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

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Long-Term Therapy with Bevacizumab in Hereditary Hemorrhagic Telangiectasia

TO THE EDITOR: Management of severe epistaxis resulting from hereditary hemorrhagic telangiectasia (HHT) can be invasive, and its effect is not durable in reducing the frequency and severity of bleeding events. Several reports have shown the efficacy of bevacizumab in treating patients with HHT.[1-3] We describe the long-term outcome of a patient who received multiple repeat courses of intravenous bevacizumab for severe HHT.

The patient, a 62-year-old man with severe HHT-related epistaxis, required blood transfusions and intravenous iron therapy to maintain a baseline hemoglobin level ranging from 5 to 7 g per deciliter. He received four intravenous infusions of bevacizumab (at a dose of 5 mg per kilogram of body weight) every 2 weeks. The epistaxis completely resolved, and the hemoglobin level improved to 13 g per deciliter. After approximately 1 year without treatment, he had a progressive relapse of epistaxis and a decline in the hemoglobin level to 8 g per deciliter. Retreatment with bevacizumab resulted in the cessation of epistaxis and a concomitant rise in the hemoglobin level to 16 g per deciliter. To date, the patient has had three treatment courses of bevacizumab with favorable responses and without adverse effects (Fig. 1).

A relapse in epistaxis after treatment with bevacizumab was reported by Bose et al.[2] and was probably due to the short half-life of bevacizumab (20 days)[4] and spontaneous regeneration of vascular endothelial growth factor[5] in the absence of bevacizumab. In our patient, retreatment with bevacizumab resulted in the same degree of improvement of anemia and epistaxis as with the first course, confirming the underlying mechanism of disease and the efficacy of bevacizumab over the course of the disease.

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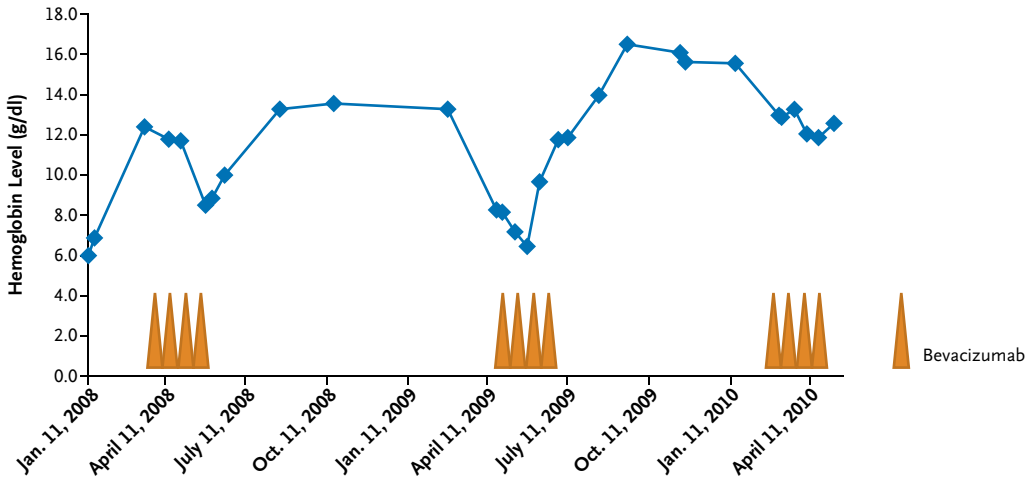

Figure 1. Hemoglobin Response to Multiple Bevacizumab Treatments in the Patient.

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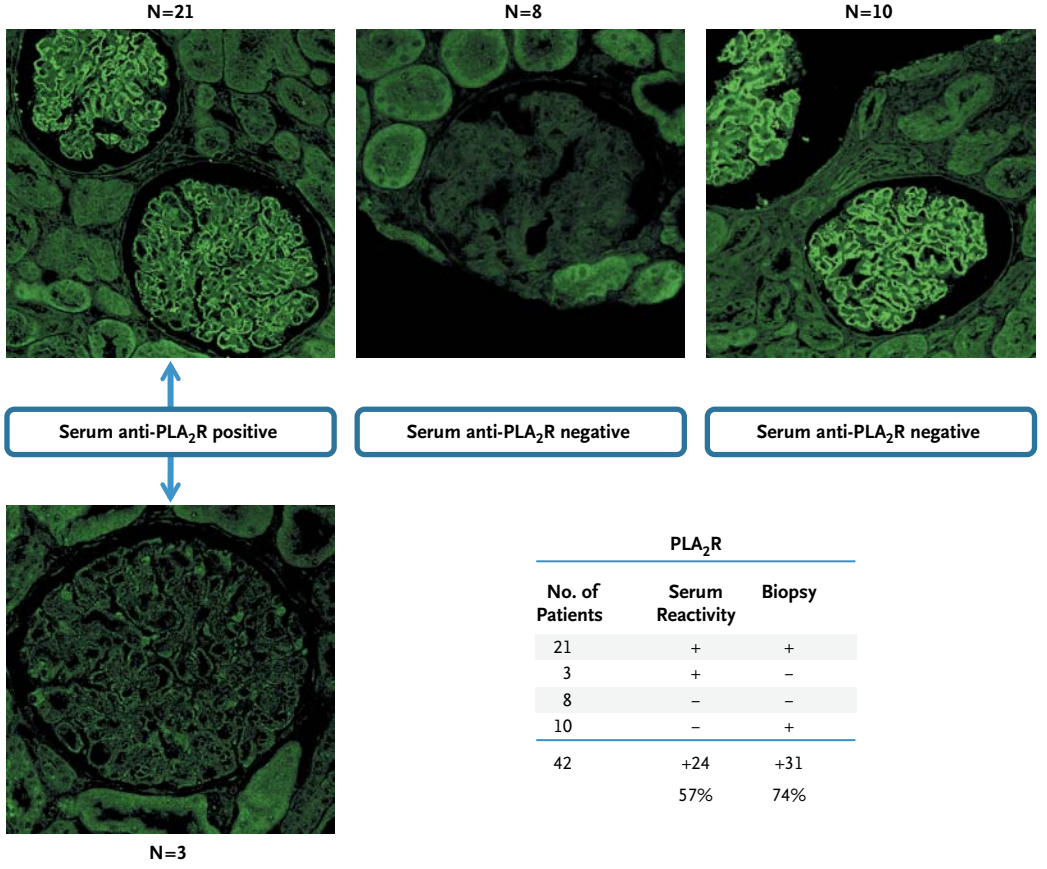
PLA_2R Autoantibodies and PLA_2R Glomerular Deposits in Membranous Nephropathy

TO THE EDITOR: Membranous nephropathy is a common cause of the nephrotic syndrome in adults. Treatment is controversial and challenging because of the heterogeneity of the disease and a lack of reliable biomarkers.[1,2] M-type phospholipase A_2 receptor (PLA_2R) was recently identified as a major target antigen involved in idiopathic membranous nephropathy in adults.[3] Circulating



	PLA_2R	
No. of Patients	Serum Reactivity	Biopsy
21	+	+
3	+	–
8	–	–
10	–	+
42	+24	+31
	57%	74%

Figure 1. Correlation between Circulating PLA_2R Autoantibodies and PLA_2R Glomerular Deposits.

After the assessment of PLA_2R autoantibody in 42 serum samples obtained from patients with biopsy-proven membranous nephropathy, PLA_2R was assessed in glomerular deposits on immunofluorescence assay in the corresponding paraffin-embedded biopsy sample from each patient with the use of antirabbit PLA_2R antibody, followed by goat Alexa 488–conjugated antirabbit Fab IgG antibody (Molecular Probes). Staining with the secondary antibody was negative in all biopsy samples. A total of 21 patients with circulating PLA_2R autoantibodies had PLA_2R in glomerular deposits, although 3 patients with a high circulating level of PLA_2R autoantibodies did not have detectable glomerular PLA_2R (serum sensitivity, 57%). Of the 18 patients with no detectable PLA_2R autoantibodies in serum, 10 had PLA_2R in glomerular deposits (biopsy sensitivity, 74%).