Bevacizumab therapy before autologous stem-cell transplantation for POEMS syndrome

POEMS is an acronym for a rare multisystemic syndrome encompassing polyneuropathy (P), organomegaly (O), endocrinopathy (E), monoclonal gammopathy (M), skin changes (S) and additional features variably expressed [1]. POEMS syndrome is associated with high vascular endothelial growth factor (VEGF) serum levels. This angiogenic factor likely plays a pathogenic role, in particular for neuropathy, possibly via alteration of endoneurial vessels [2]. Treatment options are still debated, but recently autologous stem-cell transplantation (ASCT) appears to be effective. This approach for POEMS patients, however, was associated with severe morbidity, mainly respiratory failures that appeared to be related to neuromuscular damage [3].

We report a 45-year-old woman presenting with a rapidly progressive sensorimotor polyneuropathy involving all extremities, multiple sclerotic bone lesions, skin hyperpigmentation and hemangiomas, hepatomegaly, peripheral edema and papilledema. A monoclonal immunoglobulin A λ protein was detected (5 g/l) with a bone marrow plasmocytosis (15%). Platelets were 600×10^9/l and cerebrospinal fluid proteins were 30 g/l. Electromyographic and nerve conduction analyses confirmed neuropathy with axonal abnormalities. Within few months appeared walking impossibility, swallowing difficulties and respiratory distress. Serum VEGF was highly elevated at 9700 pg/ml (normal range: 62–707).

Steroids treatment was declined by the patient. ASCT was considered at high risk because of her poor condition (Karnofsky score of 50%), neurological defects and respiratory failure. We hypothesized that VEGF inhibition may relieve neuropathy. Bevacizumab therapy was initiated at 10 mg/kg every 2 weeks. Pain relief was observed after two infusions, followed by major improvement in walking and breathing within 10 weeks. This was correlated with a drop in VEGF level (61 pg/ml) and a significant improvement in electromyographic and nerve conduction studies. Treatment was continued for 4 months, and further clinical improvement was observed, confirmed by electroneuromyography and pulmonary function tests. Hepatomegaly and skin abnormalities remained unchanged. Karnofsky score improved at 80%, allowing ASCT conditioned with melphalan (200 mg/m^2) to be realized in better conditions. The procedure was well tolerated, and clinical outcome was excellent with a Karnofsky score at 90% 1 year after the procedure.

Rapidly evolving neuropathy may hamper to carry out ASCT in POEMS patients. Neurological defects in our POEMS patient has been partially reversed by bevacizumab therapy, further supporting the role of VEGF in this complication. The large biological and clinical heterogeneities of POEMS syndrome could explain variable sensitivities to anti-VEGF therapy [4, 5]. Our report indicates that some patients may benefit from bevacizumab to improve their clinical condition before applying more standard treatments.

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