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Metastases to the heart in the course of bile duct cancer (*adenocarcinoma cholangiogenes*)

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The diagnosis of metastases to the heart (MH) is seldom observed in clinical practice.
Literature shows that MH were observed at autopsy in histological specimens of 8.4% patients with primary neoplasms. In men they were derived from mesothelioma, malignant melanoma, and lung carcinoma, whereas in women – from malignant melanoma, lung and renal cancer. Sarcomas and lymphosarcomas also cause MH.
The presence of MH or their lack has significant therapeutic implications as they worsen the prognosis of survival.
Metastases to the heart, in most cases, have been diagnosed at autopsy. There are very few clinical reports dealing with diagnosis of intravital presence of MH.
There is no description of their derivation from bile ducts in accessible literature.
We describe a case of MH in a patient aged 69 yrs. with a long-term history of arterial hypertension, after severe cerebral stroke and pulmonary oedema with carcinoma from bile ducts (adenocarcinoma cholangiogenes). The precise final diagnosis of the cancer type was based on microscopic examination of the samples taken at autopsy. The malignant cells indicated moderately differentiated tubular adenocarcinoma cholangiogenes Immunohistochemical examination showed a positive reaction to cytokeratin 19 and 7 and negative reaction to cytokeratin 20. In the heart and lung samples micrometastases of moderately differentiated tubular adenocarcinoma were found, which allowed us to diagnose micrometastases to the heart spreading through the coronary vessels.
The described case, as well as medical literature, shows the necessity to look for the presence of MH, even while diagnosing malignancies, which seldom cause metastases.

Przerzuty do serca w przebiegu raka dróg żółciowych (*adenocarcinoma cholangiogenes*)

Przerzuty do serca (MH) są nieczęsto rozpoznawane w codziennej praktyce lekarskiej.
Dane literaturowe podają, iż MH występują w 8,4% badań histologicznych tkanek pobranych autopsyjnie od chorych z pierwotnym nowotworem. U mężczyzn przerzuty do serca występują najczęściej w przypadku międzybłoniaka, czerniaka złośliwego i raka płuc, a u kobiet czerniaka złośliwego, raka płuc i nerki. Mięsaki i chłoniaki złośliwe również dają przerzuty do serca.
Obecność MH ma znaczenie dla wyboru metody leczenia. Ich obecność pogarsza rokowanie.
W większości przypadków MH są rozpoznawane na podstawie badania pośmiertnego. Niewiele jest opisów literaturowych rozpoznania przerzutów do serca za życia chorego.
W dostępnej literaturze nie ma opisu MH w przebiegu raka dróg żółciowych (adenocarcinoma cholangiogenes).
Artykuł dotyczy opisu 69-letniej chorej z rakiem dróg żółciowych i przerzutami do serca. Chora ta od lat miała nadciśnienie tętnicze, oraz przebyła udar mózgu i obrzęk płuc. Ostateczne rozpoznanie typu nowotworu zostało postawione na podstawie badania mikroskopowego tkanek pobranych w trakcie badania pośmiertnego. Naciek nowotworowy był zbudowany z umiarkowanie zróżnicowanego cewkowego gruczolakoraka dróg żółciowych. W badaniu immunohistochemicznym stwierdzono dodatnią reakcję na cytokeratynę 19 i 7 oraz ujemną na cytokeratynę 20. W skrawkach z serca i płuc uwidoczniono

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mikroprzerzuty umiarkowanie zróżnicowanego gruczolakoraka cewkowego. Rozpoznano mikroprzerzuty do serca, szerzące się drogą naczyń wieńcowych.
Opisany przypadek, a także dane literaturowe wskazują na konieczność poszukiwania obecności MH nawet wtedy, kiedy u chorego występuje nowotwór rzadko powodujący przerzuty.

Key words: cancer of bile ducts (*carcinoma cholangiogenes*), primary neoplasm of the heart, metastases to the heart
Słowa kluczowe: rak dróg żółciowych (*carcinoma cholangiogenes*), pierwotny nowotwór serca, przerzuty do serca

The diagnosis of metastases to the heart (MH) is seldom made in clinical practice. The presence of MH or their lack has great therapeutic implications. According to Silvestri and al. [1], metastases to the heart observed at autopsy in histological specimens are present in 8.4% patients with primary neoplasms and are more common in younger patients..

We report the case of MH in a patient with carcinoma from bile ducts (*adenocarcinoma cholangiogenes*).

Case description

A 69-year old woman (hospital reg. no. 301/03) with a long-term history of arterial hypertension, after severe cerebral stroke and pulmonary oedema, with a 3-year – earlier diagnosed hypochronic anaemia and carbohydrate intolerance was hospitalised due to epigastric pain, weakness, and loss of weight. The symptoms had been increasing for 2 months. A few days before hospitalisation, an abdomen ultrasonographic examination had been performed in an outpatient department. The examination showed a great number of heterogenic and hypoechogenic irregular structures in both liver lobes. In the right liver lobe a 1.5 cm calcification could be observed, as well as non-enlarged intrahepatic ducts and the choledochus. The portal vein system had normal dimensions and non-thickened wall gallbladder was described which was echo-negative.

The patient had smoked 10 cigarettes per day for 20 years and had given up smoking 2 months before hospitalisation. In family anamnesis: the patient's father had died due to cerebral stroke and her daughter had breast cancer.

On admission the doctor diagnosed pain on palpation in the right subcostal area, scoliosis in the lumbosacral part of the vertebral column, asymmetry of tendon reflexes (L > R), considerable hypoacusis and slowness of the cognitive processes (26 points MMSE scale). Laboratory results showed: leucocytosis (14 600 l/ml), slight hypochromia and microcytosis of erythrocytes. The erythrocyte count and the hemoglobin level were normal. Serum aminotranspherases, alkaline phosphathase and gammaglutamyl-transpeptidase activity were increased.

Urinalysis showed trace amounts of protein.

The serum level of the Ca 125 antigen was over 600 U/ml (normal: 35 U/ml) and the level of alphafetoprotein was within normal range. The blood glucose curve was incorrect.

ECG showed a regular sinus rhythm of 72 bpm, slight depression of the ST segment, flat (+-) T wave in leads I, aVL,V6 and a 2 mm ST segment depresson in leads V4 and V5. Ultrasonocardiographic examination revealed: dilatation of both the left cardiac cavities, thickening of the interventricular septum, impaired diastolic compliance of the left ventricle, III/IV degree mitral insufficiency, 1st degree aortic insufficiency and 2nd degree tricuspid insufficiency, as well as thickening of the mitral leaflets. During this examination the hypokinesis of the whole heart was registered with EF of 40%.

Chest X-ray examination revealed higher lung markings, especially in lower parts; the silhouette of the heart was adequate to the patient's age.

Gastritis was observed on endoscopy and an observable polyp (of 1cm) on a short pedicle in the the first part of the sigmoid was found during coloscopy.

For the first six days of hospitalisation the patient was in good overall condition. Then, over a few hours, the abdominal pain increased, the patient showed symptoms of hepatic failure, acute renal insufficiency, shock, pulmonary oedema, and disseminated intravascular coagulation with evident anaemia. On physical examination her abdomen was tense and flatulent. Lacerating pain was present in the epigastrium. Laboratory examination showed the aminotranspherase activity of a few thousand U/ml.

ECG registered ST depression of 6 mm in the precordial leads (from V2 to V6) and negative T waves in II, III, aVF, V3-V6 leads.

Despite intensified treatment the patient died.

Neoplasma (suspected as primary carcinoma of the liver) was diagnosed in macroscopic autopsy. Symptoms of haemorrhagic diathesis in the brain, stomach and intestines, pulmonary and cerebral oedema and shock kidney were an additive finding. On addition we observed intensified atherosclerosis of the aortal arcus and the abdominal aorta.

The hepatic tumor was multifocal, with widely distributed greyish-white nodules of variable size involving the entire liver. Microscopically, the carcinoma cells indicated moderately differentiated *tubular adenocarcinoma cholangiogenes* (Figure 1). Immunohistochemical examination showed a positive reaction to cytokeratin 19 and 7 (Figure 2) and a negative reaction to cytokeratin 20 (Figure 3). In the heart (Figure 4) and lung (Figure 5) samples we found micrometastases of moderately differentiated *tubular adenocarcinoma.*

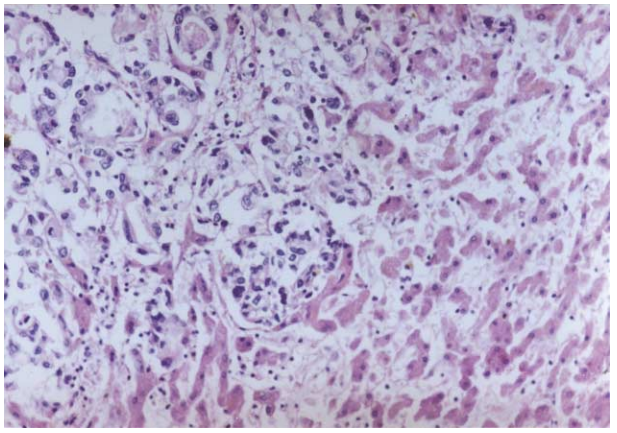

Figure 1. Photomicrograph of the liver tumor shows moderately differentiated *tubular adenocarcinoma* (HE;200x)

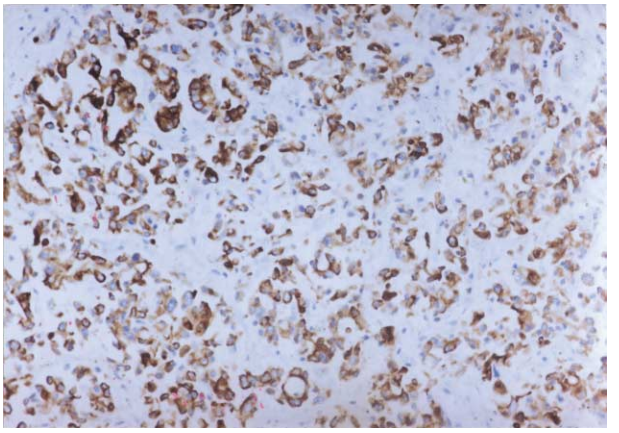

Figure 2. Photomicrograph of the liver tumor shows positive cytokeratin 7 staining (CK7;200x)

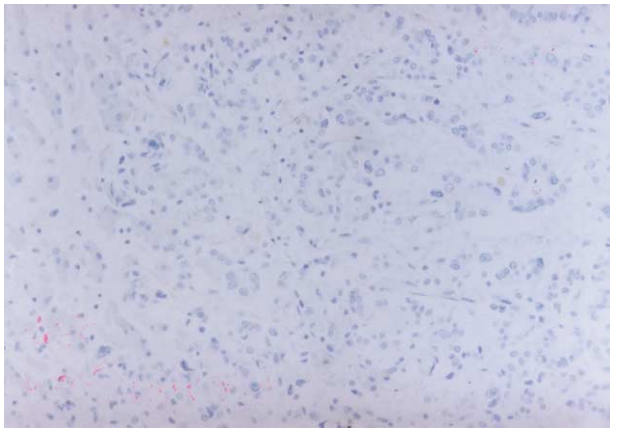

Figure 3. Photomicrograph of the liver tumor shows negative cytokeratin 20 staining (CK20;200x)

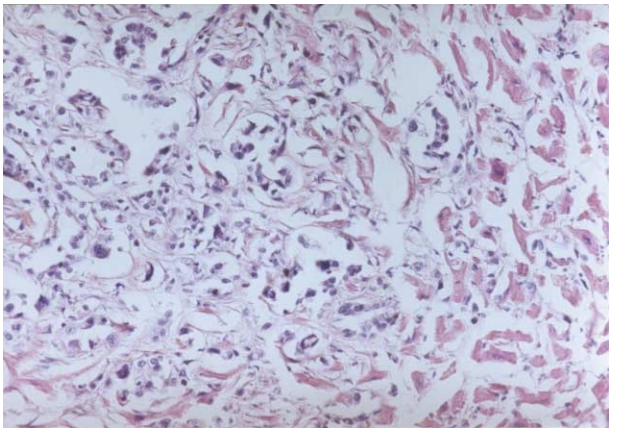

Figure 4. Photomicrograph of the myocardium shows *adenocarcinoma micrometastases* (HE;200x)

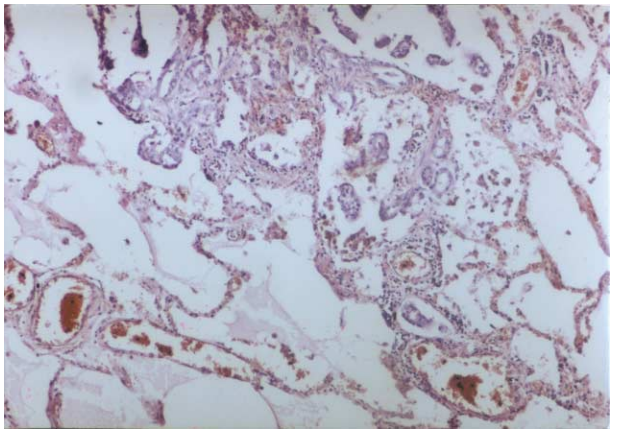

Figure 5. Photomicrograph of the lung shows *adenocarcinoma* metastases (HE;100X)

Microscopic examination showed carcinoma of the bile ducts (*adenocarcinoma cholangiogenes*). The heart and lung samples were also taken for microscopy. In both those organs we discerned the presence of *adenocarcinoma micrometastases*. The immonohistochemical staining of these samples was not performed as material with micrometastases was not avalaible.

Discussion

Metastases to the heart are more frequent than primary heart neoplasms and their occurrence worsens life prognosis.

Metastases to the heart and pericardium spread in four ways: retroactively through lymphatic vessels, with either the arterial or the venous blood stream, and by direct infiltration [2]. Silvestrii and al. [1] observed during autopsy, that in men metastases to the heart are derived from mesothelioma, malignant melanoma, and lung carcinoma (100%, 50% and 31% respectively), whereas in women – from malignant melanoma, lung and renal cancer (42%, 26% and 20% respectively). Sarcomas and lymphosarcomas also cause metastases to the heart [2-6].

There is no description of MH derivation from bile ducts in accessible literature. Metastases to the heart, in most cases, have been diagnosed at autopsy [1, 2, 4, 7]. There are very few clinical reports dealing with the intravital diagnosis of metastases to the heart [2-6, 8]. The location of metastases can be in the endocardium, in the valvular endocardium, the myocardium and the pericardium.

MH can cause elevation of the ST segment, which should compel the doctors to differentiate between its MH origin and myocardial ischaemia [8]. If the MH are located in the left heart atrium, they can cause, or be symptomatic of, mitral stenosis [5]. Rupture of the right atrium induced by MH causes cardiac tamponade [4]. Atrial fibrillation, peripheral embolisms (3), heart failure and chest pain (2) were also described in literature.

X-ray examination, ultrasonocardiography, computer tomography and magnetic resonance imaging are all helpful in the diagnostic processes [2, 5, 6].

In this particular case the diagnosis of MH was stated during autopsy.

Disorders in ECG examination occurring during the patient's life could be connected to earlier, carelessly treated arterial hypertention with organic complications including acute left ventricular failure.

The multiorgan insufficiency, directly causing death, was probably due to the progression of neoplastic disease, while the massive dissemination of neoplasmatic cells before the patient's death could have caused the intensified ECG disorders.

The precise final diagnosis of the type of cancer was based on microscopic examination which allowed us to discern micrometastases to the heart spreading through coronary vessels.

The described case, as well as medical literature, show the necessity to look for the presence of MH, even while diagnosing those neoplasms which seldom cause metastases. The presence of metastases to the heart directly implicates the choice of medical treatment and survival prognosis.

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