
Cardiac Tumors: Classification and Epidemiology

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Introduction

The precise prevalence of primary cardiac tumors in the general population is still unknown and is based on old postmortem studies.

In a study of 12,485 autopsies carried out in the time interval 1972–1991, Lam et al. reported a rate of 0.056% for primary (56 cases per 100,000 autopsies), and of 1.23% for secondary tumors (123 cases per 10,000 autopsies) [1]. However, epidemiological data are strongly influenced by when and where the data have been collected and do not necessarily reflect the real incidence in the population.

For instance, at the Mayo Clinic the autopsy prevalence of primary cardiac tumors was 0.05% in the time interval 1915–1930; when, with the

advent of cardiac surgery, it became a referral center for diagnostic and therapeutic purposes, the autopsy prevalence had a threefold increase up to 0.17%, in the time interval 1954–1970 [2].

As far as secondary cardiac tumors, an investigation performed at our University in the time interval 1967–1976 revealed that among 7,460 autopsies the cause of death was malignancies in 1,181 cases (15.33%) [3], in 74 of which cardiac metastases occurred. This accounted for 1% of all autopsies and 6% of those with malignancies.

Anyway, it is generally agreed that autopsy prevalence of primary cardiac tumors is 1 out of 2,000 and that of secondary cardiac tumors is 1 out of 100 autopsies, with a secondary/primary cardiac tumors ratio of 20:1.

Classification of Cardiac Tumors

Although a classification of tumors can be based upon cellular organization (proliferative reaction, hamartoma, cyst, and true neoplasm, either benign or malignant) or tumor histotype (mesenchymal, epithelial, mesothelial), it is easier to follow the classic distinction between benign and malignant, differentiating cardiac and pericardial tumors [4].

The World Health Organization recently convened a group of pathologists to put forward a new classification of primary cardiac tumors (Table 2.1).

Although some neoplasms or tumor-like lesions have been ignored (cysts of pericardium,

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Table 2.1 Histological classification of tumors of the heart, World Health Organization (from Travis et al. [4])

Benign tumors and tumor-like lesions	
Rhabdomyoma	8,900/0
Histiocytoid cardiomyopathy (Purkinje cell tumor)	
Hamartoma of mature cardiac myocytes	
Adult cellular rhabdomyoma	8,904/0
Cardiac myxoma	8,840/0
Papillary fibroelastoma	
Hemangioma	9,120/0
Cardiac fibroma	8,810/0
Inflammatory myofibroblastic tumor	8,825/1
Lipoma	8,850/0
Cystic tumor of the atrioventricular node	
Malignant tumors	
Angiosarcoma	9,120/3
Epithelioid hemangioendothelioma	9,133/3
Malignant pleomorphic fibrous histiocytoma (MFH)/undifferentiated pleomorphic sarcoma	8,830/3
Fibrosarcoma and myxoid fibrosarcoma	8,840/3
Rhabdomyosarcoma	8,900/3
Leiomyosarcoma	8,890/3
Synovial sarcoma	9,040/3
Liposarcoma	8,854/3
Cardiac lymphoma	
Metastatic tumors	
Pericardial tumors	
Solitary fibrous tumor	8,815/1
Malignant mesothelioma	9,050/3
Germ cell tumors	
Metastatic pericardial tumors	

blood cysts), this classification has the merit of unifying the terminology. Since cardiac tumors have been variously named, we will add the synonym for each histotype. According to this last classification, cardiac tumors are grouped into three categories, i.e., benign tumors and tumor-like lesions; malignant tumors; and pericardial tumors.

According to the morphology code of the International Classification of Diseases for Oncology (ICD-0) [5] and the Systematized Nomenclature of Medicine (<http://snomed.org>) the biological behavior is coded /0 for benign tumors, /3 for malignant tumors, and /1 for “borderline” or uncertain behavior.

Malignant Cardiac Tumors, Grading and Staging

Given their low frequency, there is no grading system for malignant cardiac tumors and we have to refer to the criteria used for soft tissue neoplasms [6]. The main parameters in non-cardiac soft tissue tumors are the mitotic index and the extent of tumor necrosis [7, 8].

Three grades of malignancy are usually recognized: G1, low grade; G2, intermediate grade; G3, high grade.

The FNCLCC (Fédération Nationale des Centre de Lutte Contre le Cancer) system is based on a score obtained by evaluating three features: tumor differentiation, mitotic rate, and amount of tumor necrosis. A score is attributed independently to each of the three parameters and the final histological grade is the sum of the three attributed scores (Table 2.2) [8].

As a general rule, grading should be used only for untreated primary soft tissue sarcomas and should be performed on representative material (for instance, tissue obtained through endomyocardial biopsy cannot be used for grading purposes).

Concerning the epidemiology and prevalence of various tumor histotypes, the data are also not uniform in the literature. Being a rare disease, the published numbers of primary cardiac tumors frequently reflect a referral bias. This is for instance the case of the data reported by the series of the Armed Force Institute of Pathology (AFIP) in Washington [9], which remains the most quoted histopathology publication on cardiac tumors, based upon 386 cases of primary cardiac tumors. The rates of 35% for primary sarcomas and of only 29% for myxomas, clearly reflect the referral bias of data derived from pathology tertiary centers, where only the most difficult cases are sent for expert opinion.

The difficulty in obtaining real epidemiological data on primary cardiac tumors is emphasized by the nonreliability of both autopsy and surgical pathology series, since in the former there is the selection bias of dead patients during hospitalization and in the latter that of indication to surgery

Table 2.2 Parameters of the grading system for sarcomas of the Fédération Nationale des Centres de Lutte contre le Cancer (FNCLCC)

Tumor differentiation	
Score 1	Sarcomas closely resembling normal adult mesenchymal tissue (e.g., low-grade leiomyosarcoma)
Score 2	Sarcomas for which histological typing is certain (e.g., myxoid fibrosarcoma)
Score 3	Undifferentiated sarcoma, angiosarcoma
Mitotic count	
Score 1	0–9 mitoses per 10 HPF ^a
Score 2	10–19 mitoses per 10 HPF ^a
Score 3	≥20 mitoses per 10 HPF ^a
Tumor necrosis	
Score 0	No necrosis
Score 1	<50% tumor necrosis
Score 2	≥50% tumor necrosis
<i>Histological grade</i>	
Grade 1 (G1)	Total score 2, 3
Grade 2 (G2)	Total score 4, 5
Grade 3 (G3)	Total score 6, 7, 8

Modified from Trojani et al. [8]

^aA high-power field (HPF) measures 0.1734 mm²

(see for instance rhabdomyoma) or tumor resectability (see for instance primary malignant cardiac tumors with infiltration and metastases).

We herein refer to the clinicopathologic experience of the University of Padua, Italy in the time interval 1970–2010.

Epidemiology of Primary Cardiac Tumors 1970–2010 at the University of Padua

In the time interval 1970–2010, 267 primary cardiac and pericardial tumors have been studied, including 239 bioptic (89.5%) and 28 autoptic (10.5%) (Fig. 2.1). This is mostly a biopsy-based experience, thus emphasizing that nowadays cardiac tumors are uncommonly fatal, with the exception of the rare primary malignant forms.

Among the consecutive 239 bioptic primary cardiac tumors (135 female, age ranging 1 day–85 years, mean 48 ± 22 years, median 53), only 26 (10.5%) were malignant and 213 (89.5%) benign (Fig. 2.2).

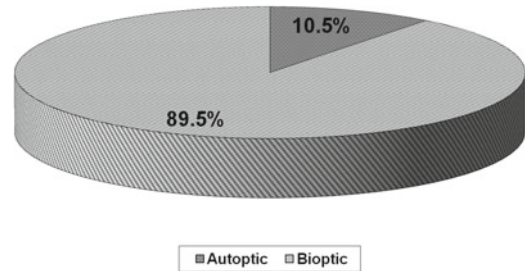


Fig. 2.1 Primary cardiac and pericardial tumors, University of Padua Medical School (1970–2010): 267 cases, 239 (89.5%) bioptic and 28 (10.5%) autoptic

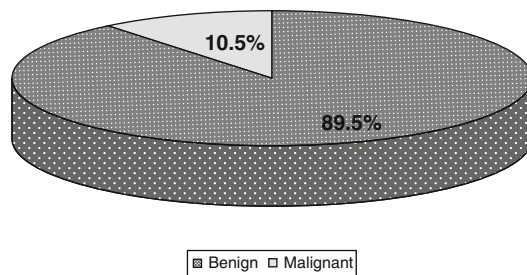


Fig. 2.2 Primary biptic cardiac and pericardial tumors, University of Padua Medical School (1970–2010): 239 cases, 213 (89.5%) benign and 26 (10.5%) malignant

In eight cases (3.5%) the diagnosis was achieved through preoperative biopsy: endomyocardial in four cases (right atrium angiosarcoma in three and fibrosarcoma in one, respectively) and thoracotomic in four cases (two right ventricular fibromas, one left ventricular hemangioma, and one left atrial malignant schwannoma). Cardiac transplantation was performed in three cases (1.25%, all with cardiac fibroma).

Primary Malignant Biopptic Cardiac Tumors

The population consists of 26 patients, 15 male and 11 female, age ranging 21–80 years, mean 50 ± 13 . They died within 6 months from clinical onset, with the exception of three cases, i.e., a 21-year-old woman with left atrial leiomyosarcoma, who was still alive 96 months after surgical resection and adjuvant chemotherapy [10]; and two cases operated of right atrial angiosarcoma who were alive at a follow-up of 12 and 18 months, respectively. The most prevalent histotype was leiomyosarcoma and angiosarcoma (19% each) and undifferentiated sarcoma

(15.5%). The various tumor histotypes are illustrated in Fig. 2.3.

Tumor location was the left atrium in eight (three undifferentiated sarcomas, two leiomyosarcomas, one fibrosarcoma, one malignant fibrous histiocytoma, and one malignant schwannoma); the right atrium in eight (five angiosarcomas, one B cell lymphoma, one fibrosarcoma, and one malignant fibrous histiocytoma), the right ventricle in two (one leiomyosarcoma, one malignant fibrous histiocytoma), the pulmonary artery in two (leiomyosarcoma), and the pericardium in four (malignant mesothelioma in three and undifferentiated sarcoma in one); finally, in two lymphomas cardiac involvement was diffuse without any chamber predilection.

Primary Benign Biopptic Cardiac Tumors

A consecutive series of 213 biopptic benign cardiac tumors have been studied in the same years, mean 48.1 ± 22.5 , median 53 years. Figure 2.4 illustrates the various histotypes.

Cardiac myxoma is the most frequent primary cardiac tumor. A consecutive series of 141 surgi-

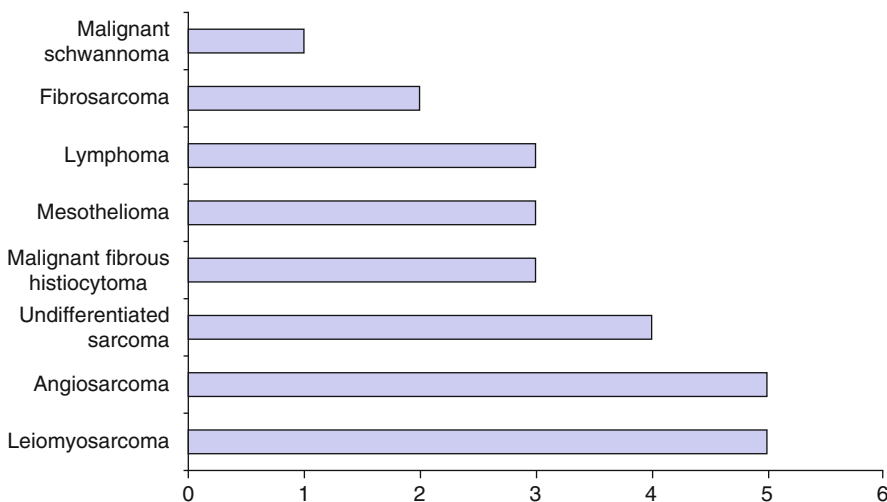


Fig. 2.3 Primary biopptic malignant cardiac and pericardial tumors, University of Padua Medical School (1970–2010): 26 cases. Prevalence of various tumor histotypes

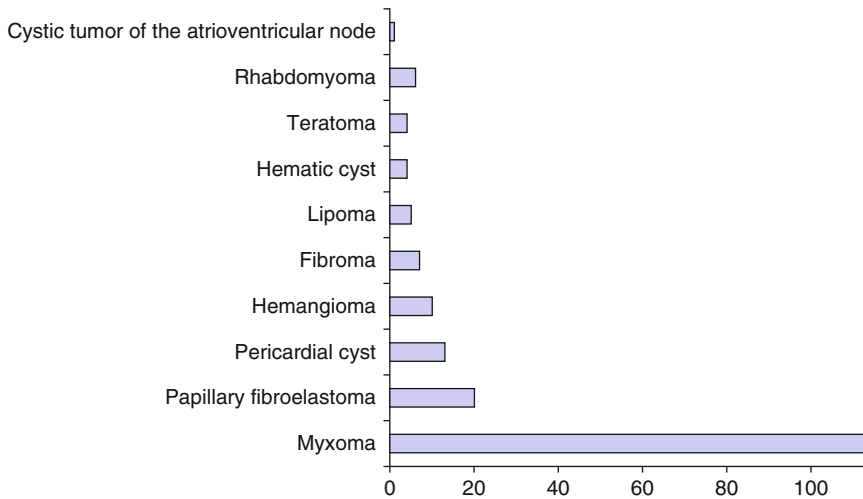


Fig. 2.4 Primary bioptic benign cardiac and pericardial tumors, University of Padua Medical School (1970–2010): 213 cases. Prevalence of various tumor histotypes

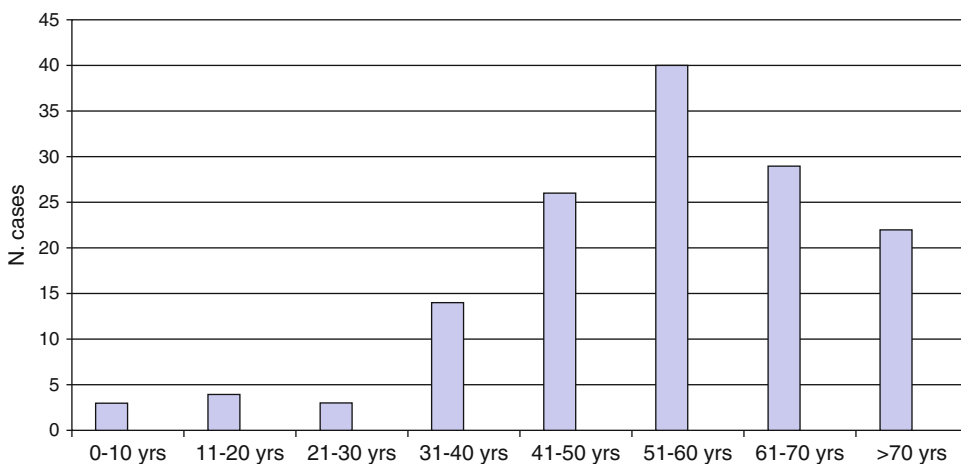


Fig. 2.5 Cardiac myxoma, University of Padua Medical School (1970–2010): 141 bioptic cases. Distribution according to age intervals

cally resected myxomas has been collected, representing 59% of all primary bioptic cardiac tumors and 66% of benign bioptic cardiac tumors. The majority were female (88, 62.5%), the age range was 2–85 years (mean 54 ± 16 , median 56).

Figure 2.5 reports the distribution of cardiac myxomas per age, showing a peak of incidence in people 50–60 years of age; only six cases (4%) have been surgically resected in the pediatric age (<18 years).

Location of cardiac myxoma was mostly the left atrium (116 cases, 82.5%), followed by the right atrium (22 cases, 15.5%), and exceptionally the ventricles (the right ventricle in two cases and the left ventricle in one case, 2%) (Fig. 2.6). In our experience, a valvular location was never observed. The weight ranged from 2 to 125 g (mean 38 ± 24) and the surface was smooth in 65% and villous in 35% of cases.

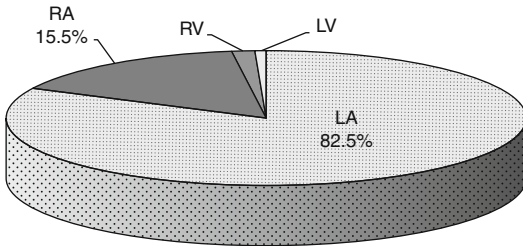


Fig. 2.6 Cardiac myxoma, University of Padua Medical School (1970–2010): 141 bioptic cases. Distribution according to tumor location (LA left atrium; LV left ventricle; RA right atrium; RV right ventricle)

As far as clinical presentation is concerned, signs and symptoms of hemodynamic obstruction were present in 60% of cases, constitutional symptoms in 30%, embolic phenomena in 16%, while one-fourth of patients were asymptomatic and myxoma was an incidental finding during echocardiographic examination (Fig. 2.7).

Papillary fibroelastoma (or endocardial papilloma) represents the second most frequent primary cardiac tumor after myxoma. Twenty cases have been surgically resected in 19 patients (8.5% of all primary bioptic cardiac tumors and 9.5% of benign bioptic cardiac tumors), 11 female, age ranging 24–78 years, mean 57 ± 17 , median 52.5 years. The location was the valvular endocardium in 16 (aortic valve in 6, mitral valve in 5, tricuspid valve in 4, and pulmonary valve in 1) and the mural endocardium in 4 (left ventricular cavity and/or papillary muscles in 2 and left atrial cavity in 2) (Fig. 2.8). In 10

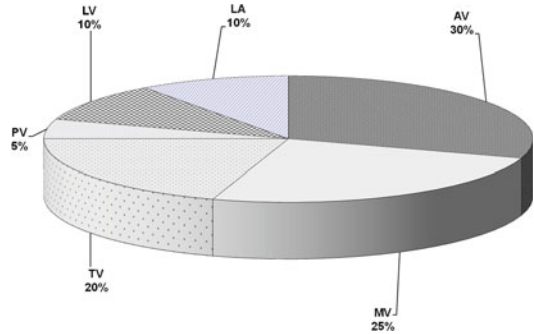


Fig. 2.8 Papillary fibroelastoma, University of Padua Medical School (1970–2010): 20 bioptic cases. Distribution according to tumor location (AV aortic valve, LA left atrium, LV left ventricle, MV mitral valve, PV pulmonary valve, TV tricuspid valve)

patients, the diagnosis was incidental during routine echocardiography (seven) or during cardiac surgery (three), while in the remaining nine patients it was achieved due to signs and symptoms of myocardial ischemia (six cases), heart failure (two cases) or arrhythmias (one case).

Hemangioma. Ten patients were studied, 4 males, age ranging from 2 days to 73 years, mean 30 ± 30 years, median 19 years. Cardiac hemangioma was intramural in 2 (left ventricular free wall and atrial septum, one each), intracavitary in 7 (right atrium in 2, right ventricle in 2, left atrium in 1, left ventricle in 1, mitral valve in 1), and pericardial in 1. The diagnosis was achieved during echocardiographic examination (nine cases) or intraoperatively (one case).

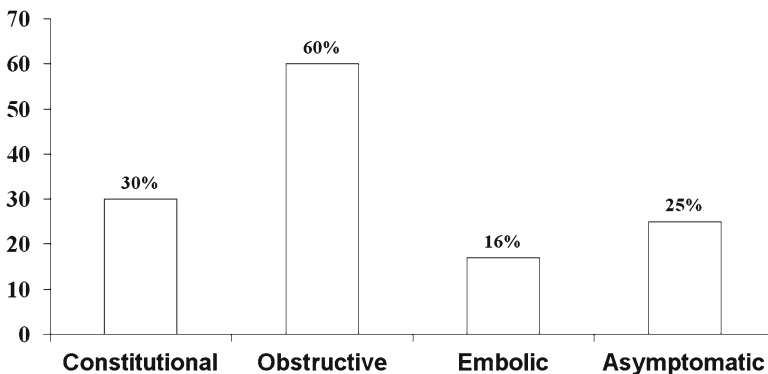


Fig. 2.7 Cardiac myxoma, University of Padua Medical School (1970–2010): 141 bioptic cases. Clinical presentation

Fibroma. Seven patients, four female, age ranging 1 month–40 years (mean 6 ± 14 years, median 6 months) were studied. The fibroma was located in the interventricular septum in three, right ventricular free wall in two, and left ventricular free wall in two. In three cases, surgical resection was not feasible and cardiac transplantation was performed.

Hematic cyst. Four cases were collected, all in infants (two male and one female, age ranging 4–11 months) but one (a 70-year-old woman). Two of them occurred in the setting of a congenital heart disease (hypoplastic right heart and tetralogy of Fallot, respectively). They were located at the level of the tricuspid valve in two, of the right atrium in one, and of inferior vena cava orifice in one.

Teratoma. Four patients, one male and three female, age ranging 1 month–35 years (median 1 month) were operated, all but one presenting with congestive heart failure since birth and with radiographic and echocardiographic evidence of pericardial mass.

Rhabdomyoma. Six patients, three female and three male, age ranging 7 days–4 months (mean 46 ± 47 days, median 22 days), had a surgically resected rhabdomyoma. In all, cardiac rhabdomyoma had an intracavitary growth with obstructive symptoms, at the level of the left ventricular outflow tract in four and of the right ventricular outflow tract in two.

Lipoma. Five surgically resected cases have been studied, including a 75 year old woman with lipomatous hypertrophy of the interatrial septum. The remaining four cases are true lipomas, with either an intracavitary growth (on the mitral valve—male 24 year old—and in the right atrium—male 61 year old and female 85 year old) or pericardial (male 64 year old).

Cystic tumor of the atrioventricular node (or Tawarioma). One surgically resected case has been examined in a full heart specimen coming from cardiectomy for heart transplantation (male 39 year old, dilated cardiomyopathy).

Pericardial cyst. Thirteen cases, 10 male and three female, age ranging 22–68 years, mean 48.5 ± 13 , median 52 years have been collected. These tumors represent the third most common primary cardiac and pericardial tumor in our bioptic experience, after myxoma and papilloma.

Primary Cardiac Tumors in the Pediatric Age (<18 years)

The pediatric experience (<18 years) consists of 29 cases (12% of all primary bioptic cardiac tumors), 13 female and 16 male, age ranging 1 day–18 years, mean 43 months, median 4 months.

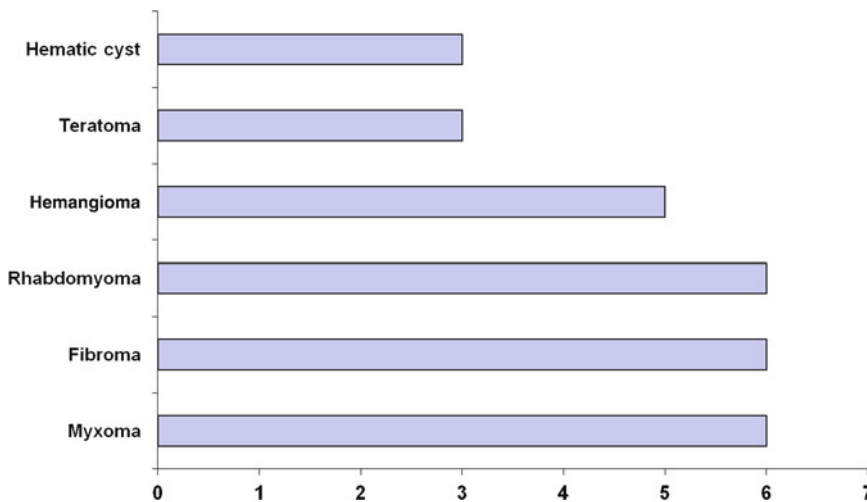


Fig. 2.9 Primary cardiac tumors in the pediatric age, University of Padua Medical School (1970–2010): 29 bioptic cases (12%). Prevalence of various tumor histotypes

They are all benign primary cardiac tumors, consisting of 6 myxomas (21%), 6 fibromas (21%), 6 rhabdomyomas (21%), 5 hemangiomas (17%), 3 pericardial teratomas (10%), and 3 hematic cysts (10%) (Fig. 2.9).

References

1. Lam KY, Dickens P, Chan AC. Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med.* 1993;117:1027–31.
2. Wold LE, Lie JT. Cardiac myxomas: a clinicopathologic profile. *Am J Pathol.* 1980;101:219–40.
3. Terribile V, Fassina A. Le neoplasie secondarie del cuore. In: *Il problema delle metastasi. Atti del XIV Congresso Nazionale della Società Italiana di Patologia* (Catania, 3–6 novembre 1977). Roma: Società Editrice Universo, 1978. p. 426–31
4. Travis WD, Brambilla E, Muller-Hermelink H, Harris CC. Pathology and genetics of tumours of the lung, pleura, thymus and heart. Lyon: IARC Press; 2004.
5. Fritz A, Jack A, Parkin DM, Percy C, Shanmugarathan S, Sobin L, Whelan S. International classification of diseases for oncology. 3rd ed. Geneva: World Health Organization; 2000.
6. Fletcher CDM, Unni KK, Mertens F. World Health Organization classification of tumours. Pathology and genetics of tumours of soft tissue and bone. Lyon: IARC Press; 2002.
7. van Unnik JA, Coindre JM, Contesso C, Albus-Lutter CE, Schiodt T, Sylvester R, Thomas D, Bramwell V, Mouridsen HT. Grading of soft tissue sarcomas: experience of the EORTC soft tissue and bone sarcoma group. *Eur J Cancer.* 1993;29:2089–93.
8. Trojani M, Contesso G, Coindre JM, Rodesse J, Bui NB, de Mascarel A, Goussot JF, David M, Bonichon F, Lagarde C. Soft-tissue sarcomas of adults: study of pathological prognostic variables and definition of a histopathological grading system. *Int J Cancer.* 1984;33:37–42.
9. Burke AP, Virmani R. Tumours of the heart and great vessels. 3rd ed. Washington, DC: Armed Forces Institute of Pathology; 1996.
10. Mazzola A, Spano JP, Valente M, Gregorini R, Villani C, Di Eusanio M, Ciocca M, Minuti U, Giancola R, Basso C, Thiene G. Leiomyosarcoma of the left atrium mimicking a left atrial myxoma. *J Thorac Cardiovasc Surg.* 2006;131:224–6.