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Patient Case: How Would You Treat a Newly Diagnosed PNH Patient with Near Normal Hgb?

Announcer:
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Dr. Broome:
Hi, I'm Dr. Catherine Broome, Associate Professor of Medicine at Georgetown University Lombardi Cancer Center in Washington DC. And we're going to talk today about a newly diagnosed PNH patient with a near normal hemoglobin, and what are some of the factors that go into treatment decisions for these patients?

So we have a 34-year-old female with several months' history of fatigue, mild dyspnea on exertion, superficial thrombophlebitis in her lower extremities bilaterally. Her laboratories you can see here, a pretty mild hemoglobin, a total bilirubin which is mildly elevated, and an elevated reticulocyte count. Peripheral smear was unremarkable. And flow cytometry does confirm the diagnosis with a granulocyte clone of 10.2% and a red cell clone of 5.3%.

So what are some of the most common symptoms? You can see them listed here, most common symptoms are going to include dyspnea, abdominal pain, anemia, fatigue, chronic renal insufficiency, thrombosis is there as well at 39%. If you look here, all of these symptoms that we talked about can be relatively nonspecific, but they do have some significant impacts on quality of life. And patients will develop a variety of different impacts on their daily life including trouble walking, trouble exercising, problems getting household work done, problems with work with regards to missing work, no flexibility in planning, the normal rhythm of their life is affected, they miss things because they're too tired to do them. This can certainly impact their relationships with family and friends, etc.

If we look at symptoms ever experienced, most patients will say that they have experienced fatigue, abdominal pain, other pain, including back and leg pain, sexual difficulties, headaches, cognitive difficulties, difficulty sleeping, which you can imagine, can all have a significant impact on quality of life.

So in addition to the numbers, right, laboratory features of PNH, which we're all familiar with, including on the bone marrow examination, either hypo or normocellular, we might see erythroid hyperplasia and some dysplasia, we might see iron deficiency, we might see abnormalities in renal function and hepatic function. And we may also see some mild reductions in white blood cells and platelets related to potential splenomegaly which can be related to portal or splenic vein thrombosis.

Uncontrolled or excessive complement activation has a variety of effects, which you can see here including endothelial cell activation and cytokine activation. Thrombosis in PNH is one of the side effects that leads to the most significant morbidity and is the most common cause of mortality. Venous thromboses are more common than arterioles. Thrombosis can occur in any PNH patient, including those with a very small clone size.

This is a multifactorial pathogenesis, which involves hemolysis and nitric oxide. It involves platelet activation from CD59 deficiency. It involves platelet consumption, endothelial cell perturbation, and the inflammatory effects of complement activation.

So symptoms associated with thromboembolic events need to be considered as part of a comprehensive clinical assessment for patients with PNH. And again, clone size does not necessarily correlate to symptom severity.

So how would we approach this patient? Here are some data to guide us looking at pegcetacoplan, which is a C3 inhibitor, in patients that have a hemoglobin at or above 10 as a baseline. And you can see that the vast majority of these patients had significant improvements in their hemoglobin, their LDH, and their FACIT-Fatigue scores.

So what are reasons to consider treatment in this 34-year-old patient with a small clone size but evidence of hemolysis and thrombosis? Fatigue mediated in part by complement activity, thrombosis mediated in part by complement activity, and ongoing hemolysis, again, mediated by complement activity.

Thank you very much.

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