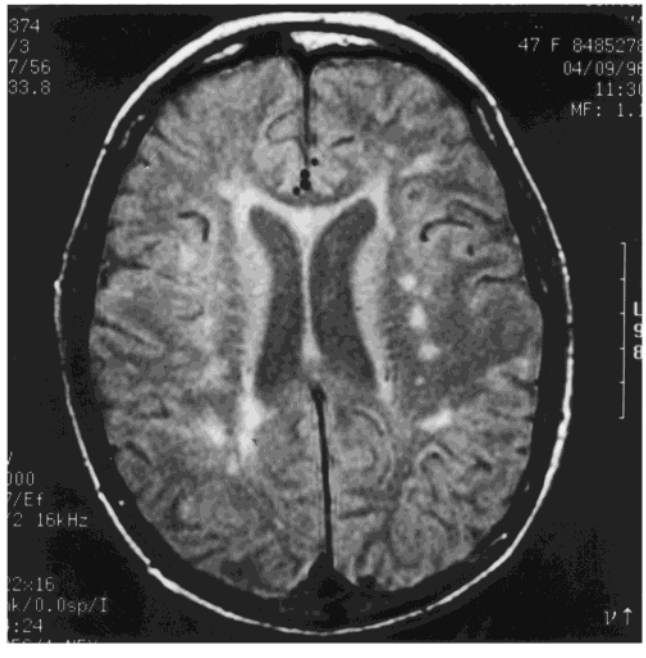

Figure 4 Axial T-2 weighted MRI 12 months following BMT showing no change in multiple periventricular white matter lesions (TR 2000, TE 17). No new lesions are seen.

months of follow-up. Furthermore, she has noted symptomatic improvement and neurological examination is now normal other than the pale right optic nerve. Her MRI scan remains stable with no evidence of new lesions.

BMT has been proposed as treatment for patients with severe and progressive MS and clinical trials are currently underway.[2] There are significant potential risks of performing BMT in this population including profound and prolonged immunosuppression, poor tolerance of fever and infection, and possible adverse effects of high-dose chemotherapy upon the central nervous system. Furthermore, BMT for MS in humans is complicated by the fact that there is an increased familial risk of MS, and some

asymptomatic family members of MS patients have abnormal MRI scans and/or CSF findings. Thus, there is a theoretical concern regarding the use of related donors for treatment of MS patients with BMT.[3] For these and other reasons, it has been proposed that autologous BMT could be an initial approach to the treatment of MS with BMT in humans.

In conclusion, although there are significant potential risks of using allogeneic and autologous BMT in humans with MS, our patient tolerated BMT well. Furthermore, she had subjective improvement in symptoms, objective improvement of her neurological examination, and MRI stability. Continued follow-up will be of interest to determine the duration of the clinical and MRI stability.

References

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