

Unwelcomed Guest to the Heart: Secondary Cardiac Localization of Non-Hodgkin's Lymphoma: About a Case and Review of Literature

Soumia Faid^{1a}, Amina Samih^{1b}, Nadif Meryem^{2a}, Nadia Loudiyi^{2b}, Zaimi Achraf^{3b}, Najat Mouine^{3a}, Ilyass Asfalou^{4b}, Aatif Benyass^{a,b}

^aClinical cardiology department, Mohamed V training Military Hospital, Mohammed V University, Rabat - Morocco.

^bNon-invasive Cardiology exploration Department, Mohamed V training Military Hospital, Mohammed V University, Rabat - Morocco.

*Corresponding author: Soumia FAID, Department of cardiology, Mohamed V training Military Hospital, University of Mohammed V. Rabat, Morocco

soumiafaid800[at]gmail.com

Abstract: Cardiac involvement in non-Hodgkin's lymphoma is rare and often seen at a very late stage in the course of the disease. Its frequency is certainly underestimated because 20% of patients who die from lymphoma presented with cardiac involvement at autopsy. We report the case of a 47-year-old male patient, with a history of an ALK + anaplastic large cell lymphoma since 2013, in complete remission, presents with dyspnea, deterioration of his general condition with clinical tumor syndrome signing the relapse of his disease and whose extension assessment revealed a right intra-auricular mass with slight extension to the inferior vena cava. The diagnosis of secondary lymphomatous cardiac localization was retained and the patient received his chemotherapy sessions. The response was spectacular with melting of the tumor syndrome and on echocardiographic control a total disappearance of the mass. The patient has been in complete remission for 3.5 years. The cardiac manifestation is a rare and often unrecognized entity. The prognosis is reserved, an early diagnosis through a rigorous screening is mandatory for an early effective management.

Keywords: Chemotherapy; Heart; Lymphoma; secondary localization

1. Introduction

Cardiac involvement in non-Hodgkin's lymphoma (NHL) is rare and often seen at a very late stage in the course of the disease [1]. It is rarely reported in large series of the literature, although it is found in 20% of postmortem of NHL [1]. This is certainly due to the insidious nature of this condition; while some patients are admitted with cardiac manifestations [2], majority presents non-specific symptoms. In this article, we report a challenging case of an unusual secondary localization during the recurrence of the NHL.

2. Case Report

We report the case of M.B, a 47-year-old man, followed since 2013 for malignant non-Hodgkin's anaplastic cell lymphoma ALK + (antigen Ki-1) initially located in the lymph nodes. The patient has already been treated with CHOP-type chemotherapy (including cyclophosphamide, doxorubicin, vincristine and prednisone) with achieved remission for 5 years.

He was admitted to our cardiology department with complaints of dyspnea with legs swelling, night sweating,

fever and prominent tiredness. He reported a weight loss of 6 kg upon 2 months involuntarily. Clinical examination revealed a tumor syndrome consisting in painless diffuse lymphadenopathy with splenomegaly, no other abnormalities except regular tachycardia at 128 beats / min, of a sinus rhythm on ECG. There were no infectious signs on the chest x-ray.

The laboratory results revealed hyperleukocytosis at 18,000 / mm³, an inflammatory type anemia at 8 g dl⁻¹, and a slight thrombocytopenia with an inflammatory syndrome. LDH was elevated to 4.5 times normal. His HIV status was negative. There was no lymphomatous invasion on bone marrow biopsy.

The injected thoraco-abdominal CT scan showed a mediastinal lymphadenopathy with a right intra-atrial mass, without signs of compression.

Transthoracic echocardiography showed a large heterogeneous polylobed echogenic mass occupying almost the entire right atrium (figure 1), poorly mobile, with discrete extension to the inferior vena cava, measuring 58 * 47mm without any significant hemodynamic obstruction. The valvular structures, the function and dimensions of the right and left ventricles were normal.

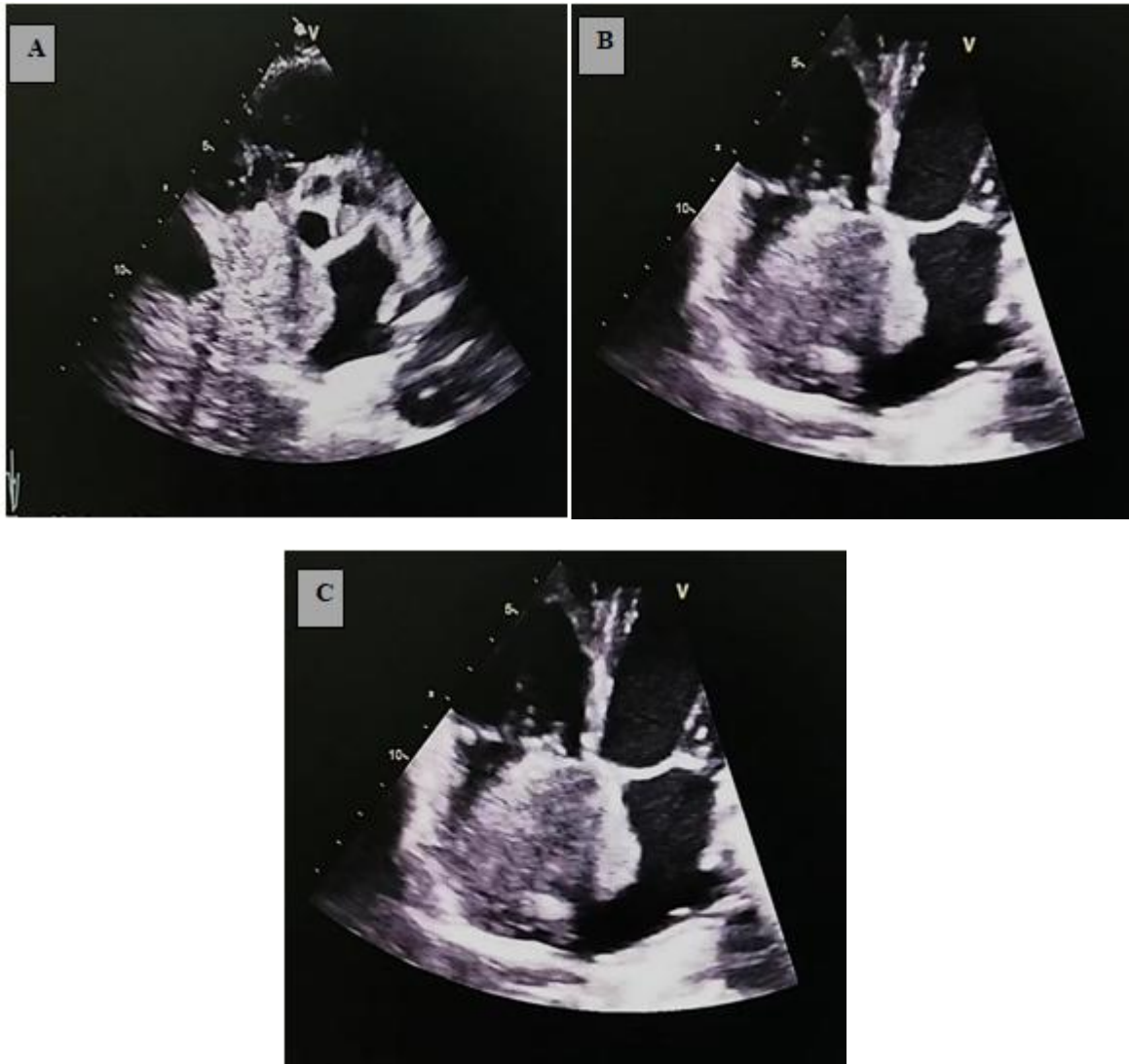


Figure 1: Transthoracic echocardiography views showing in parasternal short axis (A) and in four chambers views (B) the presence of a large echogenic mass in the right atrium measuring 58 * 47 mm, with a discrete extension towards the inferior vena cava visualized on the subcostal view (C) Cardiac MRI confirms and analyzed the cardiac mass showing the isointense signal in T1, hyper-signal in T2 with late phase contrast enhancement (figure 2).



Figure 2: Transthoracic echocardiography in parasternal short axis view showing in the control the disappearance of the mass.

The diagnosis of cardiac secondary localization of the lymphoma was then retained and our patient received chemotherapy with high dose of corticosteroid therapy

associated with a targeted treatment based on Brentuximab Vedotin. The evolution was marked by a striking reduction of lymphadenopathy and splenomegaly from the first two courses. After 8 courses, the TTE control showed a total disappearance of the mass. The patient is currently 3.5 years of complete remission.

3. Discussion

Malignant non-Hodgkin lymphomas (NHL) have a secondary cardiac location in about 20% of cases. Most often, secondary sites of systemic NHL rather than primary cardiac lymphoma [3, 4]. The primary cardiac involvement being exceptional.

Cardiac lymphomatous localization can occur either by hematogenous or lymphatic dissemination or by contiguity from an intrathoracic lymphomatous tumor. [5]

The cardiac involvement of NHL, although rare, is frequently found at autopsy of patients who have died of lymphoma. This is due mainly to its insidious incidence; the

clinical signs are discreet or even absent, explaining the discrepancy between the frequency of anatomical damage (at autopsy) and the scarcity of the clinical manifestation of these locations. Moreover, the revealing symptomatology of the cardiac location is not specific. It is related to the damaged cardiac structure. [6]

All cardiac structures can be affected with a clear predilection for the pericardium and myocardium.[6]Among the clinical manifestations revealing this impairment, the congestive heart failure syndrome in case of myocardial impairment, arrhythmias in case of atrial or septal impairment, signs related to pericardial effusion, in particular tamponade, superior vena cava syndrome or even myocardial infarction. However, it is fundamental to separate primary cardiac NHLs, where cardiac manifestations are prominent and are at first line, from secondary locations where general or functional manifestations of NHL are predominant and the discovery of cardiac involvement is often fortuitous.

Our observation illustrates one clinical revealing mode of a secondary lymphomatous cardiac location. General signs were the major and at first line complaints of the patient (deterioration of the general condition, fatigue with peripheral lymphadenopathy and splenomegaly); with a rhythm disorder as a simple sinus tachycardia. It was through the assessment of the extension of the disease that cardiac involvement was diagnosed.

EKG changes are non-specific but help to draw attention to secondary cardiac damage. It may show either conduction [7] or rhythm disorder as in our patient, or repolarization disorders with microvoltage suggestive of pericardial effusion, or even signs of a myocardial infarction.

Therefore, it is important to regularly check the electrocardiogram in patient with NHL and to perform a cardiac ultrasound, if there is any doubt or abnormalities, and which must be part of the pre-treatment assessment for any NHL, given the potential cardiac chemotoxicity of the used protocols.

Transthoracic cardiac ultrasound (TTE) is the best tool for the diagnosis of cardiac involvement in NHL, it demonstrates which heart tunic is affected. Most often, TTE shows fixed or mobile tumor vegetations, often poly-lobed, present on the valvular or endocavitary endocardium, with predilection for the right cavities rather than the left [8] as pictured in our patient where the mass occupied the right atrium. Pericardial involvement is described as the most frequent, and often results in a more or less abundant pericardial effusion, sometimes responsible for tamponade and often associated with tumor infiltration of this tunica [8]. There are infiltrating forms of the myocardium, rarer, represented by a localized thickening in most cases, giving a shiny appearance to the pathological myocardium and responsible for segmental kinetics alteration.

TTE remains also a simple and non-invasive means of monitoring the response to treatment of these cardiac locations. It allowed as matter fact, in our patient, to follow

the progress under chemotherapy until the disappearance of the tumor mass.

CT scan is performed in the NHL extension assessment and can help in the diagnosis by showing intracardiac or pericardial masses. It has been helpful to establish the etiological diagnosis of a cardiac mass when it is associated with mediastinal lymph node involvement.

However, it is nuclear magnetic resonance imaging (MRI) that represents the best non-invasive radiological examination for the detection of cardiac lymphomatous tumor locations particularly with a sensitivity of over 90% [9]; MRI allows to specify precisely the intra- and extra cardiac limits of the mass [6,10]. We performed a chest CT scan on our patient as part of the extension assessment which showed the intra-cardiac mass, which was better analyzed by MRI.

The lymphomatous nature of cardiac mass is suggested when it is associated with other peripheral or mediastinal lymph node locations. The biopsy of an accessible lymphadenopathy with histological and immunohistochemical study makes it possible to confirm rapidly the diagnosis of lymphoma.

The treatment of cardiac localizations of NHL involves the usual chemotherapy with or without radiotherapy. The response to chemotherapy of cardiac location, at same time as the other nodal location, may constitute an argument confirming its lymphomatous origin [11]. For our patient, we concluded that his anaplastic large cell lymphoma (ALK+) had relapsed, with secondary cardiac localization given the clinical context with his history and the good response to chemotherapy.

The prognosis of lymphomatous secondary cardiac location remains very reserved despite some prolonged remissions reported through literature [11-13]. In fact, the majority of observations report the early death of patients; delay in diagnosis is surely the main cause. In addition, the results of therapeutic protocols used are less encouraging, compared to those of other systemic forms of lymphomas [8].

Our patient was lucky to be taken care of on time since he had history of NHL; the diagnosis of lymphomatous secondary cardiac localization was retained and without any delay, the chemotherapy was started and we obtained a complete remission (clinically and echocardiographically) with an uneventful follow-up of 3.5 years.

4. Conclusion

Cardiac lymphoma is a rare and often unrecognized entity due to its polymorphic clinical expression. Echocardiography and MRI are the best diagnostic methods for these locations. Histological examination, although difficult to obtain, confirms the diagnosis. These locations are getting more frequent given the increase of cases of acquired immunosuppression; their prognosis is often reserved in short term due to late diagnosis with an incomplete response to chemotherapy.

References

- [1] Mikdame M, Ennibi K, Bahrouch L, Benyass A, Dreyfus F, Toloune F. Cardiac locations of non-Hodgkin's lymphoma: about 4 cases. *Journal of Internal Medicine*. 2003; 24 (7): 459-63. Google Scholar
- [2] Jonavicius K, Salcius K, Meskauskas R, Valeviciene N, Tarutis V, Sirvydis V. Primary cardiac lymphoma: two cases and a review of literature. *J CardiothoracSurg* 2015; 10: 138
- [3] Lam KY, Dickens P, Lam Chan AC. Tumors of the heart, A 20-year, experience with review of 12485 consecutive autopsies. *Arch Pathol Lab Med* 1993;117:1027-31.
- [4] Aboulafia DM, Bush R, Picozzi VJ. Cardiac tamponade due to primary pericardial lymphoma in patients with Aids. *Chest* 1994;106: 1295-9.
- [5] Mc Donnell PJ, Mann RB, Bulkley BH. Involvement of the heart by malignant lymphoma: a clinicopathologic study. *Cancer* 1982;49: 944-51
- [6] Delmas-Marsalet B, Molinié V, Jary L, Teillet-Thiebault F, Estagnasié P, Barge J, et al. Cardiac localization of non-Hodgkin lymphoma: two case reports and review of the literature. *Nouv Rev FrHematol* 1995; 37:223-30.
- [7] Roubille F, Massin F, Cayla G, Gahide G, Gervasoni R, Macia JC, Serre I, Pasquie JL, Sportouch C, Leclercq F. Intra-cardiac lymphoma with right heart failure: a therapeutic emergency in two patients. *Arch Mal Coeur Vaiss*. 2007; 100(12):1025-9. PubMed | Google Scholar
- [8] Msaad S, Yangui I, Ketata W, Ayadi H, et al. Manifestations thoraciques revelatrices de lymphomes : a propos de 17 cas. *La tunisiemedicale*. 2008; 86(2):105-13. PubMed | Google Scholar
- [9] Ceresoli GL, Ferreri AJ, Bucci E, Ripa C, Ponzoni M, Villa E. Primarycardiaclymphoma in immunocompetent patients: diagnostic and therapeutic management. *Cancer* 1997;80:1497-506.
- [10] Daus H, Bay W, Harig S, Schneider G, Feiden W, Schieffer H. Primary lymphoma of the heart: report of a case with histological diagnosis of the transvenously biopsied intracardiac tumor. *Ann Hematol* 1998;77: 131-9.
- [11] Ghannem M, Godard S, Trylesinski A, Duhamel P, Philippe J, Sabbah L, et al. Lymphome malin non-Hodgkinien à localisation cardiaque : à propos d'une observation. *Ann Cardiol Angéiol* 1995;44: 345-8
- [12] Cracowski L, Tremel F, Nicolini F, Bost F, Mallion JM. Localisation myocardique chimio-sensible observée au cours d'un lymphome malin non-Hodgkinien. *Arch Maladies CœurVaiss* 1997; 11:1527-31.
- [13] Agarwala B, Rubin CM. Intracardiac lymphoma in a child: successful treatment with chemotherapy alone. *PediatrCardiol*. 2000; 21(4):401-2. Google Scholar.

Author Profiles



Soumia Faid: Resident of Cardiology, assigned to Clinical cardiology department at Mohamed V training Military Hospital, Rabat - Morocco.

Amina Samih: Resident of Cardiology, assigned to Non-invasive cardiology exploration department, Mohamed V training Military Hospital, Rabat - Morocco.

Nadif Meriem: Resident of Cardiology, assigned to Clinical cardiology department at Mohamed V training Military Hospital, Rabat - Morocco.

Nadia Loudiyi: MD, Cardiologist assigned to Non-invasive cardiology exploration department, Mohamed V training Military Hospital, Rabat - Morocco.

Zaimi Achraf: MD, Cardiologist assigned to Non-invasive cardiology exploration department, Mohamed V training Military Hospital, Rabat - Morocco.

Najat Mouine: PhD, Head of Clinical cardiology department at Mohamed V training Military Hospital, Rabat - Morocco.

Ilyass Asfalou: PhD, Head of Non-Invasive Exploration Department, Mohamed V training Military Hospital, Rabat - Morocco.

Aatif Benyass: PhD, Head of the Cardiology center of Mohamed V training Military Hospital, Rabat - Morocco.