Hello!

This is Johana Fajardo. I am one of the members of the AAHFN Education Committee and I would like to welcome you to our second Online Journal Club article review which includes a blog with questions for collegial discussion regarding a research article. Please participate in the blog which can be found on the AAHFN website.

In the future, I hope that you will join us regularly and perhaps even consider submitting an abstract to lead a journal review.

Today’s article review is the second of a 3-part series on amyloidosis. So let’s begin...

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Introduction

The article’s title is AL Amyloidosis for the Cardiologist and Oncologist written by Ronald Witteles¹, MD, FACC & Michaela Liedtke MD and It’s an expert analysis article. While the article is somewhat extensive, the information is current and well explained to the audience. After reading this article, the reader will have a comprehensive understanding of AL amyloidosis with cardiac involvement as well as important aspects of its diagnosis and management.

The article opens with a brief description of what amyloid light chain (AL) amyloidosis is, along with its pathophysiology, including the distinction among systemic and localized AL amyloid. Although the primary characteristic of AL Amyloidosis is the production of monoclonal immunoglobulin light chains in the bone marrow into the blood stream, that then accumulate in major organs such as the kidneys or the heart, other sources of AL production can occur throughout the body. If amyloid deposits are only found at the site of the production itself rather than in the blood stream, it is thought that the AL amyloidosis is localized rather than systemic. Localized deposits of amyloid routinely do not require any
treatment unless it is for cosmetic reasons (i.e. skin lesions) or symptomatic relief (i.e. laryngeal deposits to alleviate voice changes). The article focuses primarily on systemic AL amyloidosis which is a more common and much more serious condition in regard to management and survival.

Furthermore, the article goes on to explain that while systemic AL amyloidosis almost commonly arises from clonal light chains produced in the bone marrow, there are 2 other conditions with similar presentation including Monoclonal Gammopathy of Undetermined Significance [most commonly referred as MGUs] and Multiple Myeloma, which can lead to confusion and misdiagnosis. Laboratory workup including Kappa/lambda ratio and immunofixation studies must be done to establish a diagnosis and if negative, all 3 conditions would be ruled out. However, abnormal studies are insufficient to detect AL amyloidosis and for this reason, the diagnosis of AL amyloidosis can only be confirmed by tissue biopsy, more commonly from the organ where AL amyloid deposits have occurred such as the heart. Nevertheless, a bone marrow biopsy is routinely indicated as up to 15% of AL amyloidosis patients present with multiple myeloma. Cardiac red flag signs and symptoms that should raise the suspicion for AL amyloidosis include unexplained persistent troponemia, heart block, atrial arrythmias, increased ventricular thickness on echocardiography and/or low voltage:mass ratio, when comparing ekg voltage with ventricular mass. Non-cardiac clinical features would depend on other organ involvement including macroglossia, nephrotic syndrome, elevated alkaline phosphatase, periorbital purpura or dysphagia among others.

Once the diagnosis is made, stratification of the disease will guide treatment. The severity of cardiac involvement remains the primary prognostic factor in AL amyloidosis and hence, it is routinely stratified by using cardiac biomarkers including NT-proBNP and troponin. The article then elaborates on the different treatments as the goal of therapy focuses on decreasing the pathologic light chain levels with the least toxicity possible. High dose chemotherapy with or without autologous stem cell transplant remains the main therapy for AL amyloidosis. It is important to note that while these therapies were developed and approved for the treatment of myeloma, they are widely useful for treating AL amyloidosis, as both conditions arise from a clonal plasma disorder. Immunomodulators are another group of agents used to treat AL amyloidosis and more recently, they have been added to chemotherapy regimens along with steroids to attack light chains in a
comprehensive manner. The side effect profile is certainly high particularly when it relates to cardiovascular toxicities including fluid retention, hypertension, and thromboembolic events. Noncardiac side effects include myelosuppression, neuropathy and stomatitis among others. Importantly, overall survival is tightly correlated with the degree of hematologic response, emphasizing the importance of moving to a different line of therapy quickly when a treatment is not adequately effective in reducing light chain production.

As with other types of amyloidosis, therapy must have a dual approach by stopping amyloid production while treating organ deposition. In the case of cardiac involvement, the mainstay of symptomatic therapy is volume management while reducing complications from hypotension, thrombosis and/or arrhythmias. Standard heart failure therapies are poorly tolerated and anti-arrhythmic agents such digoxin have traditionally been avoided given the risk of toxicity despite normal serum levels. Anticoagulation is key but must be used with caution on patients with thrombocytopenia secondary to chemotherapy. While pacemakers may benefit some patients with symptomatic bradycardia and heart blocks, ICD placement has been routinely thought to be contraindicated due to the lack of benefit in patient’s survival. However, recent studies have demonstrated that in selected patients who meet the life expectancy threshold and who have evidence of ventricular arrhythmias in telemetry may still benefit from ICD placement. Lastly, as survival rates improve with more effective chemotherapy treatments, candidacy for heart transplantation is being considered in Expert centers although AL amyloidosis patients have a much higher transplant waiting list mortality than other patients. However, the 2018 revision to the U.S. heart transplant allocation system listed amyloidosis as status 4, given those patients a higher status than other diagnosis.

While comprehensive, this article aimed to demystify AL amyloidosis by taking the time to explain both hemo/oncological and cardiac lingo so that readers of both specialties could gain an understanding of this complex multisystem disease. Nurses, especially those working closely with patients with heart failure secondary to amyloidosis, may benefit from this type of articles that demonstrate and encourage a multidisciplinary approach to improve patient outcomes and overall survival.
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