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722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Opsoclonus-Myoclonus Syndrome and Acquired Von Willebrand Syndrome As Manifestations of Graft-Versus-Host Disease

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Background:
Opsoclonus-myoclonus syndrome (OMS), known as dancing eye syndrome, is a rare neurological disorder characterised by a triad of opsoclonus (rapid, involuntary eye movements), myoclonus (uncontrolled muscle twitches) and ataxia. The syndrome is usually seen in children, often associated with neuroblastoma, and is extremely rare in adults. The pathogenesis is thought to be immune in nature and aetiology is variable although most cases are associated with solid tumors or after an infection. Treatment involves a combination of managing the underlying condition and immunosuppression. Acquired von Willebrand disease is a rare acquired bleeding disorder with a range of different aetiologies including lymphoproliferative, myeloproliferative, cardiovascular and autoimmune disorders. The pathogenic mechanism, in most cases is due to increased plasma clearance of von Willebrand factor (vWF) caused by such mechanisms as antibodies, cell adsorption, shear stress or increased proteolysis. Therapeutic approaches focus on prevention of bleeding through supportive treatment, and management of the underlying cause. To the best of our knowledge, this is the first case of opsoclonus-myoclonus syndrome with concurrent acquired von Willebrand disease as manifestations of graft versus host disease.

Case:
Here we present the case of a 47-year-old man presenting with opsoclonus myoclonus syndrome and concurrent acquired von Willebrand disease as manifestations of graft versus host disease. The patient had a background of relapsed myeloid sarcoma after haploidentical allogeneic haematopoietic stem cell transplant with subsequent chemotherapy to achieve full remission. He received donor lymphocyte infusion as consolidation therapy to enhance the graft-versus leukaemia effect. Six weeks following donor T cell infusion of 1 x 10^6 CD3 cells/kg, he presented with initial features suggestive of graft versus host disease (GVHD) of the digestive tract and subsequently developed neurological manifestations in the form of rapid, repetitive, involuntary and multidirectional eye movements; tremors and ataxia. Further tests prior to planned invasive testing revealed an additional new diagnosis of acquired von Willebrand disease, requiring supportive von Willebrand factor concentrate infusion. Multiple extensive investigations including cerebral MRI imaging, cerebrospinal fluid analysis and paraneoplastic antibodies were all negative for associated malignancy, infection, other autoimmune disorder or disease relapse. Skin, bone marrow examination and cross-sectional imaging confirmed complete remission with complete donor chimerism in all blood cell lineages. The patient commenced steroid immunosuppression for treatment of gastrointestinal GVHD with complete resolution of all symptoms and clinical parameters.

Conclusion:
We highlight a rare case of central nervous system involvement with graft versus host disease following cellular therapy, manifesting as the rare opsoclonus-myoclonus syndrome with associated acquired von Willebrand disease. The proposed pathological mechanism is the activation of host tissue antigen-specific T and B cells, resulting in autoantibody and cytokine-mediated effects upon neuronal tissue and coagulation proteins. Use of glucocorticoids in this case to suppress auto-antibody formation, block transcription of pro-inflammatory genes and induce lymphocyte depletion was rapidly effective and provided durable remission of symptoms, without recurrence on cessation of immunosuppression. This case highlights the need for close clinical and biochemical monitoring of patients during the risk period following allogeneic cellular therapy, for serious allo-immune manifestations not fitting classical descriptions of GVHD.

Disclosures Bulley: *Janssen:* Honoraria. **Khan:** *Jazz pharmaceuticals:* Honoraria, Speakers Bureau; *Servier Pharmaceuticals:* Honoraria; *Medac pharmaceuticals:* Honoraria; *Novartis:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Astellas pharma:* Speakers Bureau.

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