

Norovirus Gastroenteritis in Immunocompromised Patients

TO THE EDITOR: Bok and Green (Nov. 29 issue)¹ expertly summarize the epidemiologic features, diagnosis, prevention, and management of norovirus infection in immunocompromised hosts. We emphasize the authors' point about handwashing as the mainstay of prevention. A very low infectious dose is required to transmit disease.² Because data on the efficacy of alcohol-based hand sanitizers against norovirus are inconclusive, the Centers for Disease Control and Prevention recommends washing with soap and running water. The isolation of infectious patients and environmental decontamination with sodium hypochlorite-based cleaning solutions are other important strategies.³

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No potential conflict of interest relevant to this letter was reported.

1. Bok K, Green KY. Norovirus gastroenteritis in immunocompromised patients. *N Engl J Med* 2012;367:2126-32.
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Angiotensin Antibodies and Focal Segmental Glomerulosclerosis

TO THE EDITOR: Antibodies to the angiotensin II type 1 (AT1) receptor may contribute to a wide range of kidney abnormalities. Dragun et al. found that patients with refractory vascular allograft rejection without anti-HLA antibodies had serum antibodies directed at the AT1 receptor.¹ Renal podocytes express the AT1 receptor, and angiotensin II regulates and enhances the expression of transient receptor potential cation channel 6 (TRPC6), which leads to focal segmental glomerulosclerosis in animal models.² In addition, AT1-receptor antibodies may induce pre-eclampsia, with hypertension, proteinuria, and glomerular endotheliosis.³ These antibodies have also been associated with autoimmune conditions.⁴

We present a case of new-onset collapsing focal segmental glomerulosclerosis and antibody-mediated rejection that occurred 1 month after kidney transplantation in association with AT1-receptor antibodies. A 36-year-old white man with end-stage renal disease resulting from lupus nephritis type IV was referred for a third kidney transplantation, although he was already broadly presensitized. He received a kidney from a living, HLA-incompatible, ABO-incompatible donor who was not a relative under the auspices of

a kidney-paired donation. The patient underwent a desensitization protocol, given an initial positive flow cytometric cross-match and an anti-B antibody titer of 1:32. The transplanted kidney functioned immediately, and the patient was discharged with a creatinine level of 0.9 mg per deciliter (79.6 μ mol per liter).

A biopsy specimen obtained in accordance with a 1-month protocol revealed antibody-mediated rejection and focal collapsing glomerulopathy (Fig. 1A). Electron microscopy showed complete podocyte effacement (see Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Donor-specific antibodies (B37, DP1, DP11) were present at very low levels. The anti-B titer was 1:1 (detected only in an undiluted sample) and an antiendothelial cross-match was negative. New proteinuria of 2+ on a screening dipstick test was noted, but the patient's blood pressure and creatinine level were normal. AT1-receptor antibodies were detected in serum that was obtained 2 weeks before and 2 days after the biopsy. The patient received a diagnosis of antibody-mediated rejection⁵ and focal segmental glomerulosclerosis associated with alloimmune injury and AT1-receptor antibody. Plasmapheresis, intravenous immunoglob-

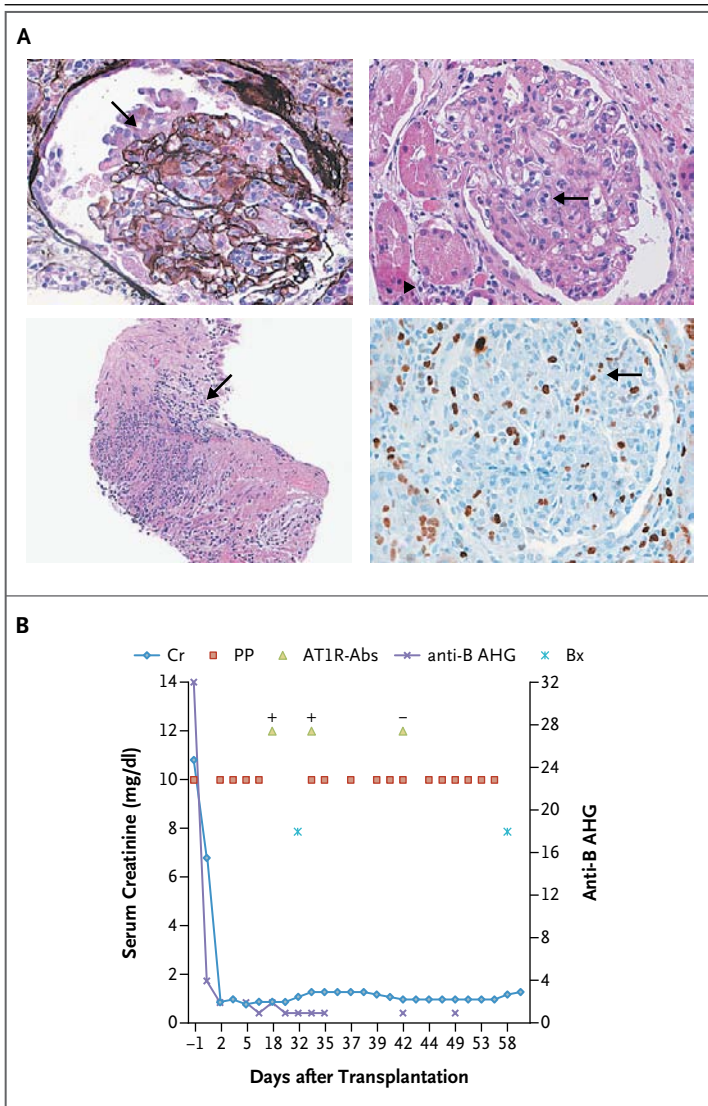


Figure 1. Biopsy Specimen Showing Antibody-Mediated Rejection and Focal Collapsing Glomerulopathy 1 Month after Transplantation and Results of Laboratory Tests before and after Transplantation.

Examination of a biopsy specimen from the transplanted kidney with light microscopy showed collapsing focal segmental glomerulosclerosis (Panel A, top left, arrow), histologic features consistent with antibody-mediated rejection, including moderate glomerulitis (top right, arrow) and focally moderate peritubular capillaritis (arrowhead), in addition to severe arteritis (bottom left, arrow) and minimal C4d staining, and podocyte proliferation (bottom right, arrow). Before transplantation, the patient underwent plasmapheresis and low-dose intravenous immune globulin therapy (100 mg per kilogram of body weight) 5 times and received a single dose of rituximab (375 mg per square meter of body-surface area). To address antibody-mediated rejection after transplantation, the patient underwent 12 sessions of plasmapheresis and intravenous immune globulin therapy as part of the desensitization protocol. Levels of AT1-receptor antibody became undetectable after the first 5 treatments (Panel B). AT1-receptor antibody levels were measured with the use of a recombinant, receptor-based, enzyme-linked immunosorbent assay in accordance with the instructions and thresholds recommended by the manufacturer (Cell-Trend). Plus indicates a positive result and minus a negative result. Anti-B AHG denotes anti-B isohemagglutinin, AT1R-Abs angiotensin II type 1-receptor antibodies, Bx biopsy, Cr serum creatinine level, and PP plasmapheresis.

ulin therapy, and losartan therapy were initiated. After the fifth plasmapheresis treatment (Fig. 1B), AT1-receptor antibodies could not be detected. A specimen obtained during a follow-up biopsy performed 2 days after the completion of plasmapheresis showed resolving lesions. At 6 months after transplantation, the patient's creatinine level was 1.3 mg per deciliter (114.9 μ mol per liter) and the urinary protein-to-creatinine ratio was 0.07. A biopsy specimen showed no antibody-mediated rejection or focal segmental glomerulosclerosis.

This case suggests that the AT1-receptor-mediated pathway may contribute not only to antibody-mediated rejection but also to de novo collapsing focal segmental glomerulosclerosis with

severe podocyte effacement. In this patient, depletion of AT1-receptor antibody with plasmapheresis and losartan therapy were associated with the resolution of antibody-mediated rejection and collapsing focal segmental glomerulosclerosis and a marked decrease in podocyte injury. We speculate that the AT1-receptor antibody may explain some cases of antibody-mediated rejection in patients without anti-HLA, ABO, and endothelial antibodies and that it may play a role in podocyte injury in association with focal segmental glomerulosclerosis.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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RESEARCH COMMUNITY FORUM

The forum, entitled “Partners in Research: How Institutions, IRBs, and Researchers Can Collaborate More Effectively,” will be held in Orlando, FL, on March 15. It is jointly sponsored by the Office for Human Research Protections and Orlando Health.

Contact Orlando Health, Conference Registrar, 1414 Kuhl Ave., MP 40, Orlando, FL 32806; or call (321) 841-5284 or (800) 648-0450; or see <http://www.orlandohealth.com/cme>.

MINDFUL PRACTICE: FOCUS ON SERIOUS AND LIVE-LIMITING ILLNESS

The workshop will be held in Batavia, NY, May 1–4. It is sponsored by the University of Rochester Department of Family Medicine and Center for Experiential Learning.

Contact the University of Rochester Center for Experiential Learning, 601 Elmwood Ave., Box 709, Rochester, NY 14642; or call (585) 275-4392; or see <http://www.urmc.rochester.edu/cpe>.

SOCIETY OF LAPAROENDOSCOPIC SURGEONS

The following meetings will be held: “Minimally Invasive Surgery Week: Annual Meeting & Endo Expo 2013” (Reston, VA, Aug. 28–31) and “AsianAmerican MultiSpecialty Summit VI: Laparoscopy & Minimally Invasive Surgery” (Honolulu, HI, Feb. 12–15).

Contact the Society of Laparoendoscopic Surgeons, 7330 SW 62nd Place, Suite 410, Miami, FL 33143; or call (305) 665-9959; or fax (305) 667-4123; or see <http://www.sls.org>.

MAYO CLINIC

The following meetings will be held in Rochester, MN, unless otherwise indicated: “Internal Medicine Recertification Course” (Huntington Beach, CA, March 13–16); “Pain Medicine for the Non-Pain Specialist” (Marco Island, FL, March 14–16); “Advanced Techniques in Shoulder Arthroscopy, Arthroplasty & Fractures” (April 26 and 27); “Mayo Clinic General Thoracic Surgery Symposium” (May 3); “Mayo Clinic Clinical Autonomic Quantitation Workshop” (May 17–19); “20th Annual Nicotine Dependence Conference” (May 20 and 21); “Disorders of the Wrist” (May 24–26); and “Mucha Symposium on Acute Care and Trauma Surgery” (Aug. 8 and 9).

Contact the Mayo School of Continuous Professional Development, 200 First St. SW, Rochester, MN 55905; or call (800) 323-2688 or (507) 284-2509; or fax (507) 284-0532; or see <http://www.mayo.edu/cme>; or e-mail cme@mayo.edu.

UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE

The “Ninth Annual Diabetes Regional Conference: Providing Patient-Centered Diabetes Care” will be held in Knoxville, TN, on March 16.

Contact Jennifer Russomanno, University of Tennessee Graduate School of Medicine, 1924 Alcoa Highway, Knoxville, TN 37920; or call (865) 305-9190; or e-mail jrussomanno@utmck.edu; or see <http://www.tennessee.edu/cme/medicine2013> or <http://www.tennessee.edu/cme/diabetes2013>, respectively.

IDWEEK 2013: ADVANCING SCIENCE, IMPROVING CARE

The meeting will be held in San Francisco, Oct. 2–6. It is jointly presented by the Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), and the Pediatric Infectious Diseases Society (PIDS).

Contact Dana Johnston, IDWeek, 1300 Wilson Blvd., Suite 300, Arlington, VA 22209; or call (703) 740-4961; or e-mail info@idweek.org; or see <http://www.idweek.org>.

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The conference will be held in Toronto, June 21–23.

Contact the American College of Chest Physicians, 3300 Dundee Rd., Northbrook, IL 60062; or call (800) 343-2227; or see <http://chestnet.org>.