Clinical Note

Metastatic and Paraneoplastic Cardiomyopathy

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It is well established fact that in the course of their evolution neoplasms can act on the different heart components: endocardium (marantic thrombocarditis), pericardium (pericarditis) and myocardium (cardiomyopathies).

In the last decade, investigations on the influence of neoplasms on the structure and/or function of the myocardium, have greatly increased.

The fact is that the action of tumors on the myocardium can not only be accomplished in a direct way through a metastatic invasion, but also indirectly either by the alterations the neoplasm produces in the body economy (anemia, hypoproteinemia, hydroelectrolytic changes) or as a consequence of the palliative treatments undergone by the patients (radio- or chemotherapy) (Table I).

Besides being acquainted with such manifestations in the tumors is in itself a highly interesting fact not only in case of an eventual heart metastasis, but also because under certain circumstances, the cardiomyopathy represents a greater and more immediate danger for the patient’s life than the neoplasm itself.

Table I. Effects of Neoplasms on the Myocardium

<table>
<thead>
<tr>
<th>1. Direct Action</th>
<th>Endocrine secretions (serotonin, catecholamines)</th>
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<td>Myocardial metastasis</td>
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<td>Cytotoxic polypeptides</td>
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<td>2. Indirect Action</td>
<td>Anemia</td>
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<td>Hypoproteinemia</td>
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<td>Hydroelectrolytic changes</td>
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<td>Antineoplastic treatment</td>
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Metastatic Cardiomyopathies

The metastatic invasion of myocardium known since last century (Hektoen, 1893)\textsuperscript{11} is not an unusual phenomenon; a great number of statistics have been published since that date, which show myocardial participation in the dissemination of different tumors (breast, lung, lymphomas, etc).\textsuperscript{21–20}

Symmers (1917)\textsuperscript{11} shows only 1.6% of myocardial metastasis in 298 autopsies practiced on neoplastic patients.

Burke (1934), describes an incidence of 4.3% of heart metastasis in 327 patients suffering from disseminated tumors.

Pollia and Gogol (1936),\textsuperscript{5} on their part, found 2% of heart metastasis in 12,000 necropsies practiced on neoplastic patients, whereas Scott and Gawin (1939)\textsuperscript{8} described an incidence of 10.9% of myocardial metastasis in 1082 disseminated tumors.

Some time later, Herbut (1942)\textsuperscript{4} presented a 5.4% of heart metastasis on 640 neoplastic patients and Prichard,\textsuperscript{14} a 3.4% in 4,375 disseminated tumors.

As to the origin of the tumors which most frequently invade the myocardium, Bisel and Wroblewski\textsuperscript{11} in 37 cases of metastatic cardiomyopathies, found in a decreasing order: melanoma (60%), breast carcinoma (33%), lung carcinoma (31%), and digestive tumors (6%).

The myocardial neoplastic involvement may take place in 3 different ways:

1—Embolism of tumor cells through the coronary vascular bed.
2—Lymphatic invasion.
3—Direct extension (lung tumors or mediastinum).

Besides, different theories have tried to explain the relatively low frequency of myocardial metastasis: metabolic peculiarities of the heart muscle, lack of lymphatic connections or the speed of the blood flow which goes through it.

Clinically, metastatic cardiomyopathies can develop without any sign or symptom, or they can manifest in a semiological, radiological or electrocardiographic investigation.

In 500 neoplasms, Bisel\textsuperscript{11} found 21% of myocardial metastasis; 8.5% of which had manifested clinically, 6% radiologically and 28.8% through the electrocardiogram.

The principal clinical manifestations of metastatic cardiomyopathies are:

1—Sudden death.
2—Unexplained heart failure.
3—Features similar to subacute bacterial endocarditis.
4—Several kinds of arrhythmias: atrial fibrillation, blocks, etc.
5—Severe coronary insufficiency.
6—Syncopal syndromes (Morgagni-Stokes-Adams).
The ECG alterations are in direct relation to the location of metastasis in the myocardium:
1—Abnormalities in the ST segment and T wave.
2—Atrioventricular block or branch block (especially right one).
3—Atrial fibrillation or flutter.

Generally, a sure diagnosis can only be possible after a necropsy, but nowadays, a pre-mortem diagnosis is more frequently attained due to the fact that we are acquainted with such cases.

**Non-Metastatic (Paraneoplastic) Cardiomyopathy**

In many cases, the physician comes across patients with disseminated neoplasms with clinical-radiological manifestations (cardiomegaly, gallop rhythm, left ventricular failure, etc) or with electrocardiographic evidence (alterations in the ST segment and T wave) showing myocardial involvement, lack of coronary or rheumatic history and with a negative result as far as myocardial metastasis in its post-mortem study (Fig. 1).

Clinically, these manifestations may develop either without any symptoms, or with slight symptoms, or with clear clinical evidence. There is frequently tachycardia (rarely bradycardia), gallop rhythm, apical systolic...
murmurs (AV-valve regurgitation), cardiomegaly or in same cases signs of congestive heart failure (Table II).

In ECG studies, we have very often observed abnormalities in the ST segment (rising or depression), and T wave. Less frequently the PR interval enlargement, premature ventricular beats, and atrial bradycardia.

These clinical-radiological and/or ECG features mentioned above can reverse with the tumor removal. On the other hand, from the point of view of the origin of the neoplasm, the greater incidence of non-metastatic cardiomyopathies has been found in bronchogenic, breast and digestive carcinomas.

Finally, we think it interesting to point out that the clinical-radiological myocardial manifestations already mentioned must be studied in the course of the neoplastic evolution, especially in those cases with lack of rheumatic or coronary precedent, in order to be able to give a correct diagnosis and determine the dissemination of the tumor (metastasis).

**Physiopathology (Paraneoplastic Cardiomyopathy)**

From a physiopathological point of view, the paraneoplastic cardiomyopathies are of a complex kind and they do not generally answer to an exclusive pathogenic cause. In this sense the action of the tumor on the myocardium can be accomplished directly or indirectly: in the first case either by the production of hormones which influence the activity and/or nutrition of the myocardium (catecholamines and pheochromocytoma\textsuperscript{18,19} or 5-hydroxytryptamine and malignant carcinoid\textsuperscript{17}) or by the action of tumor substances and myocardial cytotoxic action. Sylven (1970)\textsuperscript{20,21} has shown in the blood of neoplastic patients the presence of a polypeptide, which acts by interfering with the cellular synthesis of sound tissue, especially in certain organs (liver, myocardium, etc). This polypeptide does not present prosthetic groups in its
structure and has a molecular weight of approximately 1,900.

The neoplasm influences the general condition of the patient bringing about important alterations such as anemia, hypoproteinemia or hydroelectrolytic changes (hypokalemia, hypercalcemia) and, indirectly through this influence, may disturb the myocardial activity. Anemia, which is very common in neoplastic patients, acts on the myocardium from a nutritive point of view (hypoxia) or a hemodynamic one (concomitant hypovolemia). The hypokalemia may either be part of the clinical features of the tumor (bronchogenic cancer with ectopic production of ACT H) or may originate in a loss at gastrointestinal or urinary level (vomits, aspirasions, diarrhea, etc).

The hypercalcemia which may cause serious abnormalities in the cardiac rhythm or heart failure is seen not only in tumors with bone metastasis but also in those with ectopic production of PTH (bronchogenic cancer, etc).

Finally, different antineoplastic palliative treatments (radio-, chemo- or hormone-therapy) may influence the function or structure of the myocardium. As far as radiotherapy is concerned, Rubin has described 3 cases of myocardial fibrosis with final death, in patients with tumors in their thoracic cavity who had been treated with a high dose of radiation.

In spite of the radio-resistance of the myocardium, partial fibrosis prevailing on the right ventricle has been found and one of these cases had a disturbance of the conduction system and AV complete block.

Besides, even if so far there are no concrete experiences in relation to the action of chemotherapeutic drugs in the myocardium, it is certain that by interfering with the synthesis of nucleic acids, they will, in theory, act unfavorably in all the tissues of the economy, including the myocardium.

CONCLUSION

We make a general review of the various clinical, radiological and electrocardiographic features of the cardiomyopathies which may affect the neoplasm in the course of their evolution.

We point out the relative frequency of metastatic invasion of myocardium, especially in melanoma, bronchogenic, breast or digestive carcinomas. We also emphasize the fact that the neoplasms can alter the structure and/or function of the myocardium in a direct way (hormones and cytotoxic polypeptides) or in an indirect one, through its influence on the body economy (anemia, hypoproteinemia, hydroelectrolytic changes) and even as a consequence of the palliative treatment undergone by the patient (radiotherapy, chemotherapy and hormone therapy).

We greatly insist on the absolute need of studying the myocardial manifes-
tations above mentioned in the course of the neoplastic evolution, especially in those cases where there is no rheumatic or coronary history, so as to be able to determine in a correct way the extent of myocardial involvement (paraneoplastic cardiomyopathies) or to make the dissemination of the tumor evident (myocardial metastasis).

REFERENCES

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20. Sylven B: Gaz San 1: 3, 1970