Medical Expertise

"Development of the European Network in Orphan Cardiovascular Diseases"
„Rozszerzenie Europejskiej Sieci Współpracy ds Sierocych Chorób Kardiologicznych"

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CASE SUMMARY

The 49-years old male after exhaustive diagnostic process was finally diagnosed with multiple myeloma and appropriate complex chemotherapy was initiated. At the time of onset of chemotherapy the patient had not had any signs of cardiac diseases, however, few months later and institution of Bortezomib, he has been developing symptoms of circulatory compromise. Moreover, on echocardiography his heart become dilated with severe impairment of left ventricular systolic function (ejection fraction of only 20%). Although the chemotherapy was unsuccessful in terms of hematological remission, nevertheless, the potentially offensive treatment was prematurely stopped due to the fear that it may exacerbate already impaired cardiac state. Apart from that the patient had recurrent episodes of atrial fibrillation and flutter that also worsened hemodynamic status. Additionally, the concept of cardiac amyloidosis on the basis of multiple myeloma was coined and two biopsies of gums and abdominal tissue were harvested. However, both proved negative as no amyloid deposits were found. The second bone marrow biopsy is pending to determine the hematological status and tailor chemotherapy but in a view of overt systolic heart failure it will be very challenging.

DISCUSSION

From the cardiologic perspective the most important problem to be solved is the reason of patient's dilated cardiomyopathy (DCM). There are at least two valid explanations and one additional exacerbating factor. As the patient has been diagnosed with multiple myeloma, it has very hard to resist temptation to diagnose him with AL cardiac amyloidosis as a consequence of multi-organ infiltration of AL fibrils derived from monoclonal immunoglobulin light chains. The hart is affected in AL amyloidosis in up to 90% cases and more than half of patients develop rapidly progressive signs and symptoms of heart failure. The prognosis is generally poor with median survival of only 15 months. In this clinical setting inclusion of cardiac magnetic resonance in the diagnostic work-up could have helped with the diagnosis as global sub-endocardial late gadolinium enhancement, that likely represents interstitial expansion of amyloid, is present in 60-70% of patients. However, the most definitive diagnosis could be obtained from the endomyocardial biopsy. Due to wide deposition of AL amyloid throughout the heart cardiac biopsy is virtually 100% sensitive. Leaving aside cardiac amyloidosis, the equally probable reason of DCM could have been complex, high-dose chemotherapy

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that may have caused medications-induced DCM. Both clinical entities are highly probable in this patient and both are very serious conditions with poor outcome. There are no imaging studies that could differentiate those two disorders with high certainty. Only performing endomyocardial biopsy and detection of apple-green birefringence when stained with the Congo red and viewed under a polarizing microscope can be diagnostic for cardiac amyloidosis. As it was mentioned above there is one more contributing factor for DCM that is recurrent, uncontrolled atrial flutter and fibrillation. As the duration of atrial arrythmias is relatively short, it is highly unlikely that this is the sole mechanism of observed DCM. Nevertheless, it should be considered as an important exacerbating factor and appropriately managed.

The treatment of overt heart failure due to DCM should be in line with the current guidelines and include, whenever possible, neurohormonal blockade with beta-blockers, angiotensin II inhibitors (ACE-I) and mineralocorticoid receptor antagonists (MRA) alongside with diuretic therapy. Direct current cardioversion is effective with atrial arrythmias, however, digoxin should be avoided as binds to amyolid fibrils and can result in digoxin toxicity. Treatment of underlying disease, that is multiple myeloma, include high-dose chemotherapy coupled with peripheral autologous stem cell rescue. Unfortunately, both are contraindicated if congestive heart failure develops. The definitive treatment with heart transplantation is not generally accepted due to poor-long term survival secondary to diseases recurrence in the allograft (in case of proven cardiac amyloidosis).

EXPERT'S OPINION

Unfortunately, the presented case is very serious and very difficult to manage as it is likely that so far used high-dose chemotherapy could have inadvertently resulted in developing medications-induced DCM and overt heart failure. At this stage of very advanced heart failure the reason for it, probably does not matter for the patient's management that much. Even if performing cardiac biopsy and proven cardiac amyloidosis will not automatically change therapy as regardless of the fact what actually caused DCM whether it is drugs-mediated or amyloid, the re-start of chemotherapy is contraindicated. In case the patient status improved alongside with cardiac morphology and function, the review of cardiac biopsy indications and meanings should be performed. Given the fact that the long-term survival is poor and probably less than one year plus the fact that the presence of atrial arrythmias could result in inappropriate shocks, the implantation of cardioverter-defibrillator (ICD) should be postponed and criteria for ICD should be systematically re-evaluated with the changing clinical status.

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