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Case Report *Volume 4 Issue 1*

"De Novo" Heart Failure after Azacitidine Therapy: A New Significant Complication

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Abstract

Azacitidine (AZA) is the first choice of low-intensity treatment in myelodysplastic syndrome. Its most serious adverse effect is myelosuppression whilst cardiac complications are poorly identified. Despite the NICE guidelines encourage not to use AZA in severe congestive heart failure (HF), more data should be provided. We present a new AZA's complication: this is the first left ventricular dysfunction due to AZA's treatment in a patient with no previous cardiac history. Transthoracic echocardiogram examination was key to discontinue AZA and to initiate treatment for ventricular dysfunction. In such circumstances, cardiac follow-up is mandatory, strengthening the multidisciplinary management in oncology patients.

Keywords: Azacitidine; Adverse Effects; Cardiotoxicity; Heart Failure; Severe Ventricular Dysfunction

Abbreviations: AZA: Azacitidine; HF: Heart Failure; TTE: Treatment, a Transthoracic Echocardiogram; CVRF: Cardiovascular Risk Factors.

Case Report

A 75-year-old patient, with history of smoking, hypertension and a recent AML diagnosis, was admitted to after 72-hours history of progressive dyspnea and orthopnea without signs of infection. 8 months ago, before starting AZA's treatment, a transthoracic echocardiogram (TTE) was performed revealing no abnormalities. He had just completed 9 cycles of AZA without complications. Physical examination revealed congestive HF with sinus tachycardia and high NT-proBNP levels. Radiography revealed cardiomegaly. A new TTE demonstrated severe LV dilatation with Ejection Fraction, EF, of 15%. Coronariography showed no abnormalities and cardiac resonance (MRI) ruled out late gadolinium enhancement. Moreover, an abdominal wall fat pad biopsy excluded amyloidosis. Thus, considering this entity as an adverse effect of AZA, the drug was stopped. With a favourable response to medical treatment, our patient was discharged. During follow-up, TTE was repeated showing an overall improvement (EF 35%) and 5 months later, he is clinically stable with mild dyspnea (NYHA-II class). Despite its high mortality and morbidity rate, AZA use is rarely limited by

the occurrence of cardiotoxicity. Perino, et al. [1] described 4 cases of EF worsening, in which both cardiovascular risk factors (CVRF) and medical cardiovascular history were presented prior to AZA treatment, suggesting that the individual cardiovascular condition seemed to play a role in HF severity. On the other hand, Austrian-AZA-Registry described adverse effects in 302 patients: a total of 39 cardiac effects were documented, 23 of them LV dysfunction, 61% of who were presented prior to AZA, without any relationship between its worsening and chemotherapy [2]. In our case, the patient presented 2 CVRF but no prior cardiac history. Basal TTE was completely normal, and myocarditis, ischemia and amyloidosis were ruled out. Therefore, an association between AZA and ventricular dysfunction was biologically plausible (Figure 1).

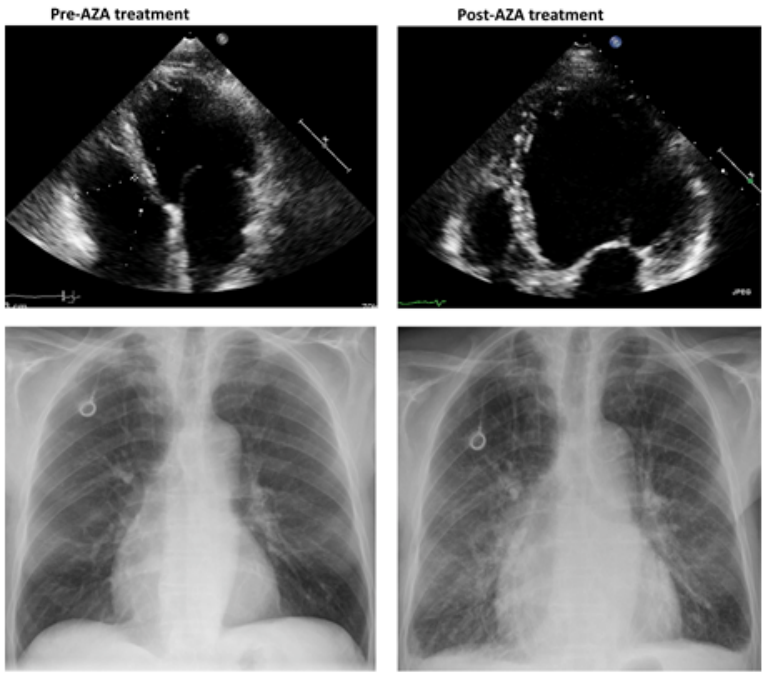

Figure 1: Progressive left ventricle structural course.

In the literature, some data of AZA cardiotoxicity were described but data about the occurrence of HF, especially in patients without cardiovascular history, are needed. Accordingly, Kambara, et al. [3] enrolled fifteen AZA-patients who developed HF, finding a relationship between the numbers of AZA's cycles (> 3, as in our patient) and their mortality. Futher more Kambara, et al. [4] investigated the risk factors for HF in the absence of CVRF but without a specific description of his cardiac involvement. The underlying cardiotoxicity mechanisms are not well known. Some authors suggested a class effect of hypomethylating agents, as far as cardiac toxicity has been well described in patients treated with capecitabine/decitabine. Others assumed the presence of an immune reaction or a dose-dependent toxicity. Given the above, and although further studies are required, potential AZA-side effects on human cardiac cells cannot be questioned.

Our case illustrates the first LV dysfunction due to AZA's treatment report, in a patient with no previous cardiac history. TTE examination was key to discontinue AZA and to initiate treatment for ventricular dysfunction. In such circumstances, cardiac follow-up is mandatory, strengthening the multidisciplinary management in oncology patients.

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