www.nature.com/bmt

LETTER TO THE EDITOR

Call for case histories of BMT in patients with coincident schizophrenia

Bone Marrow Transplantation (2013) **48,** 880; doi:10.1038/bmt.2013.30; published online 18 March 2013

Recently, the case for an immune component in the etiology of schizophrenia has regained support,^{1,2} leading to randomized controlled trials to explore treatment with immunosuppressive and anti-inflammatory drugs.³ Both postmortem⁴ and *in-vivo* studies^{5,6} provided indications for an increased proinflammatory status in the brain of patients with recent-onset schizophrenia. A common characteristic of most, if not all, autoimmune diseases (AD) is their favorable response to immunoablation and rescue with BMT. It was established in radiation chimeras more than 50 years ago that the immunological and hematological systems have a common stem cell. In the wake of this discovery came a series of investigations into the role of the BM in autoimmune disorders (AD) demonstrating that both hereditary AD and the susceptibility for induced AD could be transferred by hematopoietic SCTs and that both forms of AD in experimental animals could be cured by an allogeneic BMT from healthy donors.⁷

We therefore searched among long-term survivors after allogeneic BMT (SCT) for patients with a coexisting AD at the time of the transplant. Up to 1998, case histories of a total of 22 such patients were retrieved, all but one of whom went into CR of their AD.8 These findings did not initiate treatment of AD patients with allogeneic BMT because of the high risks of this procedure. However, after it was demonstrated both in rats with induced systemic arthritis and in rats with an experimental allergic encephalomyelitis (a model for multiple sclerosis) that autologous BMTs were potentially equally effective as allogeneic transplants, this modality has been widely explored for treating refractory AD of all sorts.9 The European Group for Blood and Bone Marrow Transplantation (EBMT) estimates that worldwide around 3000 AD patients had been treated with autologous BMT; 1200 cases were entered in the EBMT database by June 2011.¹⁰ Overall, the 5-year survival rate of the first 900 cases analyzed was 85%, with 43% PFS.

At present, around 50 000 hematopoietic SCT are registered annually. Considering a conservative prevalence estimate for schizophrenia of 8 per 1000, the registries can be expected to contain data on many survivors with coincident schizophrenia at the time of transplant. Information on the clinical course of schizophrenia after SCT would greatly enhance our understanding of the role of immune processes in schizophrenia. We have therefore asked the EBMT and the Center for Blood and Marrow Transplantation Research (CIBMTR) at the Medical College of Wisconsin about the feasibility of searching their databases for such cases. Simultaneously we call upon hematologists and

psychiatrists to inform us directly of their relevant case histories. We are submitting this appeal to the respective professional journals and websites. We think this approach may save time and money in identifying cases that are not into the databases of the international registries.

Please send the information about your cases, including identification numbers if registered, to one of us in Utrecht, E-mail: i.sommer@umcutrecht.nl

CONFLICT OF INTEREST

The authors declare no conflict of interest.

IE Sommer¹ and DW van Bekkum²

¹Department of Psychiatry, University Medical Center,

Utrecht, The Netherlands and

²Department of Molecular Cell Biology, Leiden University,

Leiden, The Netherlands

E-mail: i.sommer@umcutrecht.nl

REFERENCES

- 1 Jones AL, Mowry BJ, Pender MP, Greer JM. Immune dysregulation and self-reactivity in schizophrenia: do some cases of schizophrenia have an autoimmune basis? *Immunol Cell Biol* 2005; 83: 9–17.
- 2 Goldsmith CA, Rogers DP. The case for autoimmunity in the etiology of schizophrenia. *Pharmacotherapy* 2008; **28**: 730–741.
- 3 Sommer IE, de Witte L, Begemann M, Kahn RS. Nonsteroidal anti-inflammatory drugs in schizophrenia. *J Clin Psychiatry* 2012; **73**: 414–419.
- 4 Bayer TA, Buslei R, Havas L, Falkai P. Evidence for activation of microglia in patients with psychiatric illnesses. *Neurosci Lett* 1999; **271**: 126–128.
- 5 van Berckel BN, Bossong MG, Boellaard R, Kloet R, Schuitemaker A, Caspers E et al. Microglia activation in recent-onset schizophrenia: a quantitative (R)-[11C] PK11195 positron emission tomography study. Biol Psychiatry 2008; 64: 820–822.
- 6 Doorduin J, de Vries EF, Willemsen AT, de Groot JC, Dierckx RA, Klein HC. Neuroinflammation in schizophrenia-related psychosis: a PET study. J Nucl Med 2009; 50: 1801–1807.
- 7 van Bekkum DW. BMT in experimental autoimmune disease. *Bone Marrow Transplant* 1993; **11**: 183–187.
- 8 van Bekkum DW. New opportunities for the treatment of severe autoimmune diseases: bone marrow transplantation. Clin Immunol Immunopathol 1998; 89: 1–10.
- 9 Gratwohl A, Tyndall A. (eds). Stem cell transplantation for autoimmune disorders. Best Practice Research. Clin Hematol 2004; 17: 199–357.
- 10 Snowden JA, Pearce RM, Lee J, Kirkland K, Gilleece M, Veys P. Hematopoietic SCT in severe autoimmune diseases: updated guidelines of the European Group for Blood and Bone Marrow Transplantation. *Bone Marrow Transplant* 2012; 47: 770–790.

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-nd/3.0/