Carfilzomib, a potential front line therapy for hyperviscosity syndrome associated to plasma cell dyscrasia.

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Background:

Hyperviscosity syndrome is a clinical condition associated with plasma cell dyscrasia (Waldenstrom macroglobulinemia or WM and multiple myeloma or MM), and acute leukemia. Patients have a compatible disorder with bleeding diathesis, neurologic alterations, and less frequently central retinal venous occlusion and retinal detachment. Its treatment requires the placement of a Quinton catheter and an apheresis team. Potential serious complications of apheresis include hypokalemia, hypocalcemia, coagulopathy, immunoglobulin depletion and even mortality. Other potential complications include angiotensin converting enzyme (ACE) inhibitor-related complications, anaphylactic reactions, transfusion-related acute lung injury (TRALI) and the infectious risks of plasma or blood transfusions. The movement of extravascular IgG into the intravascular space diminishes the efficiency of IgG removal when compared to IgM. In the case of cast nephropathy without efficient tumor killing the procedure is not useful.

Cases:

We describe two cases of hyperviscosity syndrome treated with carfilzomib, a second generation proteasome inhibitor.

First Case:

A 62 year old patient with advanced MM had been transferred from a different institution comatose, and with a profusely oozing tracheostomy. He had pulmonary infiltrates and an acute kidney injury. Plasma viscosity was 2.3>H₂O with >5 g/dL of IgG. He was refractory to plasmapheresis (four procedures). After the first dose of carfilzomib he experienced resolution of the hyperviscosity syndrome in less than 12 hours. In 24 hours he regained consciousness, steadily improved and was discharged 14 days later. He is currently in a very good partial remission.

Second Case:

A 73 year-old patient with an established diagnosis of WM developed hyperviscosity syndrome with retinal changes and shortness of breath. His WM did not respond to bendamustine-rituximab. Plasma viscosity was 3.0>H₂O with >4.5 g/dL of IgM. After one plasmapheresis treatment he was started on carfilzomib. His hyperviscosity syndrome also resolved in less than 12 hours. He has developed pulmonary emboli resolved with anticoagulation. The plasmapheresis catheter was removed and WM treatment continued. One year later he is in a very good partial remission of his WM although has now developed a lung cancer for which he has elected not to seek treatment.

First Case Ig G MM

Second Case WM

	July 09 2016	July 11 2016		January 23 2017	January 27 2018
T. Protein g/dL.	9.0 g/dL	8.8g/dL		9.9 g/dL	7.0 g/dL
Ig G mg/dL	5650 mg/dL	5420 mg/dL	IgM	5.6 g/dL	5.4 g/dL
PT seconds	19.3 seconds	18.8seconds		19.3 seconds	18.8 seconds
PTT seconds	37.8 seconds	33.2seconds		34.6 seconds	3379.6 seconds
INR seconds	1.59 seconds	1.54 seconds		1.18	1.05
Eye Changes	++++	++++		+++	+++
S. Creatinine mg/dL	1.69mg/dL	1.82mg/dL		1.11mg/dL	0.73 mg/dL
Serum viscosity	2.3 relative to saline	N.D.		>3.0 relative to saline	2.1 relative to saline

Conclusion:

The dramatic clinical responses of the hyperviscosity syndrome in these two cases to carfilzomib devoid of the rebound seen with plasmapheresis raises its possibility of its use as a front line treatment in hyperviscosity associated to plasma cell dyscrasia. This is of particular interest when considering that not all the time there is readily availability of the plasmapheresis procedures. An interesting observation was the discrepancy between the dramatic clinical improvement over a relative short period of time of these patient's clinical conditions with carfilzomib when compared to the changes observed in the measured biochemical parameters suggesting a complex effect of the proteasome inhibitors upon protein metabolism, with profound physiological consequences.

Drs. Adan Rios and Aaron Ciechanover.

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