WORLD JOURNAL OF MEDICAL INNOVATIONS

Malignant pleural mesothelioma with cardiac and renal metastases: a case report confirmed at autopsy

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Article info

PATHOLOGY

Case report

Article history:
Accepted August 17, 2021

Published online
December 5, 2021

Keywords:
mesothelioma,
malignant,
neoplasm metastasis,
myocardium,
kidney

Abstract

Objectives. The presentation of case report of cardiac and renal metastases from malignant pleural mesothelioma. Material and methods. An 80-year-old male with epithelioid mesothelioma for 9 years, without asbestos exposure was admitted to hospital with multiorgan failure manifested by acute respiratory heart and renal failure. Patient died despite the resuscitation. An autopsy followed by histological examination was performed. Results. The autopsy revealed a whitish lesion up to 6.6 cm and a lot of whitish lesions measuring 0.4 cm in diameter with irregular shape throughout the visceral pleura. Left ventricular wall of the heart was with solid whitish irregularly shaped lesion placed intramurally up to 0.6 cm in diameter and left ventricular free wall was 1.6, accordingly. Right ventricular free wall was 0.6 cm. A solid whitish lesion up to 1.1 cm in diameter was found in the middle third of left kidney as well. Histologically the visceral pleura lesion was presented by epithelioid mesothelioma consisted of tubules, papillae, solid and adenomatoid pathomorphism. Some sections of the myocardium of left ventricle and cortex of left kidney were with tumor cells presence. Conclusions. A case report of unusual metastatic lesion is presented to enrich an already existing literature database. Attention should be paid to the antemortem searching of clinically asymptomatic metastases.

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Introduction.

Malignant pleural mesothelioma (MPM) is a relatively rare variant of cancer, arises from multipotential mesothelial cells of the pleura, closely related to previous asbestos exposure with an unfavorable prognosis for survival [1, 2, 3]. MPM occurs in elderly people (median age 70 years) and is more common in males than females with a ratio of 3:1, respectively [4]. Histological variants of MPM are presented by three subtypes: epithelioid (60%), sarcomatoid (10-20%) and biphasic (20-30%), which are often difficult for the pathologist to distinguish because of disease's rarity and noninformative tissue samples obtained during life-time diagnostics [5,6]. The invasion of surrounding organs is typical for MPM, and more rarely distant metastases occur [7]. There are a few reported cases of unusual sites for MPM

metastases, namely salivary glands, pancreas, stomach, duodenum, ileum, and rectum [8].

Objectives.

The presentation of case report of cardiac and renal metastases from malignant pleural mesothelioma.

Material and methods (Case presentation).

An 80-year-old male, who had an anamnesis of MPM for 9 years, was admitted to hospital with multiorgan failure manifested by acute respiratory failure (type I), heart failure, renal failure. The patient was not a smoker. Also, he did not have prior asbestos and extra-radiation exposure. Ischemic heart disease was a concomitant disease. The diagnosis of MPM was suspected on contrast-enhanced computed tomography scan and confirmed by lifetime pleural biopsy performed during thoracoscopic surgery followed by histology of postoperative biomaterial (epithelioid pattern) and immunohistochemical stains (CK 5/6 +, calretyn +, WT-1 +). Patient had combined treatment, including a platinum-based therapy and palliative care in the last year of his life. The intensive treatment was carried out, despite which clinical death occurred at the emergency medical department. Resuscitation was performed but had no effect and biological death was recorded. The body was sent for the autopsy to Pathology Department. The basis of data processing was the written consent of the legally authorized person of the deceased patient. Autopsy findings. The descendent was an elderly male of average built. During the external examination no external injury was present. The skin was clean with pale conjunctivae. Lower extremities were without edema. Visceral and parietal pleura tightly fused to throughout on both right and left sides during macroscopical examination of thoracic cavity. There was a solid whitish lesion in the visceral pleura at the level of lower lobe of right lung which reached 6.6 cm and visually invaded the lung tissue (Figure 1A).

Figure 1. Macropathologic autopsy findings: A. Part of visceral pleura with adjacent lung tissue. On the right - a whitish lesion with indistinct margins. B. Left ventricular wall with whitish lesion placed intramurally of heterogeneous structure with indistinct margins. C. Part of left kidney with subcapsular whitish lesion up to 1.1 cm in diameter.

There were a lot of whitish lesions measuring 0.4 cm in diameter with irregular shape throughout the visceral pleura. Abdominal cavity was without pathological contents, peritoneum was smooth. Gross examination of the blood vessels revealed yellowish areas of aorta's intima with multiplication of small plaques up to 0.4 cm in size some of which were with calcifications. The orifices of the mesenteric and renal arteries were passable. The pericardial cavity contained up to 50 ml of serous yellowish liquid. The heart measures were 13 x 10 x 8 cm. The myocardium was brown with a few small whitish lesions up to 0.1 cm. Right ventricular free wall thickness was 0.6 cm and left ventricular free wall was 1.6, accordingly. There was a solid whitish irregularly shaped lesion placed intramurally up to 0.6 cm in diameter (Figure 1B). Heart valves were not changed. The intima of coronary vessels was yellowish and the patency of them was preserved. The parietal thrombi and partly liquid and coagulated blood were determined in heart chambers. Bronchial wall thickening was not observed. The mucous membranes of the trachea and main bronchi were edematous covered by semi-liquid bloody mucus. During the section it was found the upper lobes and middle lobe of both lungs were variegated; lower lobes had large areas of reddish consolidation with a few pinkish zones on the front surface of lungs. The moderate amount of foamy bloody fluid was seen in the section of lungs. A solid whitish lesion up to 1.1 cm in diameter was found in the middle third of left kidney (Figure 1C). The structure of right kidney was unchanged. There were no visible tumor, infarction or obvious abnormalities in the liver, esophagus, stomach, pancreas, biliary tract, small and large intestine, thyroid, adrenal glands, spleen. The polymerase-chain reaction for acute severe respiratory syndrome coronavirus 2 of postmortem biomaterial of trachea, bronchi, and lungs was negative as well as antigen rapid test performed in the emergency department.

Histologic features. During the microscopic examination of lung tissues alveolar edema with focal inflammatory infiltration, formation of microvascular thrombosis was revealed. The lesion of visceral pleura tissue is presented by epithelioid mesothelioma with combination of tubules, papillae, solid and adenomatoid components (Figure 2A). Small fibrotic foci in the myocardium, moderate thickening and sclerosis of blood vessels walls with perivascular fibrosis were seen in paraffin-embedded myocardial tissue. Some sections from the heart and left kidney were with tumor cells presence (Figure 2B and 2C). Histopathological studies of right kidney, liver, pancreas, spleen, and stomach were unremarkable.

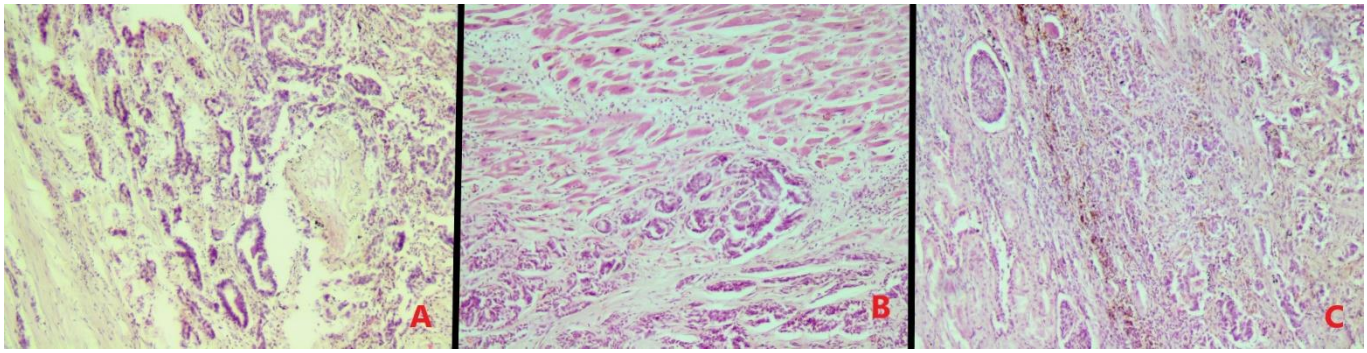

Figure 2. Histologic findings (hematoxylin and eosin-stained section; original magnification x 20 A. Epithelioid malignant mesothelioma: prominent tubular and papillar architecture, solid areas and adenomatoid structures are visualised. B. Myocardial tissue with invasion of malignant mesothelioma's metastatic lesion. C. Left kidney cortex with metastatic lesion of malignant mesothelioma.

Case Discussion.

In the present case we report about postmortem metastatic findings of the lifetime confirmed MPM. Since the antemortem diagnostics was performed in full and the determination of survival, treatment sensitivity and prognosis were definitely not our task, the routine staining methods were used. Also, electron microscopy is used occasionally in equivocal cases and not recommended for daily practice because of time- and resource-consuming and is no more useful with immunohistochemistry [9,10]. Autopsy is the gold standard for retrospective analysis of lifetime video-assisted thoracoscopic surgery and allows to find metastases not visualized antemortem [11, 12]. The difficulty in lifetime identifying MPM metastases, especially distant ones, is a major cornerstone in the search of improvement and development of new radiological protocols and has long-term significance. Since there still remains a paucity of documentation of the radiology patterns of MPM metastatic spread, just autopsy case reports and their analysis is main source of metastatic spread pathway especially in unusual, rare locations [13]. In series of S. Wadler et al., of 19 autopsies, invasion to the heart was determined in 14 (74%), with more than half to the pericardium and more than one quarter to the myocardium layer [14].

In fact, secondary cardiac tumors are 30 times as frequent as the primary ones [15]. The overall prevalence of cardiac metastasis ranges between 2.3% to 18.3% considering the theory of possibility of any malignancy to metastasize into the heart [16]. Cardiac metastases thereby are often not detected until necropsy. Most of them are clinically silent and can be suspected just during life-threating conditions like fatal cardiac tamponade or pericardial constriction. Since MPM is one of the most aggressive type of cancer the direct invasion of tumor cells into pericardial sac is possible pathway. Lymphatic spread is typical for pericardial metastases as well. Hematogenous pathway prevails for myocardial metastases placement. A case series and cohort study of cardiac metastases spreading into cardiac cavity demonstrate the pathways including invasion of lung parenchyma and permeating the vessels following by tumor embolus into left atrium via pulmonary vein. For the right-sided cardiac metastases appearance the superior vena cava should be involved and used as a pathway for tumor spreading into right atrium [17, 18]. The incidence of renal metastases detected in autopsy series is estimated between 2.36-12.6% and has a much higher prevalence than clinically antemortem ones found [19]. The exact mechanism of tumor spread to the kidneys is not sufficiently known. First pathway is hematogenous when cancer cells detached from primary location can go to the

arterial circulation following by directly to the kidney. Other mechanism is well-known as "metastasis from metastasis" and includes multiple steps: primary tumor spreads cells to one organ, then some metastatic cells are detached from there and disseminate kidneys. Also, there is pathway when some cancer cells skip some organ on the way and go specifically to another one [20]. All abovementioned different mechanisms of cancer spreading explains current unusual case with absence involving of lungs, but present cardiac and renal secondary lesions. An available literature analysis of reported cases is presented in Table I. As can be seen in previous 9 reports the median age was 68 years old with significant male predominance over female with a ratio 6:3, respectively. 8 cases were an autopsy analysis, and 1 case was the result of biopsy. 7 case reports of metastatic spreading to the heart and 2 cases of kidney secondary lesions were revealed with different histologic types of MPM.

Table I. Case reports of malignant pleural mesothelioma metastases.

№	Reference	Sex	Age (years)	Asbestos exposure	Histologic type of MPM	Cardiac metastases	Renal metastases	Location of metastases according to autopsy / biopsy
1	Olds J et al (1974) [21]	F*	63	NM*	NM	+*	-*	Left ventricle with obstruction of mitral valve
2	Walters L, Taxy J (1983) [22]	M*	70	NM	Biphasic	+	-	Right atrium with occlusion of the tricuspid orifice
3	Grellner W, Staak M (1995) [23]	M	54	+	Biphasic	+	-	Pericardium, heart.
4	Ishiyama Yet al (1998) [24]	F	78	-	NM	+	-	Tumor embolus in the left atrium
5	Sencottaiyan N et al (2006) [25]	M	71	+	Sarcomatoid	+	-	Left ventricular endocardium
6	Ushio R et al (2015) [26]	M	73	+	Epithelioid with deciduoid features	+	+	Left kidney
7	Zardawi S et al (2015) [27]	M	67	+	Biphasic	-	+	Left kidney cortex
8	Kabbash M et al (2020) [28]	M	71	NM	Epithelioid	+	-	Cardiac interventricular septum with the involvement of the endocardium
9	Fukui T et al (2021) [29]	F	62	-	Biphasic	+	-	Heart
10	Present case	M	80	-	Epithelioid	+	+	Myocardium of left ventricular wall. Left kidney cortex

*"+" present. "-" absent. M – male. F – female. NM – not mentioned.

Conclusions.

A case report of unusual metastatic lesion is presented to enrich an already existing literature database. Attention should be paid to the antemortem searching of clinically asymptomatic metastases.

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