Anaplastic large cell lymphoma with cardiac metastasis.
A case report


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**Abstract:** We present a case of an anaplastic large cell lymphoma (ALCL) in a 61 years old patient with multiple metastases including cardiac metastasis (left posterior ventricular wall). Anaplastic large cell lymphoma, ALCL is a rare condition in adult and cardiac metastasis are extremely rare. Most probably the metastatic spread was a hematogenous invasion via the coronary arteries. Initially a pulmonary small cell carcinoma was diagnosed and the patient underwent a lung partial resection. However, H&E histopathology demonstrated a specific pattern for the tumoral cells (“hallmark” cells); further immune histochemistry (RTU Peroxidase Detection System for Novocastra RTU Primary Antibodies, RE7100-CE), proved to be positive for CD 30, identifying an anaplastic large cell lymphoma, ALCL. Other markers were searched on using IHC techniques in order to confirm the affiliation to the lymphoma family (CD30, CD 3, CD 20 positive) and to exclude the affiliation to the pulmonary carcinoma and neuroendocrine tumors (Pan CK AE1-AE3, TTF1, CK 7, CD56 negative) or pluripotential hemopoietic stem cells or vascular-associated tissue including monocytes/macrophages (CD 34, CD 68 negative).

**Key words:** anaplastic large cell lymphoma, CD 30 positive, immune histochemistry, cardiac metastasis, forensic autopsy

Metastatic tumors of the heart are rather rare cases. Secondary or metastatic tumors in the heart occur more frequently than primary ones, and, according to the published series, their frequency found in necroptic material ranges from 1.6% to 20.6% [1].

The highest percentage of cardiac metastasis has been found in patients with melanoma: related to this disease the frequency may be as much as 46-71% [2].

Other neoplastic diseases which may spread metastatic emboli to the heart are pulmonary carcinoma, leukemia and malignant lymphoma, pancreatic and breast carcinoma. Most frequent localization is in the left ventricle, pericardium and valves. Right atrium involvement is particular rare [1]. On a 11.403 autopsies basis (1972-2004) Rafajlovski S. et al. found cardiac metastasis in 2.7%. Similar frequency and similar affiliation (arising especially from bronchiogenic carcinomas) is reported by many other scientists (1,8%, Wohlgemuth B, Engelstäder A. 1977 [3], Ambrosio GB, 1980, 1,71% [4]).
Metastasis can reach the heart and pericardium by retrograde lymphatic extension, by arterial, lymphatic or direct contiguous extension [5].

Even if for the secondary heart tumours (metastatic), lung cancer constitutes the most common primary location (the most common histological type being non-small cell carcinomas [6], [7]), recently some tumors with unexpected solitary metastasis to the heart, are reported such as urothelial carcinoma of the urinary bladder [8], malignant melanoma [9, 10], hepatocellular carcinoma [11], esophageal carcinoma [12], etc.

Cardiac metastasis are primary necroptic findings. Tumor may involve the heart and pericardium by one of four pathways: retrograde lymphatic extension, hematogenous spread, direct contiguous extension, or transvenous extension [13].

Myocardial metastasis are suggestive of hematogenous invasion [14]. Hematogenous metastasis to the myocardium and epicardium occur via the coronary arteries or, less commonly, by implantation of cancer fragments carried through the vena cava. The microcirculations of the lungs and liver filter most cancerous cells so that only a small number eventually reach the coronary arteries. Therefore, hematogenous metastases in the heart and pericardium are usually accompanied by evidence of hematogenous metastases in other organs [15].

Impairment of cardiac function occurs in approximately 30% of patients and is usually attributable to pericardial effusion [15]. Deaths can be attributed to cardiac tumor invasion in about one-third of patients with cardiac or pericardial metastasis, in whom death is the result of cardiac tamponade, congestive heart failure, coronary artery invasion, or sinoatrial node invasion.

Arrhythmia is the most prevalent manifestation of myocardial involvement by metastatic tumors [15].

Fig. 1 Grey-white bulky tumor in the middle lobe of right lung (7.8/7/4.5 cm)

Fig. 2 Left ventricular metastasis
CASE REPORT

History
A 61 years old male patient, with a previously diagnosed pulmonary carcinoma with multiple metastases, was admitted in the emergency ward care due to high fever, intense left abdominal pain, urinary symptoms (disuria, polakuria), disorientation, aphasia, axilar nodular enlargement, left abdominal tumour.

White blood count cell, 36,0 · 10³/µL, high values of pancreatic enzymes.

Thoracic radiography revealed a nodular opacity in the right middle pulmonary lobe and a tumoral opacity right inferior pulmonary lobe.

Abdominal echo evidenced a transsonic image (14/11 mm) in the liver.

While in the emergency unit the patient experienced a convulsive crisis with subsequent head trauma.

Imagistic investigations failed to reveal the cause of the convulsive episode (skull radiography evidenced two areas of parietal osteolysis; a CT scan revealed moderate cerebral oedema, blood densities intergyra in the Sylvian valley). A control (4 days later) brain CT scan revealed frontal and temporal contusions, hygroma, displacement (3mm) of the right ventricular, system diffuse brain atrophy. Irresuscitable cardiac arrest occurred 7 days following the admission.

Death was investigated by the police due to the accidental head trauma in the hospital.

Necroptic findings: occipital cranium fracture dissecting a right tumoral parietal bone infiltration, 3 areas of osteolysis on the left and right parietal regions, meningeal haemorrhages, large grey-white bulky tumor in the middle right lung lobe.
Anaplastic large cell lymphoma with cardiac metastasis

(7.8/7/4.5 cm)(Fig. 1), heart enlargement (11.5/10/4.5 cm), small grey-white bulky tumor in the left posterior ventricular wall (0.8/0.7/0.5 cm)(Fig. 2), tracheal lymph node enlargement agglutinated in a large tumoral mass.

**Histopathological findings**

The selected tissue samples were formalin-fixed and paraffin-embedded. Sections were cut at 5 microns and stained using the standard H&E stain.

To ensure the reliability of the experimental study, internal quality control of histopathological, HP and immunohistochemical, IHC techniques were performed as a part of an implemented and certified quality assurance system (ISO 9001/2001).

All slides were examined and photographed on a Zeiss AxioImager microscope.

**DISCUSSIONS**

Clinics, pathology, histo-pathology and imaging lead us initially to the assumption that the neoplastic disease is a pulmonary carcinoma.

The large tumor is in the lung (Fig. 3, 4) and a similar small tumor lies in the ventricular wall (Fig. 5, 6) defining a cardiac metastasis. H&E histopathology support the small cell carcinoma diagnostic.

We have performed IHC in order to confirm the diagnostic but Pan CK (AE1-AE3) and CK 7 were negative. Even more TTF1 and CK7 were negative, declining the affiliation to a pulmonary adenocarcinoma.

A negative result for CD56 excluded a neuroendocrine carcinoma either. Extensive IHC research were
undergone for a solid diagnostic: an anaplastic large cell CD30 + lymphoma, ALCL, was confirmed (vimentine positive, CD 30, CD 3, CD 20 positive)(Fig. 7-9). ALCL has a unique appearance under the microscope characterized by cells of different shapes and sizes ("hallmark" cells) and the immunopositivity for CD30.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Product code</th>
<th>Result</th>
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<tr>
<td>Pan CK</td>
<td>AE1, AE3</td>
<td>PA0909</td>
<td>Negative</td>
</tr>
<tr>
<td>CK 7</td>
<td>RN7</td>
<td>PA0942</td>
<td>Negative</td>
</tr>
<tr>
<td>TTF1</td>
<td>SPT24</td>
<td>PA0364</td>
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<td>CD 56</td>
<td>CD564</td>
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<td>Vimentin</td>
<td>V9</td>
<td>VIM-V9-R-7-CE</td>
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<td>1G12</td>
<td>CD30-R-7-CE</td>
<td>Positive (diffuse highly)</td>
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<td>LN10</td>
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<td>L26</td>
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<td>CD 34</td>
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<td>CD 68</td>
<td>514H12</td>
<td>PA0273</td>
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Table I  Cummulative IHC tabel antibodies-results. Diagnostic: Anaplastic Large Cell Lymphoma, CD30+.
*Bone marrow

The hallmark cells are of medium size and feature abundant cytoplasm (which may be clear, amphophilic or eosinophilic), kidney shaped nuclei, and a paranuclear eosinophilic region.

Occasional cells may be identified in which the plane of section passes through the nucleus in such a way that it appears to enclose a region of cytoplasm within a ring; such cells are called "doughnut" cells.

CD 34 characteristic to pluripotential hemopoietic stem cells or vascular-associated tissue is negative declining

CD 68 is also negative expressing no affiliation to the monocytes/macrophages.

Fig. 7  Positive reaction for vimentin in lung metastasis (40X)
Lymphoma is a cancer of the white blood cells, namely lymphocytes. The two main types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma.

Nearly all non-Hodgkin lymphoma cases occur in adults. Anaplastic large cell lymphoma (ALCL) is a rare type of aggressive T-cell lymphoma, comprising about 3 percent of all non-Hodgkin lymphomas in adults. This type of lymphoma can present in either the systemic (throughout the body) or cutaneous (skin) form.

There are two subtypes of ALCL, ALK (anaplastic lymphoma kinase) positive (70% of cases) and ALK negative (it specifically excludes primary cutaneous T-cell lymphomas and other specific types of anaplastic lymphoma (particularly those of B-cell lineage) with CD30 positivity): ALK negative is more commonly found in older patients over age 60.

A useful marker which helps to differentiate from Hodgkin lymphoma is Clusterin.

There are 4 clinical stages: stage IV involve wide-spread disease [16].

The case presented is an ALCL stage IV spread beyond the lymph nodes and spleen to the lung and bone marrow.

Molecular biology sustain that the vast majority of cases (> 90%), contain a clonal rearrangement of the T-cell receptor.

Oncogeneic potential is conferred by upregulation of a tyrosine kinase gene on chromosome 2 which implies several different translocations: the most common involves the nucleophosmin gene on chromosome 5. The product of this fusion gene may be identified by immunohistochemistry using antiserum to ALK protein.
CONCLUSIONS

A chronic severe pathology which normally leads to natural death may turn in some particular circumstance into a violent death. Autopsy keeps indication in sudden death of unknown cause of death. This case associate both violent mode and unknown cause of death in a hospital settlement.

Anaplastic large cell lymphoma, ALCL is a rare condition in adult.

Exceptionally rare are the cardiac lymphoma metastasis in adults [17-24]. The case presented was found to have metastasis in lung, bone marrow, lymph nodes and the left posterior ventricular wall.

Most probably the metastatic spread was a hematogenous invasion via the coronary arteries.

ALCL should be added to the list of differential diagnoses of cardiac lymphomas but notably of the cardiac metastasis.

References

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