Remission of Multiple Sclerosis Post-Liver Transplantation

Eric M. Yoshida, Virginia A. Devonshire, Alister J.E. Prout

ABSTRACT: Background: The effect of liver transplantation on pre-existing multiple sclerosis (MS) has never been reported. We report the three year post-transplant neurological outcome of a patient with MS. Case report: A Caucasian woman with MS received an urgent liver transplant for fulminant liver failure at the age of 59. Her Extended Disability Scale Score (EDSS) pretransplant was 5.0 and clinically she had cerebellar and brainstem dysfunction. Post-transplant immunosuppression consisted of tacrolimus, mycophenolate mofetil and tapering corticosteroids that were discontinued after 1.5 years. Post-transplant her EDSS decreased to 2.0 and after three years she is clinically asymptomatic with only very mild dysarthria on neurologic examination. Long-term maintenance immunosuppression consists of low dose tacrolimus. Conclusions: Combination immunosuppression with tacrolimus may have a beneficial effect on MS although an effect of donor allograft itself can not be excluded.

RÉSUMÉ: Rémission de la sclérose en plaques après une transplantation hépatique. Introduction: L’effet de la transplantation hépatique sur une sclérose en plaques (SEP) préexistante n’a jamais été rapporté. Nous rapportons le suivi neurologique d’une patiente atteinte de SEP ayant subi une transplantation hépatique trois ans auparavant. Cas clinique : Une femme caucasienne atteinte de SEP a reçu une transplantation hépatique en urgence pour une insuffisance hépatique fulminante à l’âge de 59 ans. Son score à l’échelle de Kurtzke, Extended Disability Scale Score (EDSS), avant la transplantation était de 5.0 et elle avait des signes cliniques de dysfonction cérébelleuse et tronculaire. Elle a reçu du tacrolimus, du mofétilmycophénolate et des corticostéroïdes à dose décroissante sur une période de 1.5 ans comme immunosupresseurs après la transplantation. Son EDSS a baissé à 2.0 après la transplantation et elle est asymptomaticque au point de vue clinique trois ans plus tard. À l’examen neurologique, elle ne présente qu’une légère dysarthrie. Elle ne reçoit que du tacrolimus à faible dose comme immunosupresseur à long terme. Conclusions : Bien qu’un effet de l’allogreffe elle-même ne puisse être exclu, une combinaison d’immunosupresseurs incluant le tacrolimus pourrait avoir un effet bénéfique sur la SEP.


We report the course of multiple sclerosis (MS) in a patient treated with tacrolimus, mycophenolate mofetil and tapering prednisone for three years post-liver transplantation for fulminant hepatic failure. To date the effect of solid organ transplantation on MS has not been reported in the literature. There is also little published experience with the immunosuppressive medications used and the efficacy of such combination immunosuppression in MS is unknown.

Cerebrospinal fluid analysis revealed an immunoglobulin (Ig)G: albumin index of 0.89 [normal: 0.34-0.66], an IgG synthesis rate of 10.2 mg/d [normal < 3.4 mg/d] and oligoclonal bands. Subjectively, her quality of life was reported to have significantly deteriorated as a result of her MS symptoms. A trial of interferon beta-1a was interrupted after seven weeks by the development of fulminant liver failure, as previously reported,1 requiring emergent liver transplantation. Her post-transplant immunosuppression (Table) consisted of delayed, lower dose (due to hepato-renal syndrome) tacrolimus (Prograf; Fujisawa Canada Inc, Markham ON), mycophenolate mofetil (Cellcept; Hoffmann-LaRoche Canada Inc, Mississauga ON), and tapering prednisone. Her Cerebrospinal fluid analysis revealed an immunoglobulin (Ig)G: albumin index of 0.89 [normal: 0.34-0.66], an IgG synthesis rate of 10.2 mg/d [normal < 3.4 mg/d] and oligoclonal bands. Subjectively, her quality of life was reported to have significantly deteriorated as a result of her MS symptoms. A trial of interferon beta-1a was interrupted after seven weeks by the development of fulminant liver failure, as previously reported,1 requiring emergent liver transplantation. Her post-transplant immunosuppression (Table) consisted of delayed, lower dose (due to hepato-renal syndrome) tacrolimus (Prograf; Fujisawa Canada Inc, Markham ON), mycophenolate mofetil (Cellcept; Hoffmann-LaRoche Canada Inc, Mississauga ON), and tapering prednisone. Her Cerebrospinal fluid analysis revealed an immunoglobulin (Ig)G: albumin index of 0.89 [normal: 0.34-0.66], an IgG synthesis rate of 10.2 mg/d [normal < 3.4 mg/d] and oligoclonal bands. Subjectively, her quality of life was reported to have significantly deteriorated as a result of her MS symptoms. A trial of interferon beta-1a was interrupted after seven weeks by the development of fulminant liver failure, as previously reported,1 requiring emergent liver transplantation. Her post-transplant immunosuppression (Table) consisted of delayed, lower dose (due to hepato-renal syndrome) tacrolimus (Prograf; Fujisawa Canada Inc, Markham ON), mycophenolate mofetil (Cellcept; Hoffmann-LaRoche Canada Inc, Mississauga ON), and tapering prednisone. Her
In general, the use of combination immunosuppression can be effective, but it remains to be determined whether the use of donor stem cells has been beneficial.

In terms of clinical use in MS, the use of combination immunosuppression has been reported to result in moderate or severe CNS toxicity in a small number of patients.

We cannot exclude the possibility that systemic microtoxicity, including mild to fulminant leukoencephalopathy, may be associated with some combination immunosuppression protocols.

We hypothesize that the combination of these drugs (induction followed by low dose maintenance once remission is achieved) may have produced the benefit in our patient and this approach may be worthy of further study.

In general, improvement or resolution of co-existing autoimmune diseases post-transplant are invariably attributed to the effects of long-term immunosuppressive agents, most of which have limited clinical use outside of solid organ transplantation. In our situation, an intriguing but, impossible to prove, possibility remains that the improvement was an effect of the donor organ itself. Despite its high risk, there are some reports of improvement in MS following hematopoietic stem cell transplantation.

In the stem cell setting, the immune system is ablated and then reconstituted in some percentage of cases with the best possible outcomes. An important aspect of our report lies in the fact that co-existing significant medical conditions, including MS, may be considered contra-indications to transplantation unless reports to the contrary are published.

We cannot exclude the possibility that systemic microchimerism from a donor without MS may have resulted in some disease modifying effects.
CONCLUSION

Post-transplant experience in MS is previously unreported but our experience suggests that in some cases, clinical improvement may occur after transplantation. The post-transplant clinical benefit may be a result of immunosuppressive therapy but the possibility that the donor allograft itself may have had some effect cannot be excluded.

ACKNOWLEDGEMENTS

The authors thank the University of British Columbia MS Clinic Neurologists, the Vancouver Hospital Solid Organ Transplant Clinic Nurses and the British Columbia Transplant Society.

Disclosure:
This work was presented as a poster at the ACTRIMS-ECTRIMS Meeting in Baltimore MD, September 2002.

REFERENCES