Tumor Metastasis to the Heart

By J. M. Young, M.D., and I. Ralph Goldman, M.D., F.C.C.P.

This article is a survey of 476 consecutive cases of tumor death for heart involvement. The somewhat selected group of cases (from a Veterans Administration hospital) shows an incidence of cardiac metastasis of 19.1 per cent. The bulk of tumors metastasizing to the heart were bronchogenic carcinoma, malignant melanoma, malignant lymphoma, and carcinoma of the pancreas and esophagus. Electrocardiographic changes were frequent and correlated fairly closely with the anatomic extent of the disease. The related literature is reviewed.

MYOCARDIAL involvement by neoplasms arising elsewhere in the body is no longer considered rare. A survey of the literature discloses a gradually rising incidence of myocardial metastasis as this subject is more closely explored. It has recently been estimated that more than 500 instances of tumor metastasis to the heart are now recorded, and more than 20 of these were diagnosed before death. In the earlier literature, summarized by Morris, Yater, Lisa and co-workers, Doane and Pressman, and Willis, one finds that the incidence figures were almost always below 2 per cent. Often, however, the number of tumor deaths was not mentioned. Carcinoma of the breast, lung, esophagus, pancreas, malignant melanoma, and malignant lymphoma are mentioned most frequently in the literature as the primary tumor. In fact, almost all types of tumors have occasionally metastasized to the heart. Very often the total of tumors of each kind is not given. Notable exceptions are the series of Herbut and Maisell and Willis.

Scott and Garvin found a 10.9 per cent incidence of cardiac involvement in 1082 cases of tumor death. Likewise, Dimmetye reported a figure of 8.35 per cent in 455 cases. This present report does not represent the expected frequency of cardiac metastasis in a general hospital, but rather that found in a large general medical and surgical Veterans Administration hospital which is also a reference center for thoracic surgery and for many cases of malignant lymphoma. Another factor in our high incidence is probable longer survival of our cases, since many remained hospital cases throughout their terminal course. This longer survival likely has allowed more widespread metastasis.

Material

During approximately six and one-half years 1400 autopsies have been performed, and 586 of these were upon patients who had died of tumor (41.9 per cent). Leukemia cases and brain tumors have been excluded, since the former show cardiac infiltrations frequently, and the latter almost never metastasize outside the central nervous system. (See table 1.) In 54 cases of leukemia there were 25 with myocardial infiltrations, and seven of these were of moderate or marked degree (fig. 1). Fifteen of 30 granulocytic leukemia cases and 5 of 16 lymphoid leukemia cases disclosed cardiac infiltrations.

In the remaining 476 cases of tumor death there were 91 with cardiac involvement, an incidence of 19.1 per cent. Examination of table 2 explains this high percentage since a large proportion of our cases have been bronchogenic carcinoma, malignant melanoma, malignant lymphoma, and carcinoma of the pancreas and esophagus. Six of these cases have been reported previously in detail by Lefkovitz. In all cases there were metastases to sites other than the heart.

In most of the reported series the right side of the heart has been more frequently involved than the left, but in some series more nearly equal involvement of the right and left sides has been noted. In our cases with hematogenous metastases, the right side was involved alone in but seven cases, the left side in 13 cases, and both sides in nine cases. There was bilateral involvement, considering all metastatic pathways, in 63 cases and endocardial involvement only in two cases. In the other six cases insufficient

Table 1.—Incidence of Cardiac Metastases

<table>
<thead>
<tr>
<th>Total Autopsies</th>
<th>1400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Deaths</td>
<td>586 (41.9%)</td>
</tr>
<tr>
<td>Tumor Deaths Less Leukemias and Brain Tumors</td>
<td>476</td>
</tr>
<tr>
<td>Cases with Heart Metastases</td>
<td>91 (19.1%)</td>
</tr>
</tbody>
</table>

From the Laboratory Service and Medical Service, Veterans Administration Medical Teaching Group (VAMTG) Hospital, Memphis, Tenn.
data were given to classify the extent and locations of the metastases.

The epicardial and subepicardial lymphatics were most often involved in our cases. Sixty cases showed involvement in this manner, while 29 had myocardial (hematogenous) metastases and two had endocardial implants. In the group with subepicardial lymphatic involvement, the right side of the heart, particularly the auricle, was most affected. In most cases the extent of the metastasis was grossly

FIG. 1 (top left). Subepicardial and myocardial infiltration in chronic granulocytic leukemia. (× 45)

FIG. 2 (top right). Bronchogenic carcinoma. Note dilated lymphatics filled with tumor tissue and the accompanying inflammatory reaction. (× 45)

FIG. 3 (middle left). Myocardial tumor nodules in malignant melanoma. (× 45)

FIG. 4 (middle right). Lymphocytic lymphosarcoma. Note widespread invasion and separation of muscle fibers and bundles. (× 45)

FIG. 5 (bottom). Testicular tumor with hematogenous chorionepithelioma cardiac metastasis. Note necrosis accompanying tumor. (× 45)
TABLE 2.—Tumor Types with Percentages Showing Heart Metastases

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Total Cases</th>
<th>Metastasis to Heart</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchus</td>
<td>109</td>
<td>40</td>
<td>36.7</td>
</tr>
<tr>
<td>Malignant Melanoma</td>
<td>17</td>
<td>11</td>
<td>64.7</td>
</tr>
<tr>
<td>Malignant Lymphoma</td>
<td>60</td>
<td>9</td>
<td>15.0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>33</td>
<td>7</td>
<td>21.2</td>
</tr>
<tr>
<td>Esophagus</td>
<td>33</td>
<td>6</td>
<td>18.2</td>
</tr>
<tr>
<td>Kidney</td>
<td>15</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>Testicle</td>
<td>9</td>
<td>4</td>
<td>44.4</td>
</tr>
<tr>
<td>Stomach</td>
<td>34</td>
<td>2</td>
<td>5.9</td>
</tr>
<tr>
<td>Prostate</td>
<td>27</td>
<td>2</td>
<td>7.4</td>
</tr>
<tr>
<td>Bladder</td>
<td>15</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Adrenal</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Paranasal Sinus</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lip</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

TUMORS BY TYPES

Bronchogenic Carcinoma

In the 109 cases in this group, 40 disclosed cardiac involvement. Twenty-three tumors arose in the right lung, 16 in the left lung, and one was a terminal bronchial carcinoma with bilateral involvement. In 37 of the 40 cases there was definite mediastinal involvement, and this most often was marked. The route of involvement was via the lymphatics (retrograde extension) in 34 cases and hematogenous in six. In the cases showing subepicardial tumor, the right auricle was usually more markedly involved (see fig. 2).

The pericardial sac was obliterated by tumor and adhesions in seven cases. There was significant pericardial effusion in 14 cases; this was sanguineous in eight. The heart weight was above 350 Gm. in 16 cases, but only two of these weighed more than 550 Gm.

Electrocardiographic tracings were made in 16 cases. Table 3 lists the cases and correlates the anatomic findings and electrocardiographic changes. Those showing low voltage usually had obliteration of the pericardial sac or pericardial effusion. A pattern of epicardial or myocardial involvement was present in six tracings, and in two of these, serial tracings disclosed partial resolution of the process.

Malignant Melanoma

This tumor most often involves the heart by the hematogenous pathway (see fig. 3). Eleven of our 17 cases disclosed cardiac metastases (64.7 per cent), and in eight the metastases were blood-borne. In three there was significant serous pericardial effusion. Mediastinal involvement was notable in five cases, and three of these showed subepicardial metastases. Heart weight was increased in three cases where numerous tumor nodules were present. In one case, these nodules ulcerated through the endocardium, resulting in implants between the trabeculae and on the valves. Unfortunately, in only one case was an electrocardiogram taken. This disclosed low voltage and a pattern suggestive of myocardial spread.
<table>
<thead>
<tr>
<th>Case</th>
<th>Anatomic Findings</th>
<th>Electrocardiographic Changes</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) P.M. 162</td>
<td>Obliteration of pericard. sac by fibrous adhesions and tumor.</td>
<td>Low voltage. Complete A-V dissociation. Inverted T wave in CF2. Ventric. premature systoles. This later showed P pulmonale with a prolonged Q-T interval.</td>
<td>Pos.</td>
</tr>
<tr>
<td>(2) P.M. 350</td>
<td>Many tumor nodules through subepicard. region with infiltration of outer layer of myocard.</td>
<td>Inverted T wave in CF2. Last tracing obtained 35 days before death.</td>
<td>Neg.</td>
</tr>
<tr>
<td>(3) P.M. 361</td>
<td>Subepicard. lymphatic and pericard. involvement by tumor tissue.</td>
<td>Normal ECG taken 24 days before death.</td>
<td>Neg.</td>
</tr>
<tr>
<td>(4) P.M. 374</td>
<td>Numerous tumor nodules in left aur., right vent. and I.V. septum, and one nodule present in septum between the tricuspid and mitral valve rings.</td>
<td>Pattern of left bundle branch block.</td>
<td>Pos.</td>
</tr>
<tr>
<td>(5) P.M. 482</td>
<td>Slight subepicard. lymphatic involvement with invasion of outer layer of myocard.</td>
<td>Digitalis effect. Last tracing taken 18 days before death.</td>
<td>Neg.</td>
</tr>
<tr>
<td>(6) P.M. 537</td>
<td>Sanguineous pericard. effusion. Marked subepicard. lymphatic involvement with infiltration of outer myocard. layer by tumor tissue.</td>
<td>Sinus tachycardia. changing to auric. flutter with spontaneous reversion to sinus tachycardia. T-wave changes in chest leads typical of either pericarditis or myocarditis.</td>
<td>Pos.</td>
</tr>
<tr>
<td>(7) P.M. 570</td>
<td>2 cm. tumor nodule in left aur. and involvement of subepicard. lymphatics.</td>
<td>P pulmonal which later changed to auric. flutter. Last tracing taken 3 months prior to death.</td>
<td>Equivocal</td>
</tr>
<tr>
<td>(8) P.M. 610</td>
<td>Subepicard. lymphatic involvement with myocard. infiltration in both aur.</td>
<td>Auric. fibrill. with T-wave changes in chest leads typical of myocarditis and digitalis effect.</td>
<td>Pos.</td>
</tr>
<tr>
<td>(9) P.M. 640</td>
<td>Obliteration of pericard. sac by adhesions and tumor tissue.</td>
<td>Rhythm fluctuating from sinus tachycardia. to auric. fibrill. ST and T-wave changes typical of pericarditis.</td>
<td>Pos.</td>
</tr>
<tr>
<td>(10) P.M. 721</td>
<td>Extension of tumor tissue down great vessels with invasion of pericard. at base of heart and seeding of epicard.</td>
<td>Sinus tachycardia. in tracing taken 1 month before death.</td>
<td>Neg.</td>
</tr>
</tbody>
</table>

Table 3—Correlation of Anatomic Findings and Electrocardiographic Changes

Bronchogenic Carcinoma
<table>
<thead>
<tr>
<th>Case</th>
<th>Anatomic Findings</th>
<th>Electrocardiographic Changes</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.M. 1135</td>
<td>Involvement of subepicard. lymphatics by tumor tissue.</td>
<td>Low voltage with a small Q wave and inverted T wave present in aV1. Last tracing taken 24 days before death.</td>
<td>Equivocal</td>
</tr>
<tr>
<td>P.M. 529</td>
<td>Scattered small microscopic tumor nodules in myocard. Mild left ventr. hypertrophy.</td>
<td>Low voltage. Left ventric. hypertrophy pattern which reverted to normal just prior to death. Last tracing taken 27 days before death.</td>
<td>Equivocal</td>
</tr>
<tr>
<td>(1)</td>
<td>Scattered small microscopic tumor nodules in myocard. Mild left ventr. hypertrophy.</td>
<td>Low voltage. Left ventric. hypertrophy pattern which reverted to normal just prior to death. Last tracing taken 27 days before death.</td>
<td>Equivocal</td>
</tr>
</tbody>
</table>
Malignant Lymphoma

In this series of tumor deaths, there were 60 cases with malignant lymphoma. Twelve had lymphosarcoma, and five of these showed myocardial involvement (see fig. 4). In one case the pericardial sac was obliterated, and the electrocardiogram showed low voltage, sinus tachycardia and changes consistent with pericarditis. In two other cases there was a serosanguineous pericardial effusion. The heart weight was increased in one case. There was epicardial spread in four cases and myocardial nodules in one case. The mediastinum contained tumor in three cases.

Two of seven cases of reticulum cell sarcoma had epicardial tumor, and in both the mediastinum was involved. The pericardial sac was obliterated in one case, and an electrocardiogram showed sinus tachycardia and changes typical of chronic pericarditis.

Of 39 cases of Hodgkin's disease, only two disclosed heart metastases. In both the epicardial layer was involved. An electrocardiogram in one case showed sinus tachycardia, low voltage, and changes consistent with pericarditis. Mediastinal involvement was present in both cases.

Two cases of mycosis fungoides had no cardiac metastases.

Carcinoma of Pancreas

Seven of the 33 cases of carcinoma of the pancreas had cardiac metastases. Four of these followed lymphatic pathways and involved the subepicardial region, while two showed myocardial nodules and one had implants only between the trabeculae of the right ventricle. In four cases there was pericardial effusion, and in one of these, the effusion was serosanguineous. The electrocardiogram of the last mentioned case disclosed sinus tachycardia, low voltage, and changes typical of chronic pericarditis. Mediastinal involvement was noted in three cases.

Carcinoma of the Esophagus

Six of the 33 cases in this group had cardiac involvement, and one of these showed direct extension through the pericardium. In four there was subepicardial and mediastinal involvement, and in two the metastases were blood-borne. In three instances there was pericardial effusion, one being sanguineous. One case disclosed obliteration of the pericardial sac by tumor tissue. No electrocardiograms were taken.

Carcinoma of the Kidney

Four of 15 cases in this group had cardiac metastases. Epicardial and mediastinal involvement was present in three instances, while the fourth case had endocardial implants attached to the papillary bundles of the right ventricle. The pericardial sac was obliterated by tumor in one case, and an electrocardiogram disclosed auricular fibrillation and ventricular premature systoles.

Testicular Tumors

Four of nine testicular tumors metastasized to the heart, three via the blood stream and one through lymphatic channels (see fig. 5). In one case there was bloody pericardial effusion. No electrocardiograms were taken.

Other Tumors

In both cases of carcinoma of the stomach the metastases were blood-borne. One case of prostatic carcinoma had hematogenous metastases, while in the other they were lymphatic. In the cases with carcinoma of the bladder and adrenal gland the metastases were via lymphatics, and both cases showed pericardial effusion. The other cases had hematogenous metastases, and none had significant pericardial effusion.

Discussion

The symptoms most frequently listed in cases with heart metastases are tachycardia, dyspnea, cough, cyanosis, precordial pain, arrhythmias, and edema of the lower extremities. Symptoms alone are not diagnostic of myocardial metastasis.

Clinically, the patient with cardiac metastases may exhibit a number of findings suggesting the diagnosis. In addition to the
irregularities of rhythm mentioned above, there may be a pericardial friction rub, heart failure refractory to treatment, pericardial effusion which is often bloody, diminished heart sounds, and falling blood pressure. An occasional case may show the findings of chronic constrictive pericarditis,\textsuperscript{12-16} and rarely there may be sudden death.

The roentgenographic and fluoroscopic changes may be helpful. These include large heart shadow, findings of pericardial effusion, and fixation of a border of the heart. These changes have been given attention in the following reports.\textsuperscript{3, 4, 5, 7, 17}

As stressed by Yater,\textsuperscript{4} the onset of cardiac symptoms or findings of cardiac disease without apparent cause in a patient with known malignancy is highly suggestive of cardiac involvement by tumor.

Electrocardiographic changes in cases with heart metastases have received much attention in the literature. Fishberg,\textsuperscript{18} who was the first in America to report cases of cardiac metastases diagnosed during life, in 1930 noted auricular fibrillation and flutter in his three cases, while Willis and Amber\textsuperscript{19} also in 1930 reported a case diagnosed during life in which the electrocardiogram disclosed incomplete bundle branch block, low amplitude, and T-wave changes.

In 1933 Siegel and Young\textsuperscript{20} reviewed much of the literature concerning electrocardiographic changes and felt that records in tumor cases gave some evidence as to the location of the heart metastases. Scott and Garvin\textsuperscript{8} found auricular fibrillation and flutter and auricular premature contractions the commonest changes in their series. The commonly reported changes include sinus tachycardia, auricular fibrillation and flutter, auricular premature contractions, varying degrees of A-V dissociation, ventricular premature contractions, low voltage, and changes suggestive of myocardial or pericardial involvement, but these changes by themselves are not diagnostic.

The metastatic pathways taken by tumors reaching the heart are usually listed as the blood stream, lymphatics, and direct extension, the last being unusual since the pericardium is a strong barrier.

It is at times difficult to ascertain the exact route taken in myocardial involvement. When mediastinal involvement is marked, continuous retrograde lymphatic permeation can occur, or there may be retrograde lymphatic embolization. We have accepted isolated intramural nodules as hematogenous metastases, though it seems possible that some of these may have begun from small tumor emboli in perivascular myocardial lymphatics.

Willis\textsuperscript{6} has classified involvement as arising from (a) direct nonmetastatic invasion from contiguous growths, via lymphatics, via the venae cavae, and via the pulmonary veins, and (b) true embolic metastasis by endocardial implantation and via the coronary arteries. Morris\textsuperscript{8} in 1927 felt that the hematogenous route was the most common, but one must consider the tumor type when pathways are discussed. True endocardial implants represent an uncommon type of metastasis, and these are discussed by Willis,\textsuperscript{6} Coller and associates,\textsuperscript{21} Nicholls,\textsuperscript{22} and Herbut and Maisell.\textsuperscript{7} In our series, endocardial implants occurred in a case of carcinoma of the pancreas and a case of carcinoma of the kidney. Myocardial nodules may ulcerate through the endocardium and implant within the chambers. We noted this latter occurrence in single cases of malignant melanoma, bronchogenic carcinoma, and carcinoma of a paranasal sinus. Tumors which most frequently implant on the endocardium are those of the genito-urinary tract, chiefly the testicular and kidney tumors, and those of the gastrointestinal tract. In this series no case of direct extension through the venae cavae was noted.

The supposed infrequency of cardiac metastases has been explained in several ways. Recently these were summarized by Priehard\textsuperscript{1} as (a) the strong kneading action of the heart, (b) the metabolic peculiarities of striated muscle, (c) the rapid blood flow through the heart, and (d) the restricted lymphatic connections making retrograde lymphatic extension necessary. Another factor mentioned is that the coronary arteries arise from the aorta at right
angles. Actually, for types of tumors such as bronchogenic carcinoma, carcinoma of the breast, malignant melanoma, malignant lymphoma, and carcinoma of the pancreas and esophagus, cardiac metastases are relatively common.1, 6-9, 23-26

Bronchogenic carcinoma frequently involves the heart usually by way of the mediastinal lymphatics. This mode of spread has been stressed by Morris2 and Willis.6 As early as 1912 Adler27 had noted frequent pericardial and cardiac involvement, and Simpson28 in 1929 found 62 of 139 cases of bronchogenic carcinoma with pericardial invasion. A survey of many case reports emphasizes the frequent pericardial and epicardial involvement with effusion or obliteration of the pericardial space.

It has been estimated29 that half the cases of malignant melanoma show cardiac metastases; these usually follow the hematogenous route and are extensive. Reviews emphasizing secondary melanoma in the heart30, 31 show that few electrocardiographic tracings have been obtained. Certainly, many of these cases terminally should show significant changes in their tracings. The few changes reported are low voltage, sinus tachycardia, and findings suggesting myocardial involvement.

Of the malignant lymphomas, lymphocytic and lymphoblastic lymphosarcoma most frequently involve the heart.7, 32, 33 and this was particularly prominent in our series. The method of extension may be lymphatic, infiltrative, or rarely hematogenous with formation of nodules. Epicardial and pericardial involvement with effusion is the usual finding. Reticulum cell sarcoma shows a somewhat less striking tendency for cardiac metastasis.34, 35 Hodgkin's disease, on the other hand, even less frequently shows cardiac spread. Rotting and Hoffman36 in 1952 reported five instances in a series of 63 cases. Herbut and Maisel7 had 2 instances in 13 cases, while Lucia and co-workers39 noted 3 cases in 18. Other articles concerning Hodgkin's disease with cardiac involvement are those of Harrell,37 Garvin,38 and Ritvo.39

In the malignant lymphomas the most significant involvement is usually in the epicardium and pericardium with effusion or obliteration of the sac, giving findings and electrocardiographic changes of pericarditis and even constrictive pericarditis.

Our cases of carcinoma of the pancreas and esophagus disclosed frequent epicardial and pericardial involvement, and more than half had notable pericardial effusion. This is in agreement with cases reported in the literature.

Observations and Conclusions

The diagnosis of secondary neoplastic spread to the heart offers a challenge to the clinician. If one is alert to this possibility, there are frequently symptoms, signs, and laboratory changes indicating the diagnosis, especially in the patient with known malignant disease. While such a diagnosis is usually of little importance in the patient's course, a few investigators9, 38, 40, 41 have used pericardial aspiration and/or deep roentgen therapy with beneficial though temporary results. Roentgen therapy in these cases, particularly in malignant lymphoma and small cell bronchogenic carcinoma with cardiac spread, deserves further investigation. Pericardial aspiration may help establish the diagnosis if the fluid is examined for tumor cells.

The authors, after a survey of the literature and study of this series of tumor deaths, feel that the following observations are in order.

1. Malignant tumors, particularly bronchogenic carcinoma, malignant melanoma, malignant lymphoma, and carcinoma of the breast, pancreas, and esophagus, involve the heart secondarily with relative frequency.

2. The diagnosis of cardiac spread in these cases can often be made by the alert clinician who makes use of the symptoms, signs, electrocardiographic and roentgen changes often present.

3. While there are no electrocardiographic changes pathognomonic of cardiac metastasis, certain changes do occur, and these show fairly close correlation with the anatomic changes present.

4. Deep roentgen therapy deserves further
study as a means of relieving the embarrassed heart.

**Summary**

A large series of tumor deaths was studied for cardiac metastases in a Veterans Administration hospital. The incidence of cardiac metastasis in this somewhat selected group was 19.1 per cent. The bulk of the cases were bronchogenic carcinoma, malignant melanoma, malignant lymphoma, and carcinoma of the pancreas and esophagus. Correlation of electrocardiographic changes and anatomic findings is given. Likewise, the behavior of the individual types of tumors with reference to pathologic findings is presented.

**SUMARIO Español**

Este artículo es un repaso de 476 casos consecutivos de muertes debido a envolvimiento del corazón por tumor. Este grupo de casos algo seleccionado (de un Hospital de la Administración de Veteranos) muestra una incidencia de metastasis cardíaca de 19.1 en ciento. El volumen de tumores con metástasis al corazón fueron los carcinomas bronquigénicos, melanoma maligno, linfoma maligno, y carcinoma del pancreas y el esófago. Cambios electrocardiográficos fueron frecuentes y correlacionaron bastante cercanamente con la extensión anatómica de la enfermedad. La literatura relacionada se repasa.

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