

Current status of malignant mesothelioma with liver involvement in China: A brief report and review of the literature

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Summary

Primary and secondary intrahepatic malignant mesothelioma (PIHMM & SIHMM) caused by Peritoneal mesothelioma (PM) are extremely rare tumors and their clinicopathological characteristics remain unclear. The current study presented a case of a 63-year-old female with PIHMM and a literature review of Chinese case reports of SIHMM and PIHMM was performed. The patient received curative left hemihepatectomy because of a $5.5 \times 5.0 \times 4.0$ cm mass occupying the II, III and the lateral portion of the IV segments and meanwhile tightly infiltrating the diaphragm (yellow arrow) was also observed. The pathological diagnosis was epithelial type PIHMM. Immunohistochemistry revealed that the tumor was positive for Calretinin, CK5/6, WT-1 and D2-40(N). The literature review included 11 studies and 6 case reports with a total of 293 PM patients accompanied with 31 SIHMM cases and then 3 case reports of PIHMM. SIHMM and PIHMM are extremely rare, easy to misdiagnose malignant tumors. Immunohistochemistry should be performed strictly in accordance with guidelines, which is crucial for pathological diagnosis. Comprehensive treatment of surgery combined with chemotherapy are mainstream methods for SIHMM and PIHMM. Also, exact survival data should be carefully explored so that objective evaluation of the efficacy of the treatment could be achieved.

Keywords: Malignant mesothelioma, liver involvement, China

1. Introduction

Malignant mesothelioma (MM) are tumors of the mesothelial cells which usually arise from the pleura, peritoneum, pericardium and occasionally, the tunica vaginalis. Approximately 20-35% of all the MM are peritoneal, just next to pleural mesothelioma (60-65%) (1-4). Peritoneal mesothelioma (PM) has characteristics of constant invasion of the adjacent visceral organs but infrequent metastasis to the liver (5-7). Besides secondary intrahepatic malignant mesothelioma (SIHMM), primary intrahepatic mesothelioma (PIHMM) was also reported with only less than 20

case reports from around the world so far, and is not yet included in the World Health Organization (WHO) classification of hepatic tumors (8). Therefore, PIHMM and SIHMM are too easy to misdiagnosis as HCC or metastatic liver tumors in routine clinical work.

Notably, a considerable proportion of case reports of PIHMM and SIHMM come from China. However, until now, there is still lack of a systematic summary of this rare disease in China regarding etiology, epidemiology, diagnosis, pathology and treatment. The present study provides a case report accompanied with a detailed literature review of Chinese reports, which aims to raise the awareness and improve the quality of therapeutic effects for the extremely rare PIHMM/SIHMM.

2. Materials and Methods

The current study presented a case of a 63-year-old female with PIHMM and a literature review of Chinese case reports of SIHMM and PIHMM was performed. The study was approved by the ethics committee of XinHua Hospital affiliated to Shanghai JiaoTong

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Two investigators (DZ and WJD) performed the literature search independently by using Pubmed, Embase, ISI and "CNKI (Chinese)", "WANFANG (Chinese)", "WEIPU (Chinese)" databases between January 1970 and April 2018. The search was limited to humans. The search strategy was based on the following English Medical Subject Heading terms (MeSH) and its correspondent Chinese text words: "mesothelioma", "malignant mesothelioma", "peritoneal mesothelioma", "intrahepatic mesothelioma", "primary intrahepatic mesothelioma", "secondary intrahepatic malignant mesothelioma", "SIHMM", "PIHMM". The related article's function and reference lists were used to broaden the search. The investigators and experts in this field ensured that all potentially relevant reports were identified. No restriction was set for languages or date of publication. When further information was required, the corresponding authors of relevant papers were contacted by the reviewers.

3. Results and Discussion

3.1. Characteristics of the patient

A 63-year-old female presented with upper abdominal pain that occurred when she rolled over during her sleep for half a year and was admitted to Department of General Surgery, XinHua Hospital affiliated to Shanghai JiaoTong University, School of Medicine in March, 2017.

She has no history of asbestos exposure or special pathogen infection. Laboratory examinations revealed no abnormal results concerning the blood routine index, liver and renal function, or tumor markers. Viral markers related to hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, or human immunodeficiency virus (HIV) infection were all negative. The gastroscopy examination showed a flat bulge of about 2.5×2.3 cm with a smooth surface mucous membrane in the upper part of the stomach (Figure 1A). The endoscopic ultrasonography (EUS) confirmed the above lesion as an external compression caused by the left lobe of the liver (Figure 1B). Several hypoechoic areas with clear boundary and inhomogenous internal echoes in the left-lateral lobe were detected by abdominal ultrasound. Further color Doppler flow image (CDFI) detected no blood flow signal in this lesion. The MRI revealed a 6.4×4.0 cm mass occupying the left-lateral hepatic lobe presenting an unclear boundary with the front edge of the stomach. The mass was shown as hypo-intensity on T1WI, while slightly hyper-intensity on T2WI signals (Figure 1C and 1D). Abnormal conditions were not found in pancreas, gallbladder, spleen, adrenals, kidneys, bowel loops and the pelvic cavity. There was no evidence of ascites, pleural effusion, thickening or a peritoneal malignant

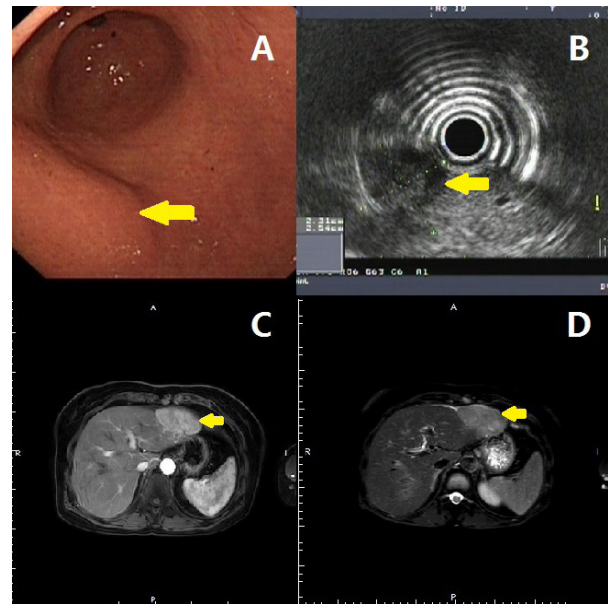


Figure 1. Diagnosis of the present case of PIHMM. Gastroscopy showed a flat bulge of about 2.5×2.3 cm with a smooth surface mucous membrane in the upper part of body of the stomach (yellow arrow) (A). The endoscopic ultrasonography (EUS) confirmed the above lesion as an external compression caused by the left lobe of the liver (yellow arrow) (B). The MRI revealed a 6.4×4.0 cm mass occupying the left-lateral hepatic lobe presenting an unclear boundary with the front edge of the stomach. The mass was showed as hypo-intensity on T1WI and peripheral serpiginous vessels were shown (yellow arrow) (C), while slightly hyper-intensity on T2WI signals (yellow arrow) (D).

tumor. The suspected diagnosis of Focal Nodular Hyperplasia (FNH) or exogenic gastric stromal tumor (GIST) was made by the MRI radiological doctor.

The patient then received an exploratory laparotomy. There was no significant ascites or metastasis sign in the abdominal cavity. A soft, $5.5 \times 5.0 \times 4.0$ cm tumor occupying the II, III and the lateral portion of the IV segments and meanwhile tightly infiltrating the diaphragm was also observed (Figure 2A, 2B and 2C). No enlarged lymph node was detected in the hepatoduodenal ligament (HDL), around the stomach, retroperitoneum or pelvis cavity except a $5.5 \times 5.0 \times 4.0$ cm nodule was found beneath the diaphragm. Therefore, complete resection of the left hepatic lobe was performed. Hepatic portal occlusion utilizing the Pringle's maneuver was conducted twice for 5 and 13 minutes, respectively. The beneath diaphragm nodule was also resected and a negative margin was obtained. The intraoperative blood loss was approximately 300 mL and a drainage tube was placed into the foramen of Winslow before abdominal closure.

No complications including postoperative bleeding, liver dysfunction or bile leakage occurred and the drainage tube was removed at the 7th postoperative day (7 POD). The patient was discharged uneventfully at 10 POD. The pathological diagnosis was epithelial type PIHMM and surgical margins were free of tumor (Figure 2D and 2E). The beneath diaphragm nodule

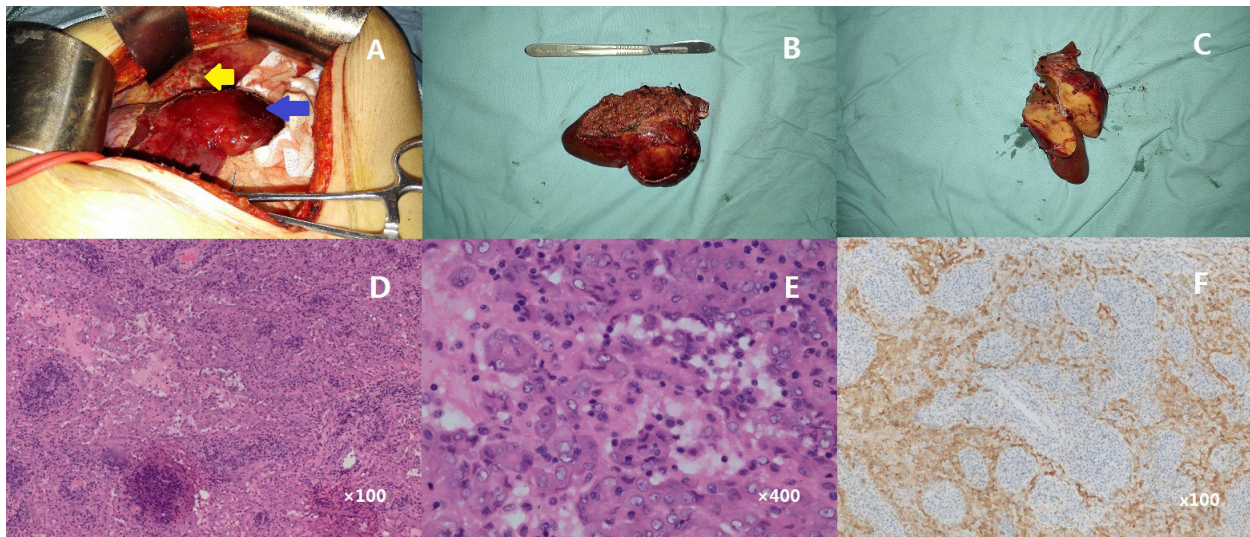


Figure 2. During the operation, a $5.5 \times 5.0 \times 4.0$ cm tumor (blue arrow) occupying the II, III and the lateral portion of the IV segments while tightly infiltrating the diaphragm (yellow arrow) was observed (A). The sample of the removed PIHMM (B). Section plane of the tumor sample (C). HE staining ($\times 100$) (D) and ($\times 400$) (E) of the tumor sample. Calretinin staining of the tumor ($\times 100$) (F).

was eventually diagnosed as cyst with lymphoid tissue hyperplasia. Immunohistochemistry revealed that the tumor cells were positive for CK7, CK19, Calretinin (Figure 2F), AE1/3, CK8, CD34, a1-AT(N), INI-1(N), B-cat(N), CyclineD1, CA125, DES, MC, WT-1(N), D2-40(N), F8(N), CD138, CD163, CD38, LCA, kp1 and partial positive for VIM, CD31, Ki-67 (10%+), CK5/6, Kappa, Lamda, S100, and totally negative for CEA, CK20, AFP, Hepa(N), HBsAg(N), HBcAg(N), HMB45(N), Glypican-3(N), TTF1, P53, TTF1, E-CAD, NapsinA, CK5, MUM1(N), SMA, CGA and SYN.

No adjuvant chemotherapy was given and the patient was disease-free survival at 13 months follow-up.

The literature review included 11 studies and 6 case reports with a total of 293 Chinese PM patients who received treatment from 1970~2016 among which 31 were patients of SIHMM (9-25). Then, three case reports with 3 cases of PIHMM were also included (26-28).

Characteristics of the included patients of SIHMM caused by PM and PIHMM plus our present case are listed in Table 1 and Table 2, respectively. The imaging and pathological diagnostic information of the included patients of localized SIHMM and PIHMM are listed in Table 3.

3.2. Epidemiology

Peritoneal mesothelioma (PM) is a rare malignancy, with an incidence of 0.1~0.2/100,000 in China. He Bei Province and Da Yao in Yun Nan Province are the two high prevalence areas of PM due to large numbers of asbestos industrial factories in the past 40 years (29,30). The male/female ratio and median age at the initial diagnosis were reported to be 2:1~3:2 and 45~70 years,

respectively, but varies a lot between different regions. The prognosis of PM is poor with a meso life span of about 1.5 years even after combined therapy (31).

The incidence of SIHMM caused by PM, including the diffuse type and the localized type of gross pathological classification, is approximately 3.8% in China and most of the diagnosed SIHMM belong to the former (32). Table 1 lists a total of 293 diffuse type PMs accompanied with 31 SIHMM cases among which 22 and 9 were metastatic and invasion patients. Then, only 10 Chinese cases of localized SIHMM have been reported and there is still no corresponding published data in other countries. Until now, no clear risk factors for liver involvement caused by SIHMM have been identified and there are also no differences between age, gender, the onset and the prognosis when comparing the two types of SIHMM.

PIHMM is even a rarer type of mesothelioma than SIHMM. To the best of our knowledge, only 15 cases of PIHMM have been previously reported worldwide in the published literature and 3 of them come from China (26-28). The characteristics of these 3 cases plus our present case are listed in Table 2. The age range of these patients were 24~63 (average of 45.75). However, contrary to the published reports in other countries, the male/female ratio of the 4 cases was 1:3. The OS of PIHMM was reported to range from 2 to 24 months whereas among these 4 Chinese patients only the present case provided follow-up data and the patient is still alive after she received surgery 13 months ago.

3.3. Etiology

Asbestos, erionite and vacuolating virus 40 (SV40) are known as the three already known risk factors for mesothelioma (33). Previous study showed that

Table 1. Characteristics of the included patients of SIHMN caused by PM

Author	Year	Type of PM	No. Of SIHMN/PM	Gender	Age (yr)	Etiology		SV40	Invasion to Liver	Metastasis to Liver	Treatment	OS
						Asbestos	Erionite					
Zhang <i>et al.</i> (9)	1973~2002	D	3/41	32M/9F	25~76	0/41	N.M	N.M	-	√	Op+Chemo	16.5 mo
Kang <i>et al.</i> (10)	1980~2012	D	5/20	13M/7F	14~79	0/20	N.M	N.M	-	√	Op+Chemo	9 mo
Guo <i>et al.</i> (11)	1985~2004	D	2/32	23M/9F	28~76	9/32	N.M	N.M	-	√	Op+Chemo	3 mo ~ 5 yr
Tong <i>et al.</i> (12)	1995~2015	D	8/21	17M/4F	23~87	1/21	N.M	N.M	-	√	Op+Chemo	3 mo ~ >2 yr
Pan <i>et al.</i> (13)	2000~2009	D	3/15	11M/4F	35~76	0/15	N.M	N.M	√	√	Chemo	3 ~ 18 mo
Shan <i>et al.</i> (14)	2000~2010	D	1/1	F	45	1/1	N.M	N.M	√	-	Op+Chemo	8 mo
Zhou <i>et al.</i> (15)	2001~2011	D	1/17	6M/11F	13~77	0/17	N.M	N.M	-	√	Op+Chemo	1 mo ~ 12 yr
Li <i>et al.</i> (16)	2003~2013	D	1/25	12M/13F	38~78	0/25	N.M	N.M	√	-	Op+Chemo	4 ~ 21 mo
Wang <i>et al.</i> (17)	2004~2010	D	4/5	4M/1F	54~73	0/5	N.M	N.M	√	-	Op+Chemo	7mo
Zhou <i>et al.</i> (18)	2005~2011	D	2/16	10M/6F	28~65	0/16	N.M	N.M	√	-	Op+Chemo	1 mo ~ >12 yr
An <i>et al.</i> (19)	2009~2013	D	1/100	70M/30F	3~83	0/100	N.M	N.M	√	-	N.M	N.M
Dong <i>et al.</i> (20)	2005	L	1/1	M	55	0/1	N.M	N.M	-	√	N.M	N.M
Zhang <i>et al.</i> (21)	2008	L	1/1	M	49	0/1	N.M	N.M	√	-	Chemo	N.M
Shan <i>et al.</i> (14)	2000~2010	L	4/4	1M/3F	51~69	4/4	N.M	N.M	√	-	Op+Chemo	5 ~ 8 mo
Zhao <i>et al.</i> (22)	2012	L	1/1	F	64	0/1	N.M	N.M	-	√	Op+Chemo	6 mo
Gao <i>et al.</i> (23)	2012	L	1/1	M	46	0/1	N.M	N.M	-	√	RFA	N.M
Li <i>et al.</i> (24)	2015	L	1/1	M	69	0/1	N.M	N.M	-	√	N.M	N.M
Zhong <i>et al.</i> (25)	2016	L	1/1	M	69	0/1	N.M	N.M	√	-	Op	N.M

SIHMN: secondary intrahepatic malignant mesothelioma; PM: D: diffuse type; L: localized type; M: Male; F: Female; Op: operation; Chemo: Chemotherapy; RFA: radiofrequency ablation; mo: month(s); yr: year(s); OS: overall survival; N.M: not mentioned.

Table 2. Characteristics of the included patients of PIHMN

Author	Year	No. of PIHMN Patient	Gender	Age	Etiology		Location of PIHMN	Size of PIHMN (cm)	Treatment	OS
					Asbestos	Erionite				
Yan <i>et al.</i> (26)	2001	1	F	46	0/1	N.M	Left lateral lobe/Left medial lobe	10 × 5.5/11 × 10	Op	N.M
Wang <i>et al.</i> (27)	2003	1	M	24	0/1	N.M	Right lobe	7 × 6 × 6	Op	N.M
Dong <i>et al.</i> (28)	2014	1	F	50	0/1	N.M	Right and left lobe	N.M	Op	N.M
Present case	2017	1	F	63	0/1	N.M	Left lobe	5.5 × 5.0 × 4.0	Op	13 mo, Still alive

PIHMN: primary intrahepatic malignant mesothelioma; M: Male; F: Female; Op: operation; mo: month(s); yr: year(s); OS: overall survival; N.M: not mentioned.

Table 3. Imaging and pathological diagnostic information of the included patients of localized SIHMM and PIHMM

Author	Type	Imaging Methods for Diagnosis				Misdiagnosis	Pathological Type			Immunohistochemistry						
		US	CT	MRI	PET-CT		Epithelioid	Sarcomatoid	Biphasic	D2-40	WT-1	Calretinin	CK5/6	AFP	CK7	Vimentin
Dong et al. (20)	S	√	√	√	N.E	HCC	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E
Zhang et al. (21)	S	N.E	N.E	√	N.E	N.M	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E
Zhao et al. (22)	S	N.E	√	N.E	√	HCC	-	-	+	N.E	+	+	-	+	+	N.E
Gao et al. (23)	S	√	N.E	N.E	N.E	CRLM	N.E	N.E	N.E	+	N.E	-	N.E	-	+	+
Li et al. (24)	S	N.E	√	N.E	N.E	Sarcoma	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E	N.E
Zhong et al. (25)	S	N.E	N.E	√	N.E	HCC	N.E	N.E	N.E	N.E	Partial +	+	N.E	-	N.E	N.E
Shan et al. (14)	S	N.E	√	N.E	N.E	No	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	N.E
Shan et al. (14)	S	N.E	√	N.E	N.E	No	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	N.E
Shan et al. (14)	S	N.E	√	N.E	N.E	No	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	N.E
Shan et al. (14)	S	N.E	√	N.E	N.E	No	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	N.E
Yan et al. (26)	P	√	√	√	N.E	Echinococcosis	-	√	N.E	N.E	+	N.E	N.E	N.E	N.E	+
Wang et al. (27)	P	√	√	√	N.E	AML	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	N.E
Dong et al. (28)	P	N.E	√	N.E	√	HCC	√	-	N.E	N.E	+	N.E	N.E	N.E	N.E	+
Present case	P	N.E	N.E	√	N.E	FNH/GIST	√	-	+	+	+	Partial +	-	+	+	Partial +

SIHMM: secondary intrahepatic malignant mesothelioma; PIHMM: primary intrahepatic malignant mesothelioma; S: secondary intrahepatic malignant mesothelioma; P: primary intrahepatic malignant mesothelioma; WT-1: Wilms's tumor-1; CK: cytokeratin; AML: angiosarcoma; CRLM: colorectal liver metastasis; HCC: hepatocarcinoma; FNH: focal nodular hyperplasia; GIST: gastrointestinal stromal tumor; N.E: not evaluated; N.M: not mentioned.

41.7~86.8% of the PM patients had a history of asbestos exposure (34-36). However, in the included studies, the rate of clear contact history of asbestos were only 3.75% (11/293), 40.00% (4/10) and 0.00% (0/4) among the diffuse SIHMM, localized SIHMM and PIHMM patients. In fact, the role of asbestos in the occurrence of PM remains to be debated. Some pathologists thought that asbestos exposure has no value in pathological differential diagnosis of mesothelioma although the role of asbestos in malignant mesothelioma pathogenesis is already confirmed by rat models. Amphibole asbestos, particularly crocidolite, has been reported to be a much more potent agent that causes PM than serpentine asbestos. However, the latter remains as a general agreement of agent and accounts for over 95% of the asbestos used around the world (14). Alarming, as the incubation period from the first exposure to asbestos to the occurrence of mesothelioma generally needs 20~40 years, this important risk factor might be overlooked in routine practice of this easily misdiagnosed disease.

In patients with no history of asbestos exposure, post-mortem examination and animal experiments showed that 30~50% might be associated with SV40 infection (37). Some other authors believe SV40 might act as a cooperative factor with asbestos and enhance its pathogenic effect. The mesothelioma-inducing role of erionite was also confirmed by rat models but unfortunately, SV40 and erionite might not be familiar to the majority of doctors and no related contact history of the above two agents could be provided in the listed Chinese case reports as well as literature from other countries.

3.4. Imaging diagnosis

Due to the rarity of mesothelioma and less radiology experience, a correct preoperative diagnosis rate of SIHMM and PIHMM is extremely low around the world. Among the 14 cases listed in Table 3, only 4 cases (28.57%) from one institute clearly declared they avoided misdiagnosis before surgery.

CT and MRI are the most frequent utilized techniques for diagnosing this tumor but the radiologic features of mesothelioma with liver involvement have not yet been clearly defined. Since hemorrhage and necrosis are very common pathological changes in SIHMM and PIHMM, In CT scan, hyper-dense components caused by hemorrhage and hypo-densities, especially in a central area, might be the necrosis lesion of PIHMM. For SIHMM patients, the CT images might indicate thickened peritoneum and omentum surrounding the liver, accompanied with an irregular nodular tumor infiltrating into the liver surface (38).

On MRI, heterogeneous hyper-dense areas of hemorrhage can be detected in T1-weighted images. The necrotic components among the solid tumor might show up as multiple cystic structures with irregular

internal septations. Contrast-enhancement is useful for detecting PIHMM. On post-contrast images, typical signs of PIHMM include peripheral serpiginous vessels, as well as a septal and increasing enhancement pattern from the periphery to the middle part of the tumor on delayed phase (39). However, a considerable number of cases do not have typical imaging features mentioned above (Figure 1C and 1D).

There were 2 listed reports, which utilized PET-CT for diagnosing SIHMM and PIHMM, respectively. However, both of them still made a misdiagnosis of hepatocarcinoma (HCC). The reason might be that although PET-CT could clearly reveal high FDG uptake in the intrahepatic tumor, no significant FDG accumulation was noted in omentum or peritoneum, thus resulting in insufficient differentiation effectiveness with other liver tumors (28). Coincidentally, hypermetabolic peripheral regions and internal septations of PIHMM might also be easily misdiagnosed as hepatic cystadenocarcinoma.

3.5. Pathology and immunohistochemistry

In gross pathology, SIHMM caused by PM could be divided into the diffuse type and the localized type. The diffuse type is generally presented as dark red or gray-white nodules of varying sizes on the peritoneum often accompanied with extensive adhesions with liver and other organs, which finally induce the "frozen" abdominal cavity. The localized type, however, is featured as multiple independent nodular lesions or accumulated masses located on the surface of liver and peritoneum (40). Ascites is the most common manifestation of PM, but it is also the major reason for misdiagnosis due to its lack of specificity and is easily confused with tuberculous peritonitis and primary, secondary or peritoneal metastatic liver tumors.

Histologically, PM includes three types: epithelial, sarcomatoid, and biphasic. Epithelial is the most common type and there were 7 cases (4 SIHMMs and 3 PIHMMs, respectively) among our listed case reports presented as epithelial type. The biphasic type has a mixture of epithelioid and sarcomatous components and each component accounts for at least 10% of the tumor.

Immunohistochemistry is the most crucial technique for pathological diagnosis of SIHMM and PIHMM. The International Mesothelioma Interest Group (IMIG) recommended that any combination of markers should contain at least 2 mesothelioma markers and 2 other cancer-related markers. Calretinin (Calcinein), CK5/6 (cytokeratin5/6, cytokeratin), WT-1, and D2-40 (Dodoplanin, peduncle) are considered to be the best markers for differential diagnosing mesothelioma (40,41). Calretinin is a calcium-binding protein commonly expressed in nerve, adipose, mesothelial, and very few adenocarcinoma tissues. Calretinin has been regarded as the most specific and sensitive antibody for

detecting epithelioid malignant mesothelioma. CK5/6, as a member of cytokeratins, is generally expressed in mesothelial squamous as well as transitional tissues, and occasionally, in certain adenocarcinoma cells. In a previous report from China containing 100 cases of diffuse type of malignant mesothelioma, the positive rate of Calretinin and CK5/6 were 93% and 79.7%, respectively. D2-40 is a monoclonal antibody, which is selectively expressed in lymphatic endothelium, lymphoid tissue-derived tumors and cancer-infiltrated lymphatic vessels. WT-1 is a DNA binding transcription factor which is localized in the nucleus. Positive staining of WT-1 is useful for detecting nephroblastoma, connective tissue-proliferating small round cell tumors, Mullerian serous carcinoma and mesothelioma. The sensitivity and specificity of D2-40 and WT-1 are significantly lower than Calretinin and CK5/6. Notably, the vast majority of the data concerning the diagnostic effectiveness of the former 4 markers came from the diffuse type of malignant mesothelioma. In our listed case reports, there were only 57.14% (8/14), 28.57% (4/14), 14.29% (2/14) and 14.29% (2/14) of the patients performed Calretinin, CK5/6, WT-1 and D2-40 immunohistochemistry examination, although their positive rate was 100% (8/8), 75% (3/4), 100% (2/2) and 100% (2/2), respectively. This might reflect that SIHMM and PIHMM were really rare diseases even for pathologists in China.

3.6. Treatment and prognosis

The treatment for PM includes intravenous chemotherapy, intraperitoneal hyperthermic perfusion chemotherapy, cytoreductive surgery and surgical resection. Surgery is the best treatment for localized SIHMM and PIHMM, even for limited recurrence tumors. Unfortunately, there has been few prognosis data of SIHMM and PIHMM due to most of the papers were cases reports without follow-up information. The mean survival time was reported to be 5~8 months for SIHMM and the present case of PIHMM from our center had 13 months of disease-free survival after curative left hemihepatectomy. For the diffuse type of SIHMM, radical resection is impossible to achieve and is not advocated due to the fact that mesothelioma can infiltrate the entire peritoneal cavity and the scars of laparotomy will cause tumor spread (42,43). Therefore, effective cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is beneficial to prolong the survival of these patients.

HIPEC can increase the local drug concentration because of its extensive contact with the tumor located in the plasma membrane and peritoneum. Pemetrexed combined with cisplatin is so far considered the first choice and standard protocol for inoperable peritoneal mesothelioma (44). For PM patients, a median survival of 31~34 months after cytoreductive surgery combined

with HIPEC as well as a 2-year survival rate of 79% after complete resection combined with HIPEC have been reported (45). In our listed case reports, the overall survival (OS) of PM patients was 1 month to over 12 years. However, clear statistics of the corresponding data specially for patients of the diffuse type of SIHMM are not available yet.

In conclusion, although the sheer number of SIHMM and PIHMM are greater in China than that in other countries in the world, they are still extremely rare, and it is easy to misdiagnose malignant tumors. The atypical imaging features and insufficient experience hinder radiologists from obtaining the correct diagnosis. Immunohistochemistry should be performed strictly in accordance with IMIG guidelines, which is crucial for pathological diagnosis. Comprehensive treatment of surgery combined with chemotherapy are mainstream methods for SIHMM and PIHMM but the prognosis is still not satisfactory. Also, exact survival data should be carefully explored so that objective evaluation of the efficacy of the treatment can be achieved.

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