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Metastatic and invasive tumours involving the heart in a geriatric population: a necropsy study

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Summary. In a series of 744 necropsied subjects with a diffuse malignant process, 57 cases of cardiac involvement were observed (50 metastatic carcinomas and 7 lymphomas or myeloproliferative disorders). The most frequent site of involvement was the pericardium and epicardium in lung or breast carcinoma, suggesting regional lymphatic invasion. Myocardial involvement was rarer and usually associated with cutaneous melanoma and lymphoma, suggesting haematogenic invasion. Endocardial involvement was exceptional. The multiple causes of heart disturbance in the elderly cloud the clinical diagnosis of such cardiac involvement; however, isolated pericardial and/or epicardial abnormalities should heighten suspicion of a neoplastic process.

Key words: Heart – Invasive tumours – Metastases – Lymphoma – Geriatrics – Necropsy

Introduction

There is a diversity of reports concerning the frequency (or rarity) of neoplastic invasion of the heart (Young and Goldman 1954; Goudie 1955; Willis 1967; Davies 1975; McAllister and Fenoglio 1978; Posner et al. 1981; Ravikumar et al. 1983). In the present study, we report our experience in a series of necropsies performed during 17 years in a geriatric institution.

Materials and methods

This retrospective study is based on 2455 complete necropsies (1453 females and 1002 males) performed consecutively by the author in the same geriatric institution between 1 January 1972 and 30 June 1989, and corresponds to 45.2% of the 5428 registered deaths during that period (3225 females and 2203 males). The patients' ages ranged between 62 years and 102 years with a mean age of 80.6 years.

Of the total number of necropsied cases, 1311 (53.5%) presented with malignant tumours or myeloproliferative diseases; of these 744 (56.8%) had metastatic or local involvement of viscera or skeleton (Table 1). The sex distribution in relation to the principal types of malignant proliferations was 628 females and 570 males for carcinomas, 7 females and 3 males for sarcomas, 57 females and 46 males for lymphomas or myeloproliferative diseases.

The pericardium and the heart (epicardium, myocardium and endocardium), including the coronary vessels, were examined mac-

Table 1. Frequency of cardiac invasion correlated with the frequency of visceral or skeletal invasion in relation to the type of tumour

Type of malignant proliferation	Number of tumour necropsied cases	Number of cases with visceral or skeletal invasion	Number of cases with cardiac invasion	Prevalence (%)
Carcinomas	1198	635 (53.0%)	50 (27 F, age range = 62–95 years) (23 M, age range = 63–94 years)	4.2
Sarcomas	10	6 (50%)	0	0
Lymphomas or myeloproliferative disorders	103	103 (100%)	7 (3 F, age range = 76–90 years) (4 M, age range = 71–82 years)	6.8
Total	1311	744 (56.8%)	57	4.3

The prevalence of cases with cardiac invasion is not significantly related to the type of malignant proliferation ($P < 0.05$)

roscopically in all cases, and all abnormalities were studied histologically by conventional methods for light microscopy. The material was fixed in 10% buffered formalin, embedded in paraffin and stained with haematoxylin and eosin; when necessary, special stains such as van Gieson, Giemsa and modified Masson's trichrome stain were used (Luna 1968).

Our criteria for defining the outer cardiac coats were those of the anatomists (Williams and Warwick 1980). We consider the pericardium to be the sac determined by the juxtaposition of an outer fibrous layer and an inner serous membrane, a complex which, in fact, is inseparable during necropsy. The epicardium is the parietal prolongation of this serous membrane.

Results

The main macroscopic and histological lesions observed are illustrated in Figs. 1–4.

Table 1 shows that cardiac invasion was observed in 57 (5.05%) of the necropsied patients presenting with a malignant process, without any increase in prevalence in carcinoma. In only 5 cases was there an absence of other visceral invasion (1 with epicardial metastases of mammary gland carcinoma and 4 with direct pericardial invasion of bronchogenic carcinoma).

Table 2 indicates the frequency (7.9%) and site of cardiac involment in necropsied subjects with carcinoma and shows the site of the primary tumour.

Carcinoma of the lung was the main neoplasm causing cardiac invasion. There was a total of 20 patients (40%) comprising 14 males and 6 females showing an age range between 63 years and 94 years with a mean age of 77.3 years. The histological types were: squamous cell carcinoma 9 cases (3 females and 6 males), adenocarcinoma 5 cases (2 females and 3 males), small cell ("oat-cell") carcinoma 3 cases (3 females) and poorly differentiated (polygonal-cell) squamous cell carcinoma 3 cases (1 female and 2 males).

Infiltrating scirrhous carcinoma of the breast was the second most frequent tumour to manifest cardiac invasion; there were 11 female cases (22%) with an age range between 62 and 90 years. Bilateral carcinoma of the breast was observed in 6 patients (55.5%).

Cardiac invasion was observed less frequently in cutaneous malignant melanoma (2 females and 2 males or 8%) and in gastro-intestinal carcinoma (4 cases or 8%). The histological types of gastro-intestinal carcinoma were: squamous cell carcinoma of the oesophagus (1 female and 1 male), undifferentiated carcinoma of the stomach (1 female) and adenocarcinoma of the caecum (1 female). Cardiac invasion was rarely observed in other carcinomas, as shown in Table 2.

Table 3 indicates the nature of lymphomas or myeloproliferative processes with cardiac invasion as well as the frequency and site of involvement. In our series of 12 necropsied cases of Hodgkin's lymphoma there was no evidence of cardiac invasion.

We also call attention to the absence of cardiac invasion in 10 necropsied sarcomas – leiomyosarcoma of the stomach (2 cases), leiomyosarcoma of the uterus,

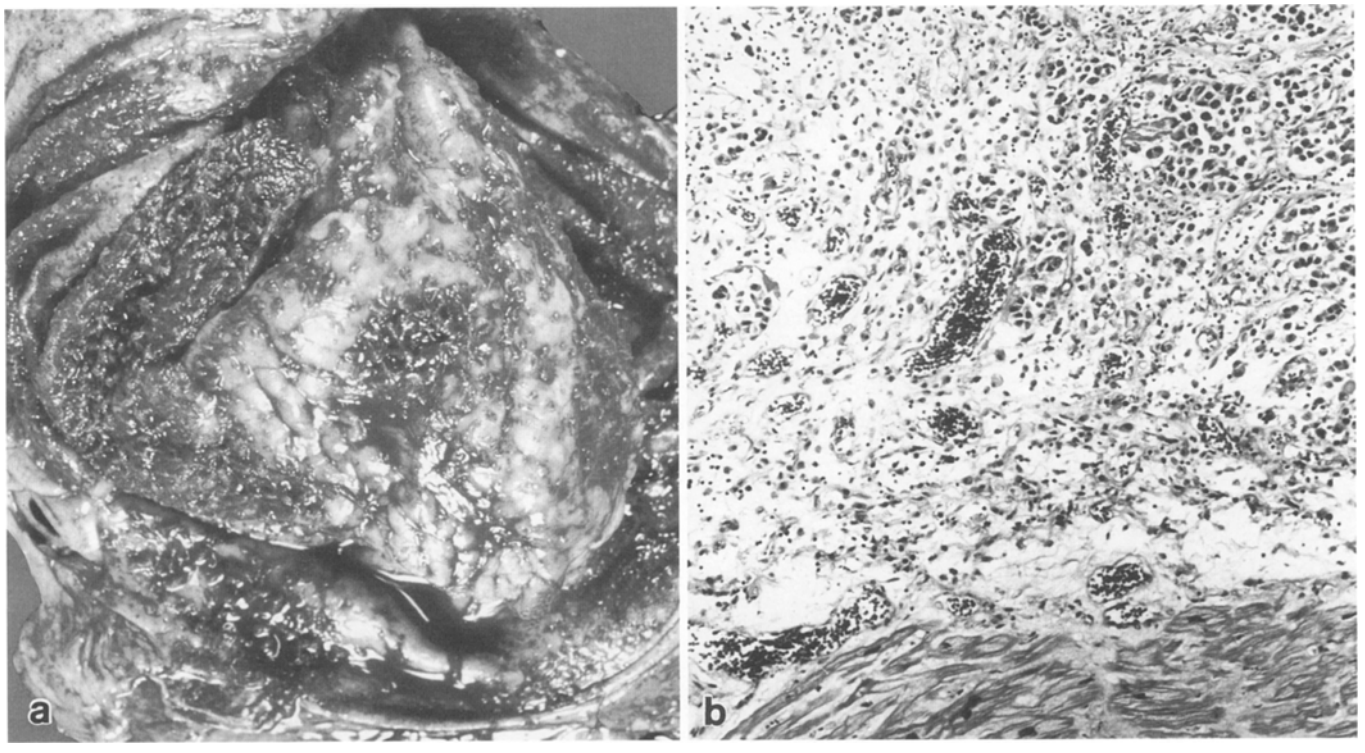

Fig. 1a, b. Peri-epicardial tumour invasion by lung adenocarcinoma. **a** *Macroscopy:* numerous tumour nodules associated with organized haemorrhagic pericarditis. **b** *Histology:* epicardial thickening by massive infiltration of compact tumour cords intermingled with organized strands of fibrinous material and erythrocytes. There is a scattered lymphoplasmacytic inflammatory infiltrate around dilated capillaries. Haematoxylin and eosin (×100)

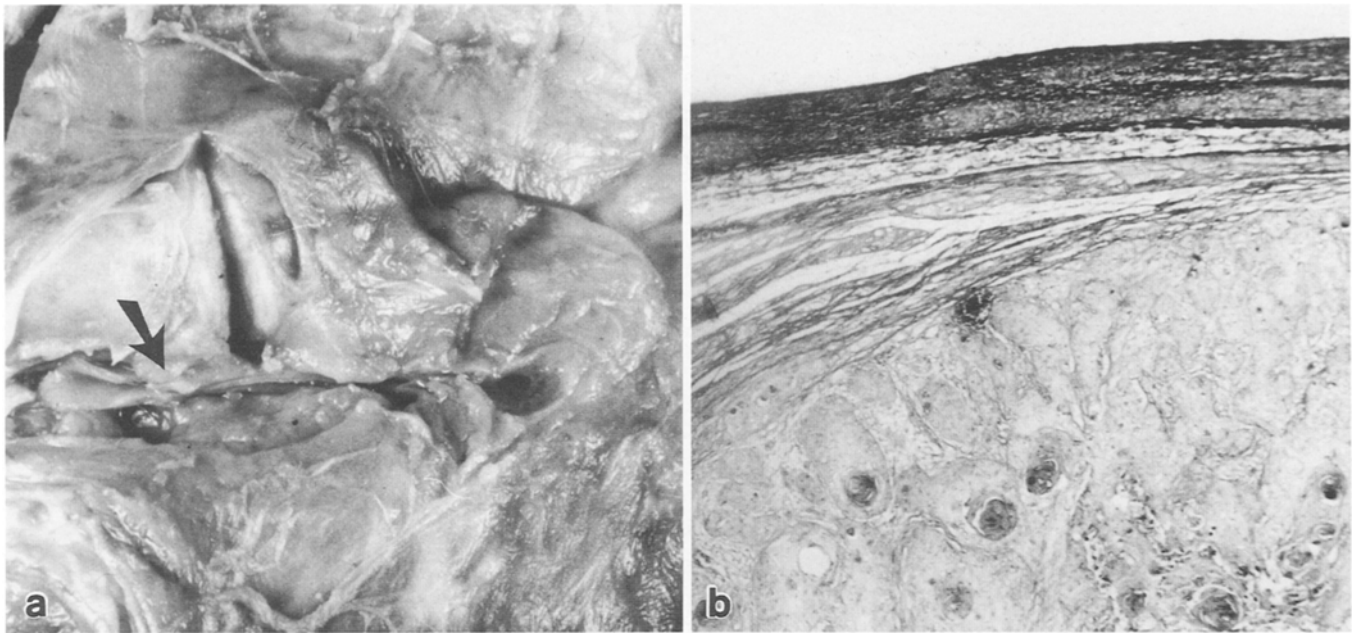

Fig. 2a, b. Nodular epicardial metastasis from squamous cell lung carcinoma. **a** *Macroscopy:* compression of the left circumflex coronary artery (*arrow*) in the posterior wall of the left atrium. **b** *Histology:* segment of the left circumflex coronary artery (*above*) adjacent to which is a nodular epicardial metastasis. Van Gieson-Resorcin-Fuchsin (× 40)

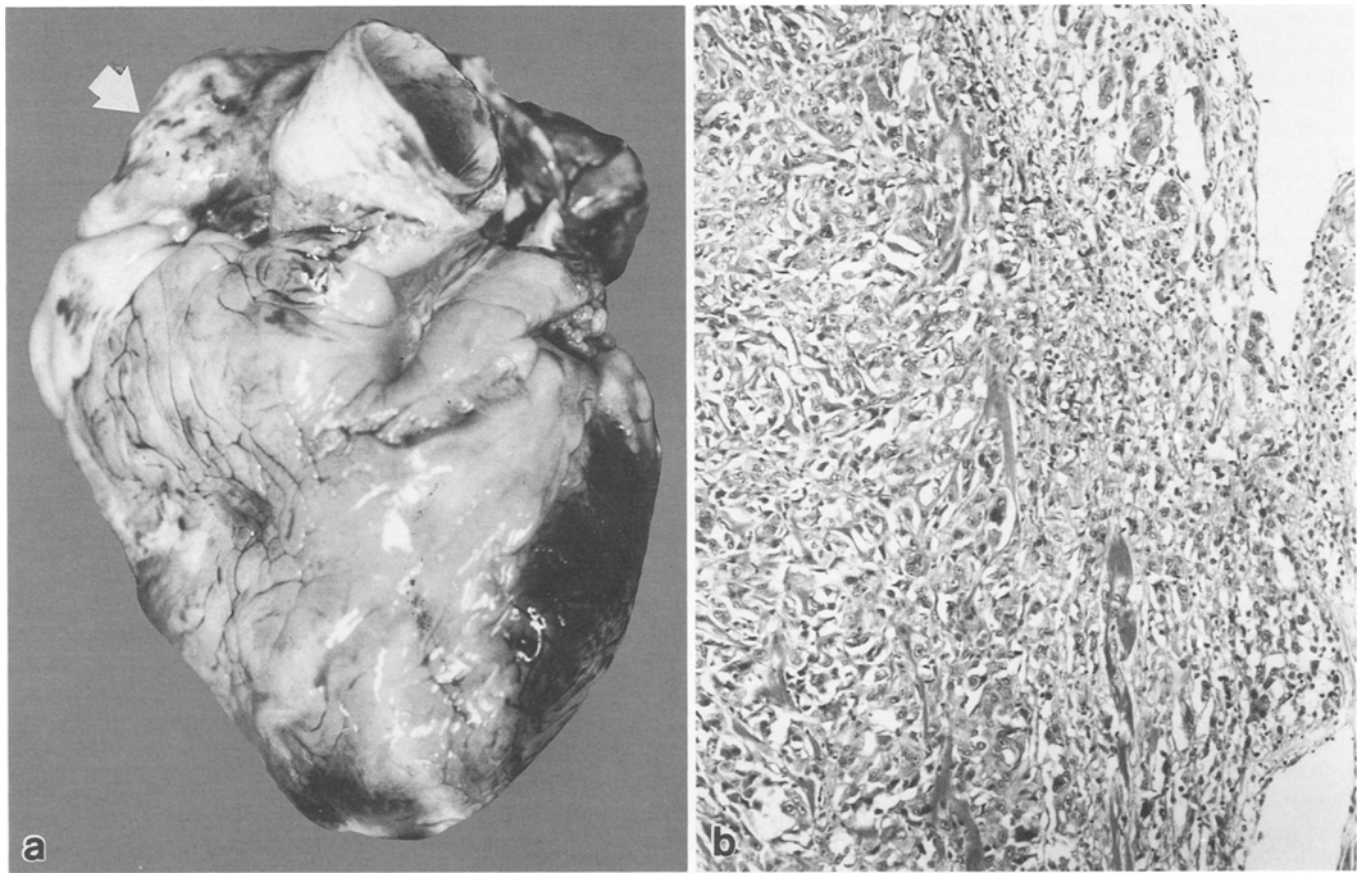

Fig. 3a, b. Invasion of the epicardium, myocardium and endocardium by squamous-cell lung carcinoma. **a** *Macroscopy:* antero-lateral view of the heart illustrating epicardial invasion of the right auricle (*arrow*) with extension to branches of the sino-atrial node. **b** *Histology:* nodular tumour infiltration of endo-myocardium (anterior aspect of the left ventricular apex showing tumour extension into the anterior papillary muscle). Haematoxylin and eosin (× 100)

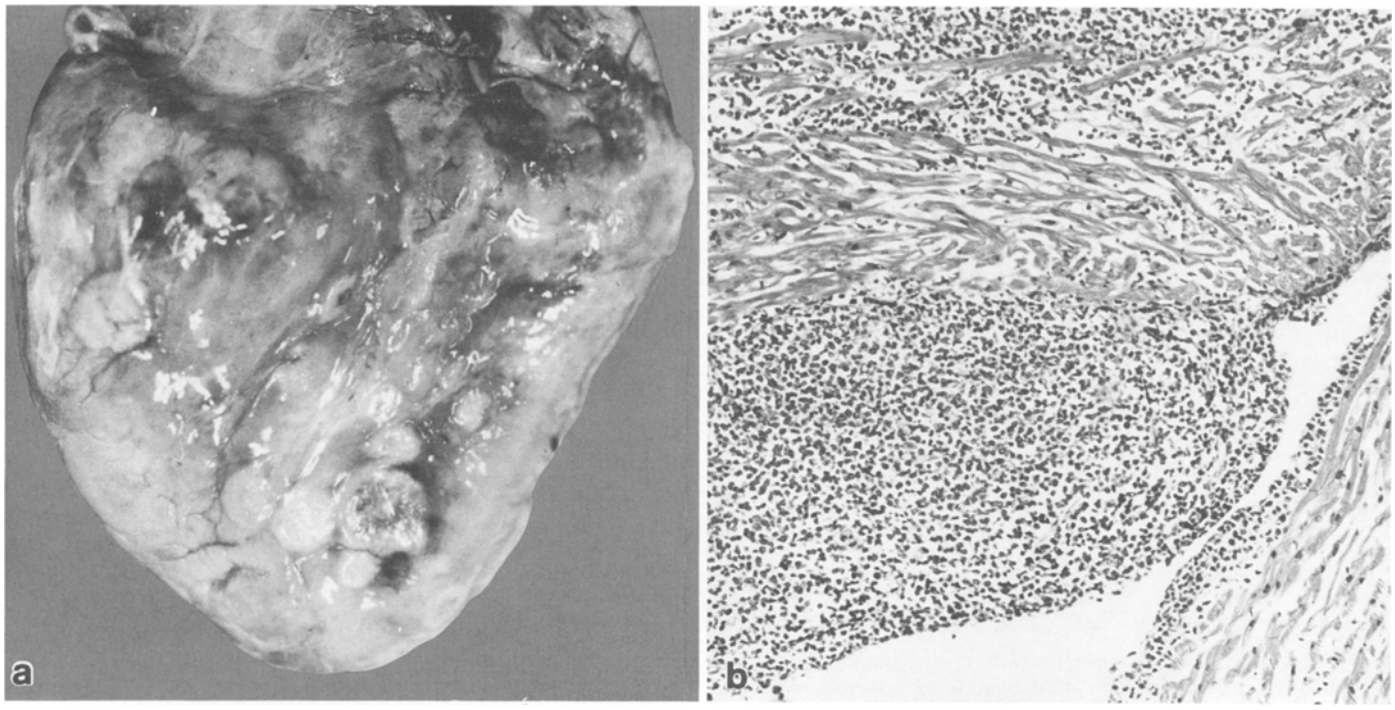

Fig. 4a, b. Invasion of epicardium, myocardium and endocardium in a case of acute monoblastic leukaemia. **a** *Macroscopy:* posterior view of the ventricles demonstrating nodular invasion of the epicardium. **b** *Histology:* nodular endo-myocardial invasion by masses of monoblastic tumour cells. Haematoxylin and eosin (× 100)

Table 2. Incidence and site of carcinomatous cardiac invasion by metastases

Site of primary tumour	Lung	Breast	Cutaneous melanoma	Prostate	Oesophagus	Vulva
Number of cases	20 (198)	11 (150)	4 (12)	2 (204)	2 (15)	2 (5)
Pericardium	14	7	0	0	1	1
Epicardium	12	8	3	2	2	2
Myocardium	4	4	4	0	1	0
Endocardium	1	1	1	0	0	0

Site of primary tumour	Thyroid	Pancreas	Colon	Stomach	Oropharynx	Ureter	Unknown primary
Number of cases	2 (12)	2 (72)	1 (109)	1 (87)	1 (13)	1 (4)	1 (6)
Pericardium	0	0	0	1	0	0	0
Epicardium	0	1	1	0	1	1	0
Myocardium	2	1	0	1	0	0	1
Endocardium	0	0	0	0	0	0	0

The figures in brackets indicate the total number of necropsied cases

neurofibrosarcoma of the retroperitoneum, mediastinal malignant schwannoma of the pneumogastric nerve, haemangio-endothelial sarcoma of the liver, Kaposi's sarcoma (not associated with AIDS), osteogenic sarcoma of the sacro-lumbar spine, sarcomatous mesothelioma of the peritoneum and gliofibrosarcoma of the brain.

Comparison of Tables 2 and 3 shows that pericardial and epicardial invasion predominates in cases of carcinoma arising from the lung or breast. In fact, in 28 of these 31 cases both layers were involved. When pericardial invasion was observed, an effusion was demonstrated in 17 cases (about two-thirds of the cases related to lung or breast cancer) but cytological examination was not performed. Myocardial invasion was generally more frequent than endocardial, particularly with regard to cutaneous melanoma. Amongst the various types of

Table 3. Incidence and site of cardiac involvement in relation to the type of lymphomatous or myeloproliferative disease

Type of lymphoma or myeloproliferative process	Chronic lymphocytic leukaemia	Acute myeloblastic leukaemia	Malignant T-cell lymphoma (mycosis fungoides)	Diffuse centrocytic lymphoma	Diffuse plasmocytoid lymphoma	Diffuse centroblastic lymphoma
Number of cases	2 (15)	1 (8)	1 (2)	1[a]	1[a]	1[a]
Pericardium	0	1	0	0	0	0
Epicardium	0	1	1	1	0	0
Myocardium	2	1	1	1	1	1
Endocardium	1	1	1	0	0	0

The figures in brackets indicate the total number of necropsied cases.

[a] In our series of 2455 necropsies 45 cases of non-Hodgkin's lymphoma were observed. However, the total number of necropsied cases was not specified for the last three columns since the nomenclature of the corresponding lymphomas had varied during the 17-year period of this study

Table 4. Clinical manifestations in correlation with the site of cardiac malignant tumour invasion

	Main clinical manifestations						
	Dyspnoea at rest	Tachycardia	Abnormal cardiac configuration (X-ray)	Irregular pulse	Tachypnoea	Central cyanosis	Pericardial friction rub
Number of cases	23	26	18	12	7	4	2
Pericardium	9	9	9	4	2	1	1
Epicardium	11	19	9	9	5	2	1
Myocardium	5	16	12	9	2	1	0
Endocardium	1	3	2	0	1	0	0

	Main clinical manifestations					
	Fever	Pleural effusion (X-ray)	Regular pulse	ECG without pathological modifications	Atrial fibrillation or flutter	Muffled heart sounds
Number of cases	11	25	28	13	10	7
Pericardium	4	11	8	3	3	3
Epicardium	5	15	18	6	6	4
Myocardium	6	10	14	6	5	2
Endocardium	1	3	4	2	0	0

lung carcinoma observed with myocardial invasion, there were 4 cases of squamous cell carcinoma and 1 case of adenocarcinoma. With regard to the myocardium and endocardium, the left side alone was involved in 9 cases and the right side alone in 3 cases. Bilateral invasion was observed in 6 cases. The left ventricle was involved in 19 cases (76.9%), the right ventricle in 11 cases (44%), the left atrium in 10 cases (40%), the right atrium in 13 cases (52.6%).

In 15 of our series of 57 patients cardiomegaly was also associated with diffuse myocardial fibrosis suggesting chronic ischaemia. In 14 cases, this finding correlated with either a chronic inflammatory valve disease (4 cases) or a degenerative age-related valve disease (10 cases); fatty infiltration of the heart was noted in 7 cases. However, we note the absence of cardiomyopathies, amyloidosis and myocarditis. Six cases of recent myocardial infarction without evidence of tumour coronary compression or tumour thrombosis were observed, 23 cases showed considerable or severe stenotic atherosclerosis of the coronary arteries.

The range of the clinical manifestations is indicated in Table 4. The main clinical manifestations were tachycardia (45.7%), pleural effusion (43.9%), dyspnoea at rest (40.3%) and an abnormal cardiac configuration (31.5%).

The main causes of death diagnosed at necropsy are shown in Table 5. In 31.6% of the cases death could be attributed to cardiac tumour invasion, namely: cardiac tamponade (6 cases), massive epi-myocardial invasion (6 cases), congestive cardiac failure consecutive to constrictive pericarditis (3 cases), coronary artery compression (2 cases) and invasion of the sino-atrial node (1 case).

Table 5. Direct cause of death in 57 patients presenting cardiac malignant tumour invasion

	Cause of death					
	Broncho-pneumonia	Multiple metasta-ses	Cardiac tamponade (haemorrhagic pericardial effusion from 200 ml to 1400 ml)	Anasarca (severe right-sided heart failure)	Myocardial infarction without evidence of coronary artery compression	Congestive heart failure
Number of cases	17	7	6	6	6	3
Pericardium	5	2	3	3	2	2
Epicardium	13	3	3	5	3	1
Myocardium	6	4	1	2	2	0
Endocardium	1	1	0	2	1	0

	Cause of death					
	Pulmonary embolism	Acute perito-nitis	Myocardial infarction with evidence of coronary artery compression	Arrhythmia (clinical) and myocardial infarction with invasion of sino-atrial node	Acute pulmonary oedema	Foreign-body obstruction of the air passages
Number of cases	5	3	2	1	2	1
Pericardium	0	1	0	0	0	1
Epicardium	1	2	2	0	1	1
Myocardium	4	2	0	1	2	0
Endocardium	0	0	0	0	0	0

Discussion

This study illustrates that cardiac invasion occurs in elderly patients with carcinomas, lymphomas and myeloproliferative disorders. This was found in about 2.3% of necropsied cases, without significant differences relating to the nature of the tumour process. However, metastasis was clearly more frequent than benign tumours of the heart, since the series of 2455 necropsied cases showed only 1 case of a massive pedunculated myxoma attached to the posterior wall of the right atrium. This incidence of malignant involvement is in agreement with the minimal values of the frequency range reported in the literature (Glancy and Roberts 1968; McAllister and Fenoglio 1978; Chan et al. 1985). In contrast to what has been reported by some authors we did not observe cardiac involvement in 12 necropsied cases with Hodgkin's lymphoma (Young and Goldman 1954; Roberts et al. 1968; McAllister and Fenoglio 1978) and in 10 cases with diverse sarcoma (Fishberg 1930; Goudie 1955; Willis 1967; Dunnick et al. 1981; Ravikumar et al. 1983). It is clear that the four cardiac layers are susceptible to invasion by any kind of malignant process with a topographical diversity of origin which is in agreement with the data in the literature (Young and Goldman 1954; Goudie 1955; Willis 1967; Posner et al. 1981; Ravikumar et al. 1983).

We emphasize the predominance of pericardial and/or epicardial tumour invasion by carcinoma of the lung and breast. There is associated pericardial effusion and concurrent infiltration of both layers in almost all of the cases. This observation is also in agreement with previous data (Young and Goldman 1954; Goudie 1955; Glancy and Roberts 1968; Yazdi et al. 1980; Del Regato et al. 1985) and suggests a role for direct extension via lymphatic channels. In cases of pericardial and epicardial invasion associated with carcinoma of the lung or breast we often observed local invasion of the pleura or the lymph nodes (24/31 cases or 77.5%). In fact, evidence of a lymphatic communication between lungs or breasts and the pericardium or epicardium has been demonstrated by anatomists (Williams and Warwick 1980; Rouvière 1981).

The above pericardial invasion must be distinguished from a non-tumour pericarditis – particularly radiation induced – a condition which may occur in patients with cancer (Goudie 1955; Hurst and Cooper 1955; Stewart and Fajordo 1971; Byhardt et al. 1975; Krikorian and Hancock 1978; Agner and Gallis 1979; Ahmed and Slayton 1980; Silver 1983). In a given patient the diagnosis may be suspected on electrocardiography, radiography or echography and further supported by the results of cytological examination of pericardial fluid (Yazdi et al. 1980; Posner et al. 1981) or by histological study of pericardectomy material (Posner et al. 1981). According to some authors, cytological evaluation of effusions in malignant pericarditis demonstrated malignant cells in 60–80% of cases (Zipf and Johnston 1972; Yazdi et al. 1980). We have noted the limits of the method in 2 cases of post mortem observed tumour pericarditis; premor-

tem cytology of pericardial fluid demonstrated malignant cells in 1 case, but not in the other.

In our 44 cases of pericardial and/or epicardial tumour invasion only 1 case of epicardial invasion had been diagnosed clinically and 3 cases of pericardial invasion has been strongly suspected. In the 4 cases the principal symptoms which had focused attention to the clinicians were tachycardia, marked dyspnoea at rest, signs of right-sided cardiac failure and absence of fever. In 1 of these cases auscultation revealed muffled heart sounds and in 2 cases, a pericardial friction rub. In 3 cases, X-rays demonstrated an enlarged heart or contralateral cardiac compression. These clinical manifestations led to echocardiographic examination which demonstrated pericardial effusion in 3 cases and increased density at the right atrio-ventricular junction in 1 case.

Myocardial invasion is seen in more than 30% of cases of necropsied cutaneous melanoma (which is spread mainly by haematogenous dissemination) but is found in only 2% of lung and breast carcinomas and even less in other carcinomas (which are spread mainly by lymphatic diffusion). This is in accordance with some published data (Glancy and Roberts 1968; Del Regato et al. 1985). In our series, myocardial infiltration was also observed in practically all types of non-Hodgkin's malignant lymphoma, as well as in lymphocytic and myeloblastic leukaemia (Goudie 1955; Roberts et al. 1968; McAllister and Fenoglio 1978; Schmidt et al. 1990).

The endocardium was rarely invaded and the valves, never. In contrast with what has been reported in secondary cardiac tumours of both children (Chan et al. 1985) and adults (Davies 1975) there was no direct tumour extension from regional veins (particularly pulmonary, superior and inferior venae cavae) into the cardiac chambers.

We therefore conclude from this study that neoplastic cardiac invasion is not exceptional in elderly subjects whose death stems from a generalized malignant process. However, neoplastic cardiac invasion is often difficult to recognize clinically, since other conditions may be the origin of a heart disturbance. The only feature which suggests a neoplastic process is the production of an effusion.

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