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Case Report

Primary Cardiac Sarcoma of the Left Atrium, A Case Report and Literature Review

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Abstract: Primary malignant cardiac tumours are extremely rare. They count for a quarter of all possible cardiac tumors, and are mostly sarcomas. For a long time, their diagnosis was made post mortem, and they were only reported through autopsy series. Since then, diagnostic and therapeutic advances have been made, making clinical diagnosis of this entity more accessible ante mortem. Nevertheless, due to their rarity, cardiac sarcomas suffer from a lack of therapeutic guidelines. Their treatment is modelled on that of sarcomas developed in other organs of the body. We report an interesting case of a 74-year-old female patient operated on for an infiltrating sarcomatous tumour of the left atrium revealed by dyspnoea associated with cardiac palpitations. Thoracic angioscan and transthoracic echocardiography led to the diagnosis of a cardiac tumour, and the thoracic-abdominal-pelvic Computed Tomography (CT) scan did not reveal any other extracardiac lesions except for a minimal non-neoplastic bilateral pleural effusion. The patient underwent an incomplete surgical procedure with R2 resection followed by adjuvant chemotherapy with doxorubicin monotherapy. The evolution under this treatment was marked by a locoregional progression of the disease with further progression in the atria, mediastinum and dorsal spine after 4 courses. A second line of chemotherapy with Dacarbazine monotherapy was initiated, but the patient died shortly after receiving two courses of the new treatment.

Keywords: Sarcoma, cardiac tumour, (CT) scan.

INTRODUCTION

Soft tissue sarcomas are uncommon cancers of mesenchymal origin with an incidence of less than 2% of all adult cancers [1]. They can arise anatomically in any part of the body, from head to toe, but primary cardiac sarcoma is an extremely rare and exceptional entity [2]. Historically, the overall incidence of primary cardiac tumours has been estimated at less than 0.03% in autopsy series. The majority of these tumours (80%) are benign, represented by cardiac myxoma. Malignant tumours of the heart represent only 20% and form a very heterogeneous group with sarcoma as the leading one [3, 4]. Nowadays, advances in diagnostic imaging allow early and accurate diagnosis of cardiac tumours antemortem. However, their diagnosis is difficult due to a non-specific clinical picture, mimicking other medical cardiac diseases.

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Surgery is the standard treatment, although it is delicate and requires improved equipment, an experienced hand and a centre specialising in cardiac surgery. Furthermore, in the absence of dedicated treatment guidelines, the place of adjuvant therapy for operated localised tumours remains to be defined as for other soft tissue sarcomas [5]. Thus, cardiac sarcomas are tumours with an appalling prognosis characterised by frequent recurrence and low short-term survival rates due to the aggressive biological behaviour known of sarcomas [6].

Considering the rarity of this disease entity, each case encountered in clinical practice is an interesting case. In this article, we describe the experience of the medical oncology department of the Regional Hospital Centre of Orleans (CHRO) in the management of a case of primary sarcoma of the left atrium diagnosed in a 74 year old woman patient, resected and then treated with adjuvant chemotherapy under which she progressed shortly thereafter and subsequently died after a short survival of 7 months after diagnosis. We also made a brief review of the literature concerning the diagnostic and therapeutic approach of primary malignant cardiac tumours.

CASE PRESENTATION

The patient was 74 years old, with no known major pathological history. She presented with a symptomatology that evolved over two months, marked by the appearance of respiratory discomfort in an intermittent mode, and then repeated and progressively worsened. After two months, there was a sensation of heart palpitations and malaise without any notion of loss of consciousness. Given the recurrent nature of this symptomatology, the patient consulted the emergencies department on the occasion of a critical episode. On investigation, the biological check-up showed an increase in D-dimers to 5 times normal. The thoracic Angioscan showed a large hypodense left intra-atrial formation with a 54 mm long axis in a dilated left atrium, without signs suggestive of pulmonary embolism (Images 1).

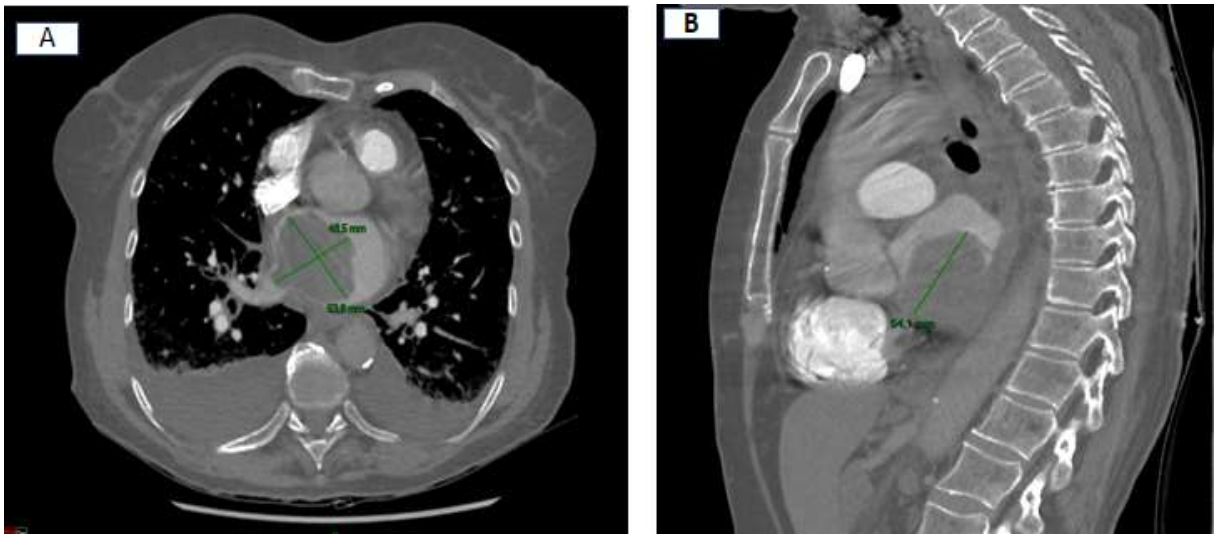

Image 1: Chest CT scan, bone window: Axial (A) and sagittal (B) sections: Large left intra-atrial tumour mass with 54 mm long axis within a dilated atrium. Note a minimal bilateral pleural effusion

The morphological appearance and lack of enhancement suggested a thrombotic rather than tissue origin. In addition, there were multiple signs of vascular overload of cardiac origin. The echocardiogram (ECG) performed was in regular sinus rhythm at 76 beats per minute, normal PR interval, fine QRS complexes with normal heart axis without repolarisation disorders. Transthoracic echocardiography showed a floating mass in the left atrium with a mean gradient of 7mmhg over the mitral valve. The right cavities were not dilated and the inferior vena cava was thin and compliant. The patient was then transferred to the cardiac intensive care unit for further management. A resection of the cardiac mass was then performed. The resection was incomplete with a macroscopic tumour residue, classified as R2, due to wall adhesion and mitral valve invasion.

On the histological examination, it was a 6 cm long tumour whose morphological and immunohistochemical characteristics corresponded to a spindle cell sarcoma, grade 3 according to the histopronostic classification of the National

Federation of Cancer Centres (FNCLCC). The extension work-up by brain CT scan was normal. The thoracic-abdominal-pelvic (TAP) CT scan did not detect any other secondary lesions elsewhere. The postoperative course was simple. The patient's general condition was preserved with a performance status (PS) of 1, and her left ventricular ejection fraction (LVEF) was 72%. The medical oncology consultation meeting decided to start the patient on adjuvant chemotherapy with Doxorubicin monotherapy, 60mg/m2 in one course every 3 weeks. The TAP CT scan performed after the 4th course of chemotherapy revealed a significant locoregional progression of the disease with the appearance of right and left intra- and retro-atrial tumour masses (Image 2 and Image 3), a large right mediastinal process compressing the large vessels (image), moderate and stable bilateral pleural effusion and lytic bony lesions of the vertebral bodies of T8 and T9 (Image 4), all this with a preserved general condition. A second-line chemotherapy with Dacarbazine was initiated, but the evolution was rapidly fatal after only two courses, id est (i.e) an overall survival of 7 months since diagnosis.

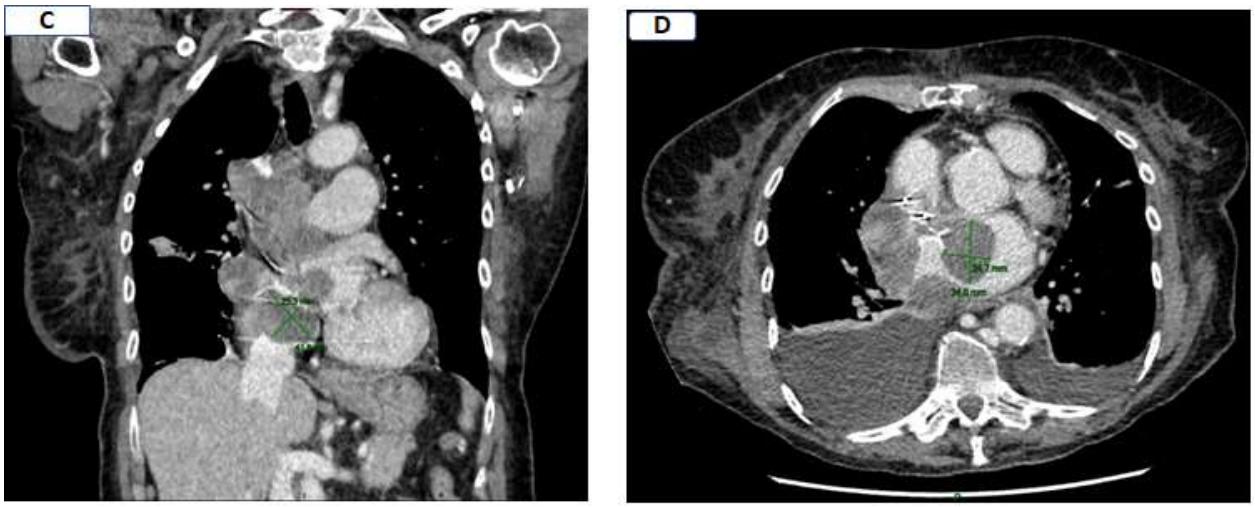

Image 2: Chest CT scan, mediastinal window: coronal(C) and axial(D) sections: right and left intra-atrial tumour lesions, with quasi-stable appearance of bilateral pleural effusion.

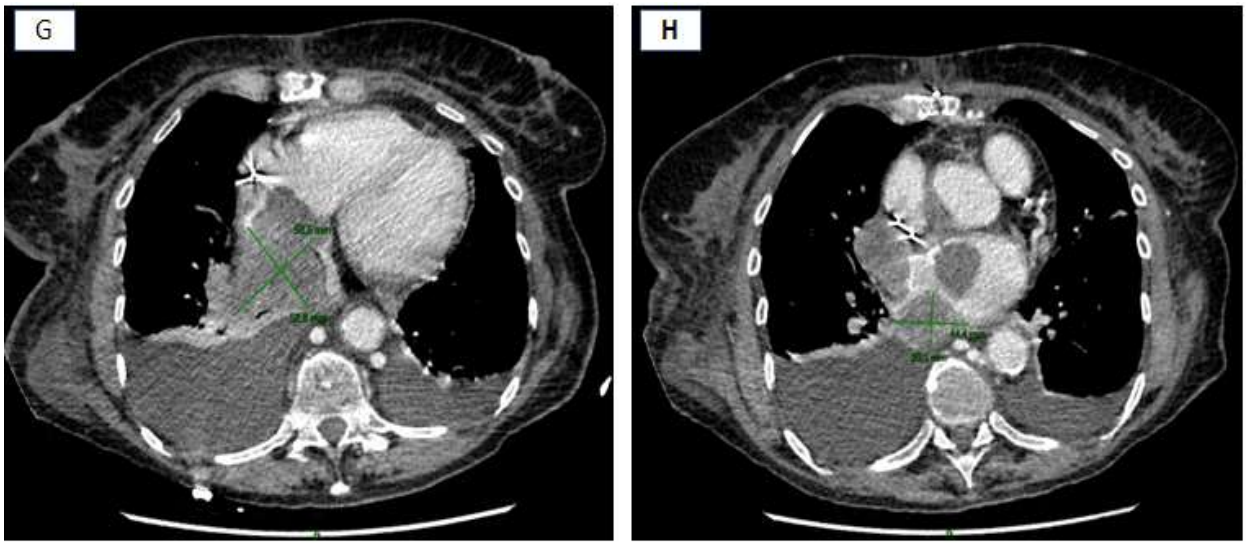

Image 3: Chest CT scan, mediastinal window: axial sections (L and H): right and left retro atrial lesions with quasi-stable appearance of bilateral pleural effusion

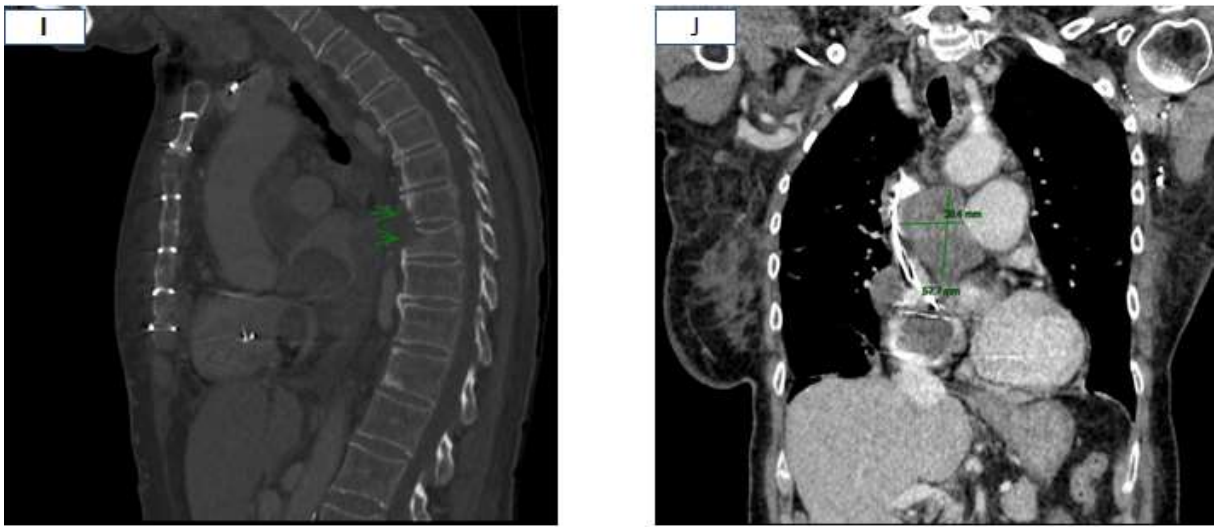

Image 4: Thoracic CT scan, bone window sagittal section (I), mediastinal window coronal section (J): lytic lesions of the vertebral bodies of T8 and T9 and a large right mediastinal tissue mass of 58 x 39 mm in contact with the large mediastinal vessels

DISCUSSION

Primary malignant tumours of the heart are so rare that very few medical oncologists can claim to have treated one in their entire career. Historically, their diagnosis has been exclusively post-mortem and reported by autopsy series. Analysing data from 22 large autopsy series published from 1934 to 1993, Reynen K. found 157 cardiac tumours in 731,309 autopsies performed (0.021%), i.e. an incidence of 2 cardiac tumours per ten thousand autopsies. Sarcoma was the most common histology [7]. It was not until 1934 that the first diagnosis of a cardiac tumour was made antemortem on the basis of clinical and electrocardiographic findings. Clarence Crafoord, a Swedish cardiovascular surgeon, performed the first successful excision of a benign heart tumour in 1954, a left atrial myxoma [8]. Since then, for those centres able to perform it, cardiac tumour surgery has become a routine operation and has improved the survival of heart cancer patients. Currently, enormous progress has been made in the field of diagnostic imaging. It is therefore possible to diagnose heart tumours at an early stage and thus to refer patients to appropriate centres for treatment, with a consequent improvement in the prognosis of treated patients. It is now understandable that the prevalence of primary malignant cardiac tumours is higher than historically reported in old autopsy series. In a 10-year retrospective monocentric series, Patel J *et al*., found that out of 94 patients treated for cardiac tumours from 1990 to 2008, the prevalence of primary malignant cardiac tumours was 28.7%, of which 77.7% were sarcomas [9]**.** More recently, a meta-analysis reviewing the literature on the epidemiology and therapeutic aspects of cardiac tumours (CT) has been published. In this meta-analysis, Rahouma M *et al*., reviewed 74 published articles dealing with primary or secondary cardiac tumours. There were a total of 8,849 cases of cardiac tumours of which 8,346 were primary cardiac tumours (PCT) and 355 were secondary malignant cardiac tumours (SMCT). Although benign PCTs represent the most common form of CT (84.6%), the prevalence of primary malignant cardiac tumours was 10%. This confirms the rarity of these entities, although their prevalence is much higher compared to historical autopsy series [10].

Primary cardiac tumours are clinically difficult to diagnose. They are very rare with non-specific symptoms mimicking those of many other cardiac pathological conditions. The extent of their clinical manifestations depends mainly on their location in the heart and their size, resulting in similar clinical pictures for both primary and secondary benign and malignant tumours [11, 12]. In our patient, the tumour was located in the left atrium. The presenting sign was intermittent and progressively worsening dyspnoea and heart palpitations. This is in agreement with the literature which reports that dyspnoea is the main symptom in the context of a cardiac tumour [10]. It is important to note that cardiac tumours have a wide variety of clinical manifestations depending on their location in the heart, and can give rise to variable clinical pictures of a cardiac nature such as cardiac rhythm disorders (arrhythmias or palpitations), or symptoms of cardiac insufficiency (shortness of breath, fainting, oedema), general constitutional signs (fever, weight loss, fatigue) or paraneoplastic signs, or pulmonary or systemic embolic accidents that can lead to sudden death [3, 13]. As such, a cardiac tumour should always be considered as one

of the diagnostic hypotheses in the presence of acute cardiac symptoms [10, 14]. However, incidental finding of cardiac tumours is also possible in patients being investigated for other medical conditions, such as breathing difficulties [5, 14].

The age of onset varies. But young adults are the most affected without gender preference. Our patient was 74 years old. In the meta-analysis by Rahouma M., et al. the average age was 42.9 years and 55% of the patients were women [10]. There is no preferred site, but the left ear is the most affected [12, 13]. In our 74-year-old patient, the tumour was located in the left atrium.

The imaging work-up is essential for the positive diagnosis of a cardiac tumour. However, the histological nature of the tumour is known after anatomo pathological examination of the surgical specimen. In our patient, the diagnosis of a tumour was made with a thoracic angioscan, transthoracic ultrasound and an assessment of the impact on the electrical activity of the heart with an electrocardiogram. In general, the etiological approach to a mass suspected of being a cardiac tumour is based on transthoracic echocardiography (TTE). This allows the size of the tumour, its location, mobility and haemodynamic consequences to be assessed [15]. Once the diagnosis of a cardiac mass has been confirmed, magnetic resonance imaging (MRI) will improve the results of TTE by specifying the degree of infiltration of the cardiac tissues by the tumour as well as the extension to neighbouring structures, and will also make it possible to predict the tumour grade [4]. As with other solid tumours, CT scan is essential for the diagnosis of a cardiac tumour to provide useful information, such as a better definition of the secondary or primary appearance of the lesion, its extension to surrounding structures and for the investigation of extracardiac locations, which can be useful for planning tumour resection and further treatment [3]. Positron emission tomography with 18-Fluorodeoxyglucose scanner (18F-FDG PET scan) offers an accurate assessment of the metabolic activity of tumours. The extent of FDG uptake by tumours improves differentiation between benign and malignant tumours. It could also be useful in assessing responses to cancer treatment. In a study of 24 patients with cardiac tumours assessed by 18FDG PET, Nensa F. et al concluded that in this indication, 18 FDG PET scan had a sensitivity of 100% and a specificity of 92% [16]. All of these elements should allow a diagnosis of the nature of the tumour to be evoked. Nevertheless, obtaining a histopathological specimen is the essential step in histological diagnosis. It has been established that resection is necessary to avoid major complications but also to establish a histological diagnosis.

In our patient, the cardiac mass was resected, but not completely because of adhesion to the walls and invasion of the mitral valve. The histological examination of the surgical specimen showed morphological and immunohistochemical features consistent with a spindle cell sarcoma, grade 3 according to the FNLCC histopronostic classification. It is established that resection is necessary to avoid major complications but also to establish a histological diagnosis. In some series, complete resection of cardiac tumours is a good prognostic factor associated with better long-term survival. In the study by Simpson et al, the survival of operated patients was 17 months for complete resection versus 6 months for incomplete resection [17]. Our patient's survival was 7 months. In their series, Li S. et al showed that when it is possible, the minimally invasive robot-assisted or mini-thoracotomy approach is to be preferred in the case of surgery for malignant cardiac tumours because it is associated with few post-operative complications compared with conventional surgery [18]. In the meta-analysis by Rahouma M. et al, the surgical procedure could also consist of heart transplantation, particularly for complex cardiac tumours that are not well suited to conventional surgery [10].

In the medical oncology consultation meeting, our patient was considered to be at high risk of progression due to the high tumour grade and incomplete resection. Adjuvant chemotherapy with Doxorubicin monotherapy was preferred to adjuvant radiotherapy. Nevertheless, the benefit of adjuvant therapy (chemotherapy or radiotherapy) in soft tissue sarcoma is not clearly established, but it remains a treatment option, particularly for patients with incomplete resection or high risk of recurrence [1].

The evolution under treatment was marked by an early progression of the tumour disease in the atria, mediastinum and the dorsal spine (Images 1, 2, 3 et 4), which appeared after 4 courses of chemotherapy with Doxorubicin. Given the context of conservation of the general state with moderate asthenia (PS 2), a second line treatment with Dacarbazine was initiated. Indeed, after the failure of Doxorubicin, there seems to be no standard treatment protocol for soft tissue Sarcoma. The choice of dacarbazine for our patient was motivated by the results of a Spanish phase II study which evaluated Dacarbazine +/- Gemcitabine [19]. With this study, although the doublet provided more

benefit in terms of progression-free survival (4.2 months vs. 2 months, p=0.005) and overall survival (16.8 months vs. 8.2 months, p=0.014), the medical oncology consultation meeting, taking into account the patient's clinical status (PS 2), preferred a light regimen with Dacarbazine alone. At this stage, other regimens were also possible, such as Gemcitabine +/- Docetaxel or Trabectidine, which were evaluated in phase II studies and still provided modest benefits in terms of overall survival or progression-free survival [20, 21]. Our patient died shortly afterwards, having received only two courses of the new treatment for an overall survival of 7 months after diagnosis.

CONCLUSION

Cardiac sarcomas are very rare cardiac disorders in oncology. Obviously, cardio respiratory symptoms such as dyspnoea and cardiac arrhythmias are the main warning signs, with the severity depending on the size of the tumour and its location in the heart. Imaging (TTE, MRI) is essential to make the diagnosis of a cardiac tumour. A CT scan or an 18-FDG PET scan is useful for the search for secondary extracardiac locations. Histological confirmation is done on the resection specimen. Surgery is the mainstay of treatment for cardiac sarcoma. Adjuvant therapy (radiotherapy or chemotherapy) may be used by analogy with the treatment of soft tissue sarcomas in other locations, particularly if high grade or incomplete resection is involved. It is known that cardiac sarcomas, even resected, have a poor prognosis with frequent recurrence and poor survival.

Conflicts of interest: None declared

Patient's Consent

We certify that we have obtained the patient's consent when she was still alive. By means of a consent form, the patient has given her agreement to have her clinical information reported in a journal. We undertook to guarantee her anonymity.

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