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AMYLOID HEART DISEASE: THE DEATHLY PROTEIN INVASION – A PERSONAL PERSPECTIVE

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The gusts of cold wind were harsh as I treaded the wild terrain of despair. As a physician, I carried the torch of hope, a bestowment that conferred immense responsibility. I felt the burden of divine expectation, from the wounded to deftly navigate this unchartered terrain and offer a respite from suffering. Upon entering the battle-zone, I could not fail to notice the despondency in their eyes — and with it a glimmer of hope from the reflection of my torch. As I approached the edge of a steep cliff, I saw him: a meek, astonished, and badly wounded man holding on to his dear life with his last vestige of strength. His desperate, helpless family stood by, with their hands tied and their voices loud with cries for help. A sense of relief dawned on them when they heard my footsteps in the distance. As I stumbled through the terrain, I tried to estimate how long his weak hands could hold on to the edge, and how fast I needed to leap and grab-on and initiate my fight with the demons of death. The fog muddled my vision; the cries of suffering numbed my senses. The terrain lay divided — this one man dangling on the edge, and the rest on the other side. I reached out to save him, but the winds of suffering were too strong for this wounded soldier. Helplessly, I watched him plummet into the abyss of darkness. There were marks of other would-be messiahs by the edge, signs of other unsuccessful attempts to save him. Consternation consumed me: I held a baton in my hand that I could not deliver, sorrow in my heart, and a sense of hopelessness and doubt looming inside me. The burden of the torch grew heavier, making me wonder if I was ever suitable to carry it.

As a heart failure and transplant specialist, there are many times I have lived the terrain described above, especially when I see the missed opportunities of end-stage heart failure patients who are referred for possible advanced therapies at a stage when our efforts are only made more heroic. One specific subgroup of heart disease patients who definitely need special attention in this regard are those with amyloid heart disease. The prose at the beginning of this passage resulted from my emotional outburst after a humbling and unfortunate experience with a patient who had a missed diagnosis of AL-amyloidosis for more than 10 months. A successful diagnosis was quickly followed by the unexpected outcome of sudden death (asystolic arrest at home) within a week, before we could initiate a transplant evaluation. All planned efforts to evaluate and bridge the patient, possibly to an amyloid transplantation protocol, remained a dream both for the medical team and the patient's family. We see many amyloid patients who are either too advanced in their disease process to be transplanted or succumb prior to or after diagnosis, depriving us of the opportunity for any lifesaving therapy. The problem is not negligence on the part of any medical provider but rather a lack of awareness, a deficit in understanding the myriad variations of the disease process, and poor prognostication tools.

Though amyloidosis is considered a rare disorder, the typical prolonged time to diagnosis makes one wonder if the true incidence is astronomical compared to those who are actually diagnosed. AL amyloidosis is the most common type of amyloidoses and is in essence a blood dyscrasia, which makes the hematologist the inherent expert in this field. Yet, the irrefutable prevalence of cardiac involvement driving mortality, over any other organ, makes the cardiologists and internists equally responsible for being well informed in concepts of diagnosis and risk stratification. A larger onus of responsibility might need to be taken up by internists, as many patients have systemic and nonspecific symptoms. Many physicians, including cardiologists, lack the experience to suspect amyloidosis and often are incognizant of the subtleties of the disease process that would elicit suspicion — for example, a symptom complex that is disproportionate to the extent of the presumed diagnosis, such as atrial fibrillation or diastolic heart failure in patients with no reported or suspected hypertension, or an electrocardiogram showing disproportionately low voltage in comparison to the extent of echo evidence of hypertrophy. A deceptively normal appearance of these patients, who may have extreme symptoms of fatigue, makes it even more challenging.

With the mode of death in AL amyloid patients being overwhelmingly cardiac, it becomes imperative for the cardiology community to get involved and take action — not only to empower ourselves with the clinical skills to suspect and diagnose this disease but also to reach out and educate the many healthcare providers who could potentially encounter such patients. Transplant centers across the country are making strides in creating multidisciplinary teams that offer cardiac transplantation, combined heart-liver transplantation, or cardiac followed by autologous bone marrow transplantation depending on the type of amyloidosis. However, based on experience from ours and other centers, the outcome of patients over the last 3 decades has barely changed due to late diagnosis and early mortality. Furthermore, none of the national organizations in the world of cardiology has addressed the issue of lack of awareness of amyloidosis.

A sense of urgency in evaluating and offering definitive therapy for patients with cardiac amyloidosis seems reasonable. As we move forward with growing technology in mechanical assist

devices, there will be more options to support individuals with amyloidosis, and it will be important to diagnose them before they encounter debilitating systemic involvement. It will be equally important to fight end-stage organ disease with organ replacement and a definitive cure such as chemotherapy and bone marrow transplantation. Hope for future amyloid patients can be accomplished through early diagnosis combined with established protocols by experienced centers that streamline and expedite efforts to evaluate and treat these patients.

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