

A clinical challenge of cardiomyopathies: Beyond the heart

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ABSTRACT

Introduction: The relation between the cancer and the heart is diverse. It can be affected all parts of the heart directly or indirectly caused by the systemic manifestation of the cancer or by cancer therapy. Paraneoplastic dermatomyositis and tumor lysis syndrome (TLS) are two examples of systemic manifestations of cancer. Being systemic, the cardiovascular system can be affected. Heart failure and arrhythmias are the main cardiac manifestations.

Case Report: A 68-year-old man with a recent diagnosis of diffuse large B-cell lymphoma waiting to begin chemotherapy, and paraneoplastic dermatomyositis, presented at the emergency department (ED) with palpitations and dyspnea with a week of evolution. At the physical examination, he presented with pulmonary edema and the novo rapid atrial fibrillation. Also, an Nt-pro BNP of 8957 pg/mL, and echocardiography with severe dilated left ventricle, with a severe reduced ejection fraction. Already in the ward, the patient developed a spontaneous TLS. The etiological interpretation was that paraneoplastic dermatomyositis and TLS were the triggers of atrial fibrillation (AF). Then, the combination of them was responsible for development of the dilated cardiomyopathy (tachymyocardiopathy). The chemotherapy regimen was changed to R-CEOP (Rituximab, cyclophosphamide, etoposide, vincristine sulfate, and prednisone).

Conclusion: This clinical case perfectly shows how the world of cardiomyopathies can be challenging and hard to understand all the complexity of the patients.

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INTRODUCTION

The relation between cancer and heart is diverse. We can have cardiac manifestations caused directly by the cancer (cardiac cancer), or in an undirected way, where cardiac achievement is a systemic manifestation of cancer; or cancer therapy-related cardiovascular toxicity. The main manifestations are cardiomyopathy and heart failure, known as cancer therapy-related cardiac dysfunction, which is a consequence of cancer treatment; myocarditis, vascular toxicities, pericardial and valvular heart diseases, cardiac arrhythmias, and corrected QT interval prolongation [1, 2]. Cancer therapy-induced cardiomyopathy emerged from the cardiotoxicity of the cancer treatment, radiation, or drugs. The main drugs involved are anthracyclines and trastuzumab [1, 2].

In 2022, the European Society of Cardiology in collaboration with the European Hematology Association, the European Society for Therapeutic Radiology and Oncology, and the International Cardio-Oncology Society published the first European Society of Cardiology guideline on cardio-oncology. The main goal is to help with prevention, diagnosis, treatment, and management of cardiovascular diseases caused directly or indirectly by cancer [1].

Polymyositis (PM) is an acquired autoimmune disease characterized by an inflammatory infiltrate of the muscle, mainly skeletal muscle. Skin (dermatomyositis), lungs,

joints, heart, and gastrointestinal tract are the extra-muscular systems the most affected [3].

Cardiac involvement is rare, and all cardiac structures can be affected [3, 4]. Clinical manifestations are infrequent and typically remain subclinical, with electrocardiogram alterations (bundle branch block, atrial-ventricular blocks, prolongation of PR-intervals, ventricular premature beats, abnormal Q-waves, non-specific ST-T wave changes) [4]. If symptomatic, normally is time-dependent of the beginning of polymyositis and it impairs the diagnosis. Congestive heart failure with left ventricular diastolic dysfunction, myocardial infarction, and arrhythmias are the most common manifestations [3]. Endomyocardial biopsy is the gold-standard technique for the diagnosis but rarely used (invasiveness). Cardiac magnetic resonance (C-MR) via late gadolinium enhancement is the best non-invasive technique to enable the diagnosis and to evaluate the effects of treatment [3, 4].

Traditional heart medication and corticosteroids in combination with other immunosuppressive drugs (such as azathioprine or methotrexate) are still cornerstones of the treatment, but sometimes cardiac achievement keeps getting worse despite the treatment or because of the treatment [3, 4].

Tumor lysis syndrome (TLS) is an emergency and life-threatening clinical condition in the world of oncology. Cairo and Bishop's laboratory and clinical criteria are the criteria most used for the diagnosis [5, 6]. Hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia are the biochemical criteria [5, 6]; the clinical criteria are acute kidney injury (AKI), seizures, heart rhythm abnormalities, and heart failure [5–7].

The risk is biggest (>5%) in cancers that have a high volume and a high metabolism rate, mainly acute leukemias, Burkitt's or acute lymphoblastic lymphoma [5], after chemotherapy or radiotherapy, but there are other risk factors. Spontaneous TLS has been reported mostly among patients with hematologic malignant diseases [7–9]. The principal cardiac manifestations are heart rhythm abnormalities, being atrial fibrillation the most frequent [10].

The most effective therapy in preventing arrhythmia during TLS remains the primary prevention that consists of recognizing the high-risk patients and giving them prophylactic treatment.

With this clinical case, we want to show how two paraneoplastic syndromes can be achieved the heart and how can be both a diagnosis challenge and a cancer therapy-related challenge.

CASE REPORT

A 68-year-old man was recently diagnosed with a diffuse large B-cell lymphoma (beginning in July 2023), germinal center subgroup, in a context of paraesophageic mass and paraneoplastic dermatomyositis (anti-transcription intermediary factor 1 (anti-TIF1) positive). He was being

awaited to begin the R-CHOP chemotherapy (Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone). For the dermatomyositis was being with prednisone 5 mg. Without other personal or familial relevant antecedents.

He presented to the emergency department (ED) on 27 July of 2023 with palpitations and dyspnea with a week of evolution. At the physical examination was observed tachypnea (30 breaths per minute), irregular tachycardia, with 170 beats per minute (bpm), and bibasal crepitations on pulmonary auscultation. Normotensive and afebrile. With skin lesions of dermatomyositis. The ED workup showed a venous gasometry with 4.3 mmol/L of lactate, electrocardiogram with atrial fibrillation (AF), radiography with vascular pulmonary cephalization, and an Nt pro-BNP of 8957 pg/mL. Kidney and liver function were preserved, without hydroelectrolytic or acid-base changes like thyroid hormone dosing.

First-diagnosed AF associated with acute heart failure, wet and warm perfil, were assumed. The patient began bisoprolol, intravenous diuretics and was hospitalized in the cardiac intermediated care unit.

In the ward, the formal echocardiography showed a severely dilated left ventricle (cor bovis) with a severe reduced ejection fraction and global hypokinemia, associated with moderated functional mitral regurgitation. The right ventricle had normal dimensions, but a mild reduced ejection fraction. With these findings and the atrial fibrillation patient's rhythm maintenance, it was assumed that rhythm control would be difficult for him, so a frequency control strategy was decided. It needed many doses increasing to get a frequency control. At the same time, he started enalapril, eplerenone and dapagliflozin, with good tolerance.

Relative to the etiology of these findings, two differential diagnoses of arrhythmia-induced cardiomyopathy were thought to occur, considering AF as the cause of cardiomyopathy; or in another way, this cardiomyopathy could be cancer associated, which was considered like cardiac manifestations of paraneoplastic dermatomyositis.

The evolution of the patient was torpid, and two days after hospitalization he was diagnosed by TLS. The biochemical alterations are shown in Table 1.

A spontaneous tumor lysis syndrome was assumed. Combining these findings the etiological interpretation was that paraneoplastic dermatomyositis and TLS were the triggers of AF. The patients started the pharmacological treatment, with allopurinol. The fluid therapy was a challenge because at the same time the patient needed intravenous diuretic. Despite the particularities of this patient, he got a good treatment response, as shown in Table 2 (two days after the treatment's beginning).

For the staff cardiovascular comorbidities developed by the patient, he became a patient with absolute contraindication to anthracyclines. For that, the initial planning of beginning R-CHOP was changed to R-CEOP

(Rituximab, cyclophosphamide, etoposide, vincristine sulfate, and prednisone).

The patient was discharged and the cardiac MRI was completed on an outpatient basis. It confirmed the hypothesis of tachycardiomyopathy, because the C-MR showed heart function recuperation, without any enhancement. In the following consultations, the patient continues with stable cardiac function.

Table 1: Biochemical findings

Biochemical parameter	Value	Normal interval
Uric acid	12.4 mg/dL	[2.4–7.2]
Sodium	137 mEq/L	[135.0–145]
Potassium	3.75 mEq/L	[3.5–5.1]
Chloride	91 mEq/L	[96.0–110]
Phosphorus	5.08 mg/dL	[2.4–4.9]
Plasmatic creatinine	0.94 mg/dL	[0.7–1.3]
Plasmatic urea	63 mg/dL	[10.0–50]
Lactate dehydrogenase	254 U/L	[85.0–240]
Aspartate aminotransferase	22 U/L	[4.0–40]
Alanine aminotransferase	16 U/L	[4.0–40]
Gamma-glutamyl transferase	47 U/L	[1.0–75]
Alkaline phosphatase	68 U/L	[40.0–126]

Table 2: Biochemical findings after treatment

Biochemical parameter	Value	Normal interval
Uric acid	3.9 mg/dL	[2.4–7.2]
Phosphorus	4.37 mg/dL	[2.4–4.9]
Lactate dehydrogenase	214 U/L	[85.0–240]

DISCUSSION

As we can see, the differential diagnosis of cardiomyopathy can be a challenge, and a patient can be a world of contributors. On the other hand, it is possible that both diagnoses are not distinct identities, but yes a chain of cause–consequence, having the same basis. Then, in retrospect, our proposal for the explanation of this case is that de acute heart failure was the “visible part” of the iceberg, and cancer is the big hidden part of it. For the next sequences, we can expose our interpretation of this clinical case.

We are facing a patient with a recent diagnosis of a hematologic neoplasm waiting to begin the first line of chemotherapy R-CHOP. He was hospitalized for AF and acute heart failure. In association, he has paraneoplastic dermatomyositis and a TLS. As said above the main

cardiac manifestations of these paraneoplastic syndromes are congestive heart failure, normally with diastolic and systolic dysfunction, reaching both ventricles; and arrhythmias, being the AF the most common [3, 11]. For that, we considered that dermatomyositis and TLS are the triggers for the development of AF.

It is known that AF is the main cause of arrhythmia-induced cardiomyopathy. Its development is more possible the longer the time of AF, and it is not necessary a very fast heart rate: ~110–120 bpm would be enough to develop cardiomyopathy. Normally it can take from a few months to years to develop [11]. This cardiomyopathy is normally a 4-chamber dilated cardiomyopathy without hypertrophy, deterioration of systolic and diastolic function, and presence of at least moderate functional mitral regurgitation [11]. Arrhythmia-induced cardiomyopathy can be divided into two subgroups: pure, when tachycardia is the only mechanism of impaired LV function; and impure, when there are other associated causes of LV dysfunction, being the most common presentation. The cessation of the arrhythmia and normalization of the heart rate results in the recovery of myocardial function, with complete recuperation on the second or third month, after normalization [11].

So, considering that the patient has a recent AF, itself does not explain the cardiomyopathy of this patient. But AF in associating with dermatomyositis and TLS can explain these findings.

The second interesting finding of this clinical case is not just the need to adapt the chemotherapy, but also the patient needs close surveillance with a multidisciplinary team done by hemato-oncologists and cardiologists. For that, this patient began the chemotherapy in the ward of hematology with frequent visits of the cardiology team. He kept stable, and one week after the beginning of chemotherapy went home. After the discharge, the patient continues with frequent hospital visits for management by the multidisciplinary teams.

CONCLUSION

This clinical case perfectly shows how the world of cardiomyopathies can be challenging and hard to understand all the complexity of the patients. Sometimes it is not possible arrive to at the basis of the problem such is the enchainment of the different contributions, as we could see in this clinical case. In the end, to make better the practice of medicine, the concept of a multidisciplinary team is the best for the management of the patients.

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Author Contributions

Dina Fernandes Neto – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability

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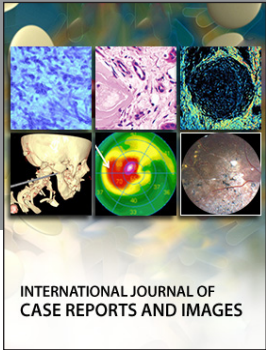
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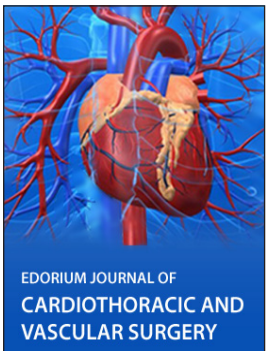


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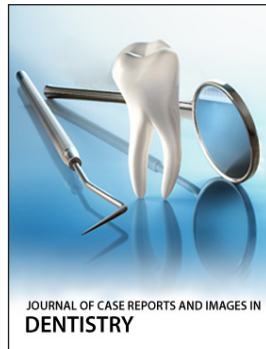
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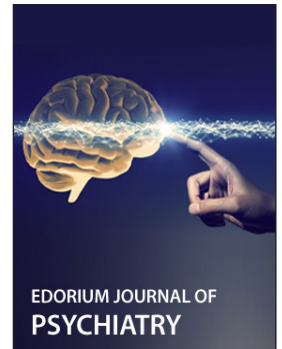
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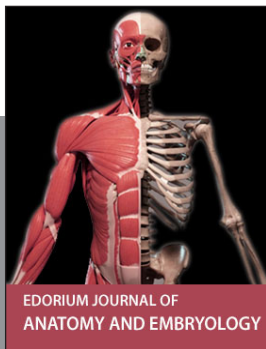
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