Managing Myeloma

Managing Myeloma Webinar Q&A with Dr. Sergio A. Giralt and Dr. Beth Faiman

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What are the symptoms of amyloidosis and what are the signs clinicians should be aware of so that patients can be captured early in the course of their disease?

Faiman: As you know, primary amyloidosis focuses on fibrils which cause misfolding of a number of proteins and deposits, they form beta-sheet fibrils and deposit extracellularly in various organs, so the symptoms of amyloid are targeted toward which organ you have the deposition. For patients with heart amyloidosis, you might have congestive heart failure signs with restrictions and some diastolic dysfunction, palpitations, or arrhythmia. If the kidney is affected, then you can have foamy urine or ankle swelling, which might be a sign of hypoalbuminemia. For nerve innervation, you can have some numbness and tingling or even autonomic symptoms, and then for skin, you can see some easy bruising, bleeding, or tongue enlargement. The symptoms of amyloidosis are targeted toward the organ and it is primarily the light chain type that hematologists and oncologists will treat.

Giralt: I think it is also important to remind community physicians and providers that if patients present with unexplained neuropathy, unexplained diarrhea, or orthostatic hypotension, particularly if they are older or have abnormal skin deposits, you must have the diagnosis of amyloid in the back of your head because if not, these patients will never be diagnosed early in the course of the disease and many of them will actually lose their chance to undergo high-dose therapy and autologous transplant, which is the most effective way of treating this disease.

Are there any specific instruments or tools recommended to assist in documenting geriatric assessment, function, and comorbidity?

Giralt: I am going to refer all our learners to a recently published ASCO special article. The first author was Dr. Supriya Mohile and the article is titled, Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy; ASCO Guideline for Geriatric Assessment. This was published in May 2018. The expert panel conclusion was that clinical trials are vital for informed medical decisions for older patients with cancer and improved cancer care. In patients' aged 65 or older, geriatric assessment, the evaluation of functional status, physical performance, comorbid medical condition, depression, and social support are essential to provide the best oncologic care. There are many instruments in the public domain available for use in practice. The panel reviewed and recommended several instruments that measure independent activity or instrumental activities of daily living (IADLs), including the Geriatric

Depression Scale and the Mini-Cog Test. In regard to assessment of prognosis without cancer, there are actually two indexes. They are both available online; one is called the Schonberg Index and the other one is called the Lee Index.

Is there a way of differentiating amyloid neuropathy from other types of peripheral neuropathy?

Faiman: Yes, absolutely. In our clinic one of the primary reasons patients are assessed for a monoclonal paraprotein is because of peripheral neuropathy. They see the primary care doctor, they go to the neurologist, and they are checked for a monoclonal paraprotein and found to have a monoclonal dermopathy. This is a very common scenario. In amyloidosis, peripheral neuropathy has been well described and it seems, although it is not entirely clear, related to the amyloid deposition within the nerve. The nerves tend to innervate in the sensory, motor, or autonomic fibers, and it creates a sensory neuropathy as the skin organ is involved. QSAR and other EMG testing can be very helpful, but again, a lot of these patients will have diabetes and other comorbid conditions that could lead to neuropathy. It is pretty much a clinical diagnosis based on sensory findings but QSAR and EMG testing can help delineate if it is a small fiber neuropathy which might be related to the amyloid paraprotein.

Would someone with insulin-dependent diabetes be ruled out for corticosteroid therapy? If not, how would it be modified and what are the statistical risks for this population?

***Faiman*:** It is very clear that there is a lot of activity with steroids in the myeloma population. Since the 1950s and the advent of prednisone to treat multiple myeloma, we know that steroids will induce deeper responses in just about every single study, so the statistical risks are hard to quantify. When a patient of mine has newly diagnosed or relapsed myeloma, I try to intensify their treatment with their oral agents, watch their hemoglobin A1c, and elicit the help of the primary care providers. Because steroids are so effective, I would not eliminate them from the treatment, but I would include the multidisciplinary team to effectively manage it. At some point when the steroids cause too much hyperglycemia, oftentimes you have decrease to very low doses, but you have to take into consideration the risk of the myeloma not being well controlled. Again, including the multidisciplinary team can really benefit that patient.

Are VTEs a risk for all patients being actively treated for myeloma?

***Faiman*:** The answer in my opinion is yes. Multiple myeloma is an inheritably coagulable state and an active myeloma diagnosis is one which further increases the risk to develop venous thromboembolic events. Patients with IMiDs and high dose carfilzomib are at an even further increased risk. The ENDEAVOR trial showed that patients with high dose carfilzomib versus bortezomib had an increased risk of thrombotic events. Everybody with myeloma in my practice is risk stratified and this can change, so at diagnosis although one might not have cardiac or renal disease or other risk factors such as surgery, immobility, etc. that would warrant therapeutic anticoagulation, just about everybody is on a low dose aspirin 81 mg. There are some studies that say it should be 325 mg, but work from our institution suggests 81 mg will suffice. Then we would employ a DOAC or enoxaparin for patients at even greater risk who

have had previous blood clots or are undergoing surgery, at least temporarily, and protect them that way.

Do you treat the biochemical relapse or do you wait for the patients to have symptomatic disease?

Faiman: We use the International Myeloma Working Group Criteria for remission and relapse (updated criteria were in 2014) primarily, and so we are really looking for about a 25% increase in M-spike or free light chains. The criteria is very specific, it can be easily access online, and we also take into consideration the biology of the disease. If somebody is a younger individual with high risk, adverse cytogenetics, or FISH, then we would be a little bit more aggressive at changing therapy with that biochemical relapse, and there are different ways of initiating treatment. Some people will wait until outside of the clinical trials, if the number gets to a 0.5 or 1.0, but it depends on adaptive response. So if they had achieved the M-spike of 0, and now they are slowly progressing toward 1.0, you are more likely to jump in before that individual has end organ damage. I know there have been other papers still looking at PET scans, restaging, and marrows.