To the editor:

Bevacizumab therapy for POEMS syndrome

The role of vascular endothelial growth factor (VEGF) in hematologic malignancies was recently reviewed in this journal. Serum VEGF is higher in POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammapathy, and skin changes) patients than other monoclonal gammapathies and is thought to play a role in its pathophysiology. Here we describe a POEMS patient with high VEGF levels, even after chemotherapy, that rapidly decreased after bevacizumab, followed by significant clinical improvement.

A 52-year-old woman presented with progressive sensory and motor neuropathy for 2 years that left her bedridden. She had lost 30 kg and had a Karnofsky score of 40. She had received empiric intravenous immunoglobulin and steroids with no improvement. She was admitted with aspiration pneumonia. She had severe wasting and weakness in distal and proximal muscles, stocking-glove painful paresthesias, absent deep tendon reflexes, and weak gag reflex. She had extensive edema and hyperpigmented skin patches. She also had significant ascites, pleural and pericardial effusions, and hepatomegaly.

Electromyographic and nerve conduction studies showed evidence of sensorimotor neuropathy with axonal features. Nerve biopsy showed mild loss of myelinated axons and no evidence of deposition diseases. Magnetic resonance imaging of head showed empty sella. Cerebrospinal fluid revealed normal cell count and elevated protein level (60 g/L). Barium swallow showed silent aspiration. She exhibited signs of hypothyroidism (thyroid-stimulating hormone [TSH], 11 IU/L) and had low follicle-stimulating hormone (FSH, 0.3 IU/L) and luteinizing hormone (LH, 0.1 IU/L). Platelets were $680 \times 10^9/L$, with normal hemoglobin and white cell count. She had normal renal and liver functions. Laboratory tests are summarized in Table 1.

Skeletal survey showed no lytic or sclerotic lesions at diagnosis and 4 months after therapy. After 2 months of therapy with melphalan and dexamethasone, she achieved a hematologic remission (near complete remission [CR]) but no improvement in the clinical status and VEGF level remained elevated. Bevacizumab was given in an attempt to decrease VEGF level. Surprisingly, after 1 week, the edema resolved and by the second week the neuropathy pain vanished and she stopped all narcotics. One month after bevacizumab, she started to use her hands to feed herself and started drinking liquids without choking. Her performance status markedly improved; she started to use her hands to feed herself and started drinking liquids without choking.

The patient met diagnostic criteria for POEMS. Her therapeutic options were limited; she was not a candidate for high-dose chemotherapy. Conventional chemotherapy, such as melphalan and dexamethasone, has limited success in alleviating symptoms even in those achieving hematologic responses. VEGF contributes to POEMS symptoms by increasing microvascular permeability, which leads to edema, increased endoneural pressure, and exposure of myelin to serum cytokines and compliments leading to demyelination. Interventions that specifically decrease VEGF level have been successful in improving disease symptoms. This is the first report of bevacizumab therapy in POEMS; the drug was well tolerated with rapid reduction in VEGF level and was associated with dramatic improvement in all features of the disease, most remarkably the painful neuropathy and edema. This case suggests that VEGF should be measured in all POEMS patients to confirm the diagnosis and monitor clinical activity. Targeting of VEGF with bevacizumab should be investigated further in therapy of POEMS syndrome.

Ashraf Badros, Neil Porter, and Ann Zimrin

Correspondence: Ashraf Badros, Greenebaum Cancer Center, University of Maryland, 22 South Greene St, Baltimore, MD, 21201; e-mail: abadros@umm.edu.

References

Bevacizumab therapy for POEMS syndrome
Ashraf Badros, Neil Porter and Ann Zimrin

Updated information and services can be found at:
http://www.bloodjournal.org/content/106/3/1135.full.html
Articles on similar topics can be found in the following Blood collections

Information about reproducing this article in parts or in its entirety may be found online at:
http://www.bloodjournal.org/site/misc/rights.xhtml#repub_requests

Information about ordering reprints may be found online at:
http://www.bloodjournal.org/site/misc/rights.xhtml#reprints

Information about subscriptions and ASH membership may be found online at:
http://www.bloodjournal.org/site/subscriptions/index.xhtml