Pembrolizumab as an effective treatment for diffuse malignant peritoneal mesothelioma with long-term survival: A case report and literature review

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Abstract. Primary diffuse malignant peritoneal mesothelioma (MPEM) is a malignant disease without standard treatments recommended. Recently, immunotherapy has revolutionized the field of tumor therapy. According to current clinical evidence, advanced MPEM may gain potential clinical benefits from immune checkpoint inhibitors. The present study reported a 61-year-old female patient with persistent low fever as the initial symptom, who was eventually diagnosed with MPEM. This patient obtained significant clinical benefits from pembrolizumab, with disappearance of symptoms, a lasting stable disease response with a progression-free survival of 10.0 months and a long overall survival of 26.2 months. The application of pembrolizumab was explored as an emerging effective treatment for patients with MPEM. In addition, the clinical characteristics, diagnosis, treatment, pathogenesis and target regulation in MPEM were discussed and previous studies were reviewed. Further evidence is needed from future extensive clinical trials.

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Introduction

Malignant peritoneal mesothelioma (MPEM) is a rare aggressive neoplasm that accounts for approximately one-fifth of all malignant mesothelioma cases (1,2). The incidence of MPEM has been reported to be 1.7/1,000,000 in men and 1.0 in women, varying widely across different areas (3). Primary diffuse epithelioid MPEM, the most dominant subtype, has remained to be fully elucidated and no consensus has been reached on how to treat it (1).

In recent years, immunotherapy has revolutionized the field of tumor therapy. Rapid progress in immunotherapy showed promising results in malignant pleural mesothelioma. According to the current limited clinical evidence, advanced MPEM may also benefit from immune checkpoint inhibitors (4).

The present study reported a case of MPEM that showed a favorable response to pembrolizumab. To the best of our knowledge, this was the first attempt to use single-agent pembrolizumab as the first-line treatment for a patient with MPEM. A review of available studies reported to date was also provided, so that improved immunotherapy strategies could be proposed for the management of MPEM.

Case presentation

In February 2021, a previously healthy 61-year-old Chinese woman developed chronic low fever lasting for >4 months with no obvious predisposing cause. The patient's body temperature ranged from 36.5 to 37.5˚C and became more elevated every afternoon. After drinking water and resting, the

patient's body temperature returned to normal and it was not treated.

Since April 2021, the body temperature rose to 38.5˚C, but the patient's general condition was fair. The patient took self-administered ibuprofen sustained-release capsules twice a day to keep the body temperature normal, while there was still intermittent fever every day. In mid-April, the patient experienced dressing difficulties due to a palpable abdominal mass and mild abdominal distension. Therefore, the patient sought medical treatment. Fig. 1 shows a timeline of the patient's clinical course. There was no abnormality in the patient's medical history, such as surgical trauma, allergy, personal or family history, or known exposure to asbestos.

The patient was admitted to the China-Japan Friendship Hospital (Beijing, China) two months later, with decreased lymphocytes (17.2%↓, normal range: 20-50%), hemoglobin (98 g/l↓, normal range: 115-150), platelets ($509x10^9$/l↑, normal range: 125-350), [C-reactive protein (CRP) 17.05 mg/dl↑, normal range: 0-5.00], coagulation indicators [prothrombin time (14.2 sec, normal range: 11-15), internal normalized ratio (1.24↑, normal range: 0.85-1.5), D-dimer (2.50 mg/l, normal range: 0-0.5), activated partial thromboplastin time (32.8 sec, normal range: 28.0-43.5) and fibrinogen (6.82 g/l, normal range: 2.0-4.0)] and tissue polypeptide-specific antigen 405.15 u/l↑ (normal range: 0-100.0), and normal tumor markers [CA242, CA125, CA199, CA724, α-fetoprotein and carcinoembryonic antigen (CEA)]. After two days, ultrasound-guided biopsy (maximum tumor size, 11.8x7.9 cm) was performed. The histological results (Fig. S1; protocol available in supplemental information and antibody details in Table SI) showed that the sample was epithelioid, with no tumor necrosis or lymphoid infiltrate. The immunohistochemical results (Fig. S1; protocol available in supplemental information) were as follows: D2-40 (2+), Wilms' tumor-1 protein (2+), AE1/AE3 (3+), Calretinin (3+), caudal-type homeobox transcription factor 2 (-), paired-box gene 8 (-), human bone marrow endothelial cell marker-1 (-), OCT3/4 (-), special AT-rich sequence-binding protein 2 (-), P63 (-), P40 (-), Cytokeratin (CK) 5/6 (-), thyroid transcription factor 1 (-), GATA binding protein 3 (2+), estrogen receptor (-), human epidermal growth factor receptor 2 (0), progesterone receptor (-), chromogranin A (-), synaptophysin (-), MELAN-A (-), CEA (-), CK7 (3+), CK18 (3+), Ki-67 (+, >30%), programmed death ligand 1 (PD-L1) (-), PD-L1 (22C3) (CPS 60%). The pathological diagnosis was diffuse epithelial MPEM.

According to the peritoneal cancer index (PCI) scoring system (5) (PCI=33), MPEM at stage III (T4N0M0) was identified. Surgical resection was not recommended after careful evaluation by surgical oncologists, as complete cytoreduction (CC-0/1) could not be achieved. The patient rejected chemotherapy and was not able to afford a two-drug combination regimen with nivolumab plus ipilimumab. In addition, the single-agent pembrolizumab, which was covered by the patient's insurance, had been approved as a second-line treatment option for malignant pleural mesothelioma (MPM). Finally, the patient agreed to this therapy regimen not only due to drug accessibility but also affordability. Thus, the patient underwent monotherapy with pembrolizumab (100 mg q21d) as first-line treatment in June 2021. After the first cycle, the patient's fever completely resolved. Fortunately, the patient had no discomfort; thus, 2-12 cycles of standard-dose pembrolizumab (200 mg Q21d) were continued from June 2021 to February 2022. Regular follow-up showed that the mass and nodular foci in the pelvic cavity had shrunk, with obvious necrosis in the center of the lesion (Fig. 2C and D). Until February 2022, the patient still showed lasting stable disease (SD) to pembrolizumab according to the iRECIST 1.1 criteria (6), and had no adverse events or new clinical symptoms.

In February 2022, MRI showed that the targeted lesion in the upper abdominal cavity was slightly enlarged; however, the patient still achieved an SD response. One month later, MRI showed shrunken pelvic lesions. Finally, the patient achieved an SD response to pembrolizumab, with a progression-free survival (PFS) of 10.0 months. Subsequently, the patient received two cycles of pemetrexed based on the first-line regimen, but no clinical or imaging benefits (Fig. 3A) were obtained. The patient was afebrile again (with a body temperature of 39˚C) but achieved symptom remission from the third-line regimen (four cycles albumin-bound paclitaxel plus pembrolizumab). Radiographic assessment (Fig. 3B) showed slight shrinkage, but the patient could not tolerate the II˚ myelosuppression and lasting abdominal distension. The regimen was changed to anlotinib and pembrolizumab (fourth-line treatment). However, the patient could not tolerate the following severe adverse events (including new symptoms such as anorexia and vomiting). The CT results showed a slight increase in the abdominal mass after one cycle of fourth-line therapy (Fig. 3C). Subsequently, the patient refused further treatment after the fourth-line regimen due to financial reasons. Follow-up was continued every month and it was found that the patient had died in July 2023. The overall survival (OS) of the patient was calculated as 26.2 months.

Discussion

MPEM is a rare, aggressive neoplasm that arises from the peritoneal lining, resulting in limited data summarizing its clinical characteristics. Most MPEMs are asymptomatic or have a nonspecific insidious onset in the early stages. Typical symptoms of MPEM include abdominal bloating, abdominal pain, nausea, vomiting, and bowel obstruction (7). The patient presented with a lasting fever as the first symptom, which is much less common. Except for a higher CRP value and low-grade fever, there were few signs of infection in this patient. According to previous observational studies, fever, as a prognostic indicator, may have a short survival (8). Thrombocytosis and anemia are common signs of hematologic paraneoplastic syndromes associated with MPEM. A paraneoplastic syndrome should also be considered. Thus, the literature on neoplastic fever and hematologic system paraneoplastic syndromes associated with MPEM was reviewed (Table I). A total of six cases with various hematologic system paraneoplastic syndrome and three with fever had been published. It seemed that these symptoms are not associated with gender or pathological patterns. Previous studies revealed that patients with MPEM and paraneoplastic syndrome appear to have a short OS and unfavorable outcomes (9). It was one reminder that more attention needs to be paid to patients suffering from lasting fever and other hematologic signs.

In the present case, pathological analysis supported the diagnosis of diffuse epithelioid MPEM, rather than benign

Table I. Literature on neoplastic fever and hematologic system paraneoplastic syndrome associated with MPEM.

Author, year	Sex	Pathological pattern	Paraneoplastic syndrome	Outcomes	(Refs.)
Selleslag, 1989	M	NA	Autoimmune hemolytic anemia	OS 3 m	(33)
Kimura, 2005	M	Decidual	Marked leukocytosis, thrombocytosis and elevated serum levels of C-reactive protein, granulocyte colony-stimulating factor and IL-6	OS 1 year	(34)
Banayan, 2006	F	NA	Weakness, anemia, recurrent jugular thrombosis/ inflammatory biological syndrome	NA	(35)
Socola, 2012	M	NA	Recurrent thrombotic thrombocytopenic purpura syndrome	NA	(36)
Thakral, 2020	F	Decidual	Leukemoid reaction	NA	(37)
Su, 2022	F	Epithelioid	Thrombocytosis, moderate anemia	OS 15 m	(9)
Chen, 2011	F	NA	Persistent high fever	NA	(38)
Hermann, 2013	M	Epithelioid	Fever of unknown origin	OS 2 m	(39)
Ishizuka, 2022	M	NA	Fever	OS 2 m	(40)

F/M, female/male; NA, not available; OS, overall survival; m, months.

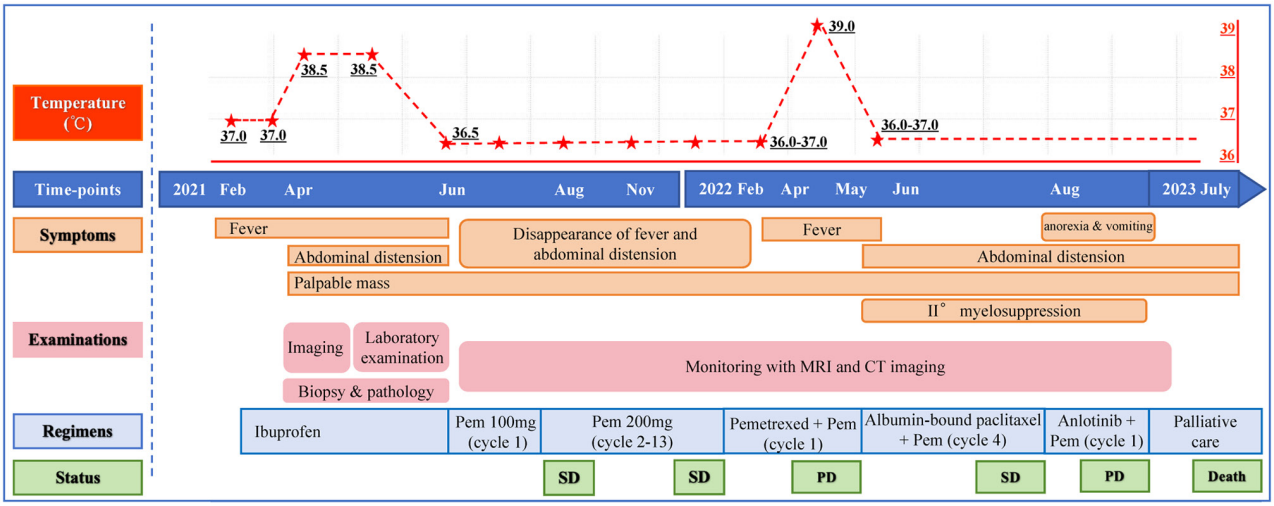

Figure 1. Timeline of the clinical course of the patient. Pem, Pembrolizumab; Tm, maximum temperature; SD, stable disease.

cystic mesothelioma. Ki-67 protein is present during all active phases of the cell cycle (G1, S, G2 and mitosis) but is absent in resting cells (G_0). Therefore, Ki-67 protein is regarded as an excellent marker of cellular proliferation and provides an inference of tumor aggressiveness. Immunohistochemical analysis indicated that the Ki-67 index was as high as 30%. Several studies have found that Ki-67 >9 or >10% is an independent indicator of poor OS benefits in malignant peritoneal mesothelioma. Ki-67 >30% suggests that the tumor grows faster than in indolent disease (10,11).

The multidisciplinary team did not recommend surgical resection for three relative contraindications (inability to achieve CC-0/1, PCI>17 and Ki-67 >9%). According to one clinical study (10), patients with Ki-67 >9% are unlikely to benefit from the procedure and should be considered for other treatment protocols. Due to limitations of clinical technology and medical equipment, hyperthermic intraperitoneal chemotherapy was not available at our hospital at the time. The absence of standard recommendations and the patient's financial situation made the therapeutic plan even more challenging. A literature review of the PubMed database was performed for eligible studies on immunotherapy in patients with MPEM, which was updated until July 2024. Key words and Medical Subject Headings terms pertinent to the intervention of interest, such as 'peritoneal mesothelioma' and 'immunotherapy' were used. Further details of the eligible studies are presented in Table II. Immunotherapy was previously applied for >1 line treatment of advanced mesothelioma. As a first-line regimen, Rizzolo *et al* (12) reported the first case using nivolumab combined with ipilimumab for MPEM in 2022 with PFS >8.0 m. In July 2023, Tang *et al* (13) reported the first OS data (23.0 months) of first-line single agent nivolumab for MPEM. In addition, two small-cohort retrospective trials and two case reports supported the possibility of pembrolizumab used to treat MPEM, while no accurate OS data of pembrolizumab as first-line treatment are currently available (11-14).

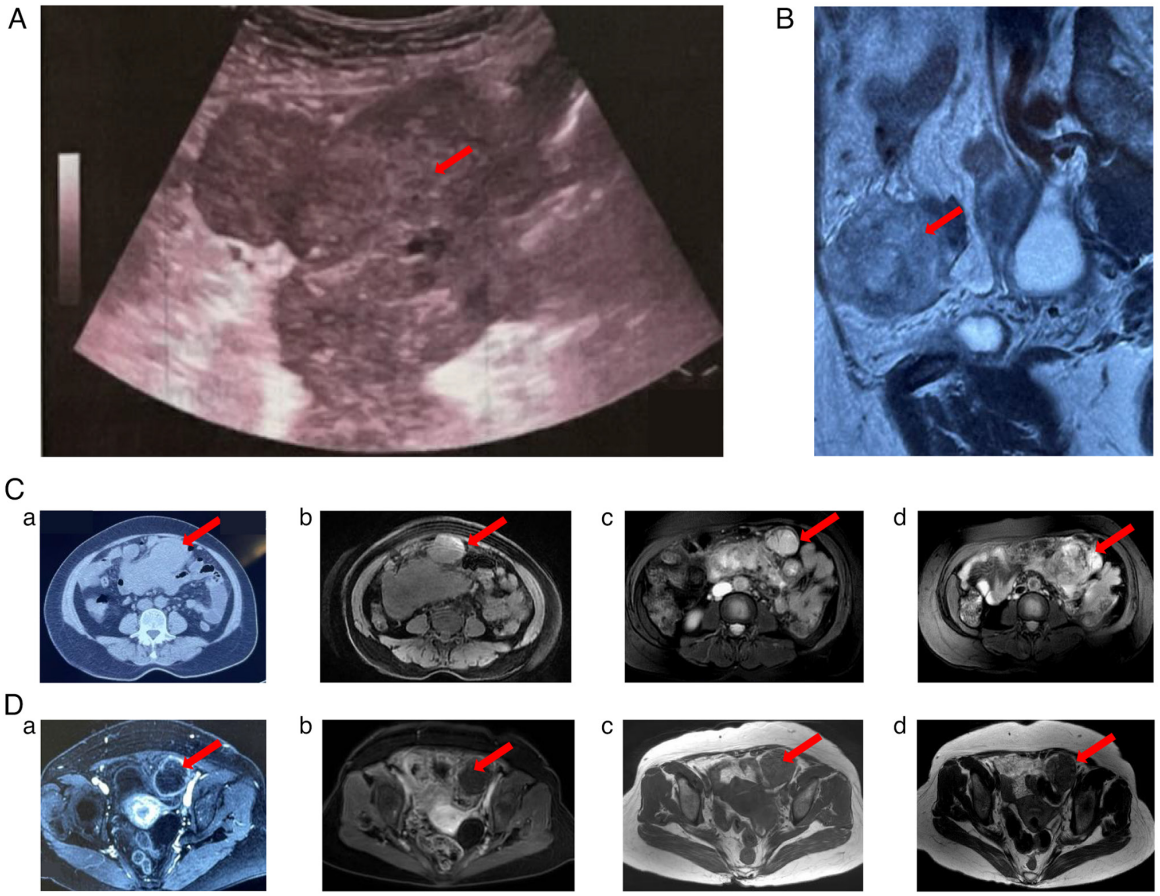

Figure 2. Imaging tests during diagnosis and pembrolizumab intervention. (A) Abdominal ultrasound showing multiple malignant, possibly cystic, and scattered solid areas in the double adnexal areas and mesentery of the abdominal and pelvic cavities (maximum, 11.8x7.9 cm). (B) Pelvic MRI showing oval mass and numerous partially fused nodules in abdominal and pelvic cavity. (C) Imaging examination showing the lesions in the upper abdominal cavity (maximum diameter: 10.4x7.1 → 8.7x6.1 → 8.5x4.5 → 10.8x5.9 cm; Ca: CT images during diagnosis; Cb-d: MRI images after 2 cycles, 8 cycles, 12 cycles of pembrolizumab intervention), with obvious liquefaction necrosis in the center of those lesions. (D) MRI showing the shrunken pelvic lesions (6.5x3.1 → 4.9x3.0 → 3.3x2.9 → 2.7x2.2 cm; Da-d: images before and after 3 cycles, 11 cycles, 13 cycles of pembrolizumab intervention). The lesion is diffuse and not solitary. To check the efficacy conveniently, the largest lesion was marked as the targeted part with red arrows.

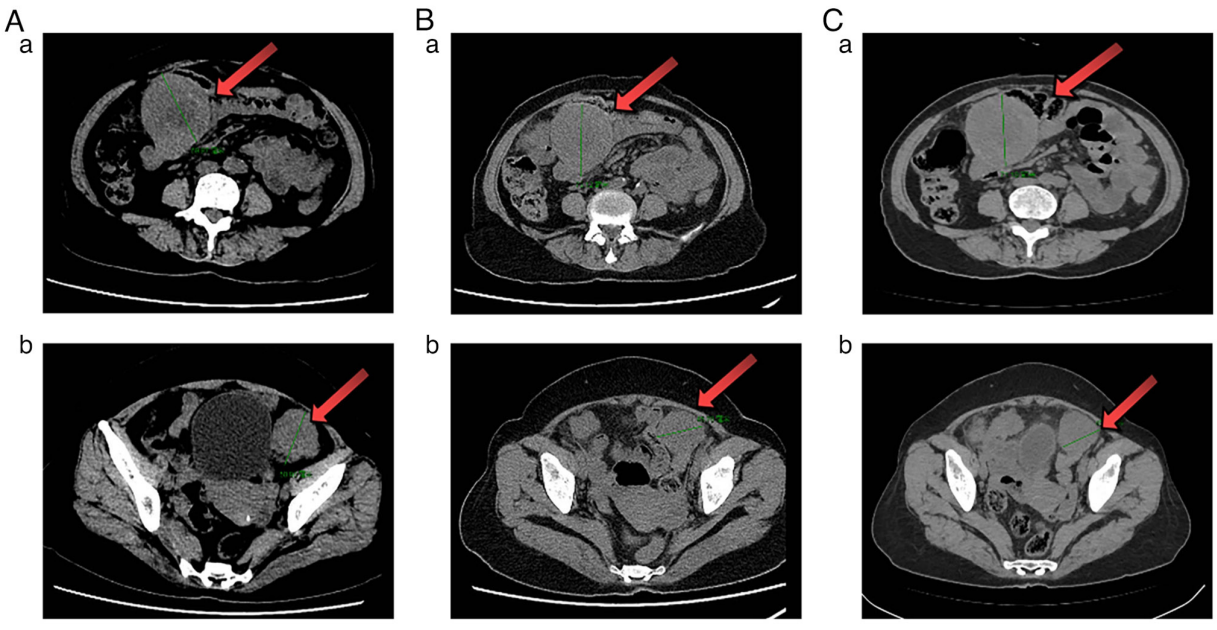

Figure 3. CT examination after first-line therapy. (A) 11.2 months, (B) 14.2 months and (C) 14.9 months after the first cycle of first-line therapy. (Aa-Ca) Cross-section in peritoneal cavity (green boundaries); (Ab-Cb) cross-section in pelvic cavity. Maximum cross-section diameter of the mass (green boundaries) in the peritoneal cavity (6.9 → 6.2x7.1 → 7.0x7.1 cm). Maximum cross-section diameter of the mass (green boundaries) in pelvic cavity (5.0 → 4.5 → 4.5 cm). The largest masses are also highlighted (red arrows).

Table II. Studies on immunotherapy for peritoneal mesothelioma.

Identification	Author, year	Disease	Trial type	Number[a]	Phase	ICI	ICI targets	Line	Outcomes	(Refs.)
NCT01649024	Calabrò, 2013	Mesothelioma	Single-arm trial	1/25	2	Tremelimumab	CTLA-4	>1	Possible encouraging effect	(41)
MESOT TREM-2012	Calabrò, 2015	Chemotherapy-resistant mesothelioma	Single-arm trial	1/29	2	Tremelimumab	CTLA-4	2	ORR 13.8%	(42)
DETERMINE	Maio, 2017	Relapsed mesothelioma	RCT	26/382	2b	Tremelimumab	CTLA-4	2/3	Not significantly prolonged OS	(43)
NCT02399371	Desai, 2019	Advanced mesothelioma	Prospective trial	8/64	2	Pembrolizumab	PD-1	>1	mPFS 4.5 m; mOS 11.5 m	(44)
JAVELIN NCT01772004	Hassan, 2019	Advanced mesothelioma	Single-arm trial	N/53	1b	Avelumab	PD-L1	>1	Possible durable disease control	(45)
NIBIT-MESO-1	Calabrò, 2021	Advanced mesothelioma	Single-arm trial	2/40	2	Tremelimumab + durvalumab	CTLA-4 +PD-L1	1/2	PFS 8·0 m; OS 16.6 m	(46)
-	Ikushima, 2020	MPEM	Case report	1/1	-	Nivolumab	PD-1	2	Hyper-progressive disease	(47)
-	Tanaka, 2020	MPEM	Case report	1/1	-	Nivolumab	PD-1	2	Remission of symptoms	(24)
-	Marmarelis, 2020	MPEM	Retrospective trial	13/13	-	Pembrolizumab	PD-1	>1	DCR 81%; mPFS 5.7 m; mOS 20.9 m	(23)
-	Kitadai, 2021	MPEM	Retrospective trial	3/26	-	Nivolumab	PD-1	2	OS 36.7 m; PFS 8.1 m	(48)
NCT03074513	Raghav, 2021	MPEM	Prospective trial	20/20	2	Atezolizumab	PD-L1	>1	ORR 40%; 1-year PFS 61%; 1-year OS 85%, PFS 17.6 m, OS not reached	(49)
-	Raghav, 2021	MPEM	Retrospective trial	29	-	Ipilimumab+ nivolumab or other single-agent ICIs	CTLA-4 +PD-1 or single-agent ICIs	>1	DCR 65.4%; mPFS 5.5 m, mOS 19.2 m	(50)
CONFIRM	Fennell, 2021	Relapsed MPEM	RCT	10/221	3	Nivolumab	PD-1	>1	mPFS 3.0 m; 1-year PFS 14%; mOS 19.8 m; 1-year OS 68%	(51)
-	Huang, 2022	MPEM	Case report	1/1	-	Unknown	Unknown	>1	OS 2.0 m	(52)
NCT02141347	Fujiwara, 2022	Mesothelioma and other solid tumor	Phase I trial	11/11	1	Tremelimumab ± durvalumab	CTLA-4 ± PD-L1	>2	-	(53)
	Rizzolo, 2022	MPEM	Case report	1/1	-	Ipilimumab+ nivolumab	CTLA-4 +PD-1	1	PFS >8.0 m	(12)
-	Peng, 2023	MPEM	Case report	1/1	-	Zimberelimab	PD-1	1	PFS 7.0 m	(54)
	Sugarbaker, 2023	MPEM	Case report	1/1	-	Nivolumab	PD-1	2	DFS 5 years	(55)

Table II. Continued.

Identification	Author, year	Disease	Trial type	Number[a]	Phase	ICI	ICI targets	Line	Outcomes	(Refs.)
-	Lal, 2023	MPEM with brain metastases	Case report	1/1	-	Nivolumab + ipilimumab	PD-1 + CTLA-4	2	PFS 21 m	(56)
-	Tang, 2023	Double primary malignant tumors with MPEM and nasopharyngeal carcinoma	Case report	1/1	-	Nivolumab	PD-1	1	PFS 12 m, OS 23 m	(13)
-	Marmarelis, 2023	MPEM	Retrospective trial	24/24	-	Pembrolizumab	PD-1	All	PR rate 21.0%, mOS 20.9 m	(27)
-	Deng, 2024	MPEM	Case report	1/1	-	Pembrolizumab	PD-1	1	DFS 33 m	(14)
-	Bairos Menezes, 2024	MPEM	Case report	1/1	-	Pembrolizumab	PD-1	2	DFS 4 years	(17)

[a]Number=(number of MPEM patients receiving ICI)/(number of mesothelioma patients receiving ICIs). MPEM, malignant peritoneal mesothelioma; ICI, immune checkpoint inhibitor; m, months; mOS, median overall survival; PFS, progression-free survival; DFS, disease-free survival; ORR, objective response rate; PR, partial response; DCR, disease control rate; PD-1, programmed cell death 1; CTLA, cytotoxic T-lymphocyte antigen; RCT, randomized controlled trial.

In general, MPEM and MPM are frequently studied together to assess the therapeutic regimens (15). Since MPEM and pleural mesothelioma are both rare lethal cancers, there are few reports on the immunological and molecular differences between them (16). Notably, only a few case reports and cohort studies have focused on MPEM, thus providing insufficient evidence for clinical guidance (11,15-17). However, differences were observed in their clinical features. The lack of prospective randomized controlled trials (RCTs) established guidelines and consensus on MPEM management poses challenges in standardizing treatments for advanced non-resectable cases. According to previous reports, MPEM usually occurs in younger women, with less emphasis on asbestos exposure as a risk factor and a lower mean age at death (18). Furthermore, mesothelioma from the pleura and peritoneum have distinct genomic profiles, and thus, various dysregulated pathways (19,20). Despite these differences, no recommendations have been proposed specifically for the treatment of MPEM at the time of diagnosis. Although approved by the Food and Drug Administration, Chinese patients were unable to obtain tremelimumab from any hospital or drug store at that time. The single-agent PD-1 inhibitor pembrolizumab has been proven to be an active agent and has been added to the National Comprehensive Cancer Network (NCCN) and Chinese Society of Clinical Oncology guidelines as a second-line treatment option for MPM (21,22). More importantly, there have been few successful attempts to obtain preliminary results on pembrolizumab for MPEM in a small-sample retrospective trial (23). In addition, the patient agreed to this therapy regimen because of not only drug accessibility, but also affordability.

An increasing number of studies, including genomic sequencing analyses, have revealed some of the possible molecular mechanisms underlying pathogenic/target regulation in MPEM (Table SII). PD-L1 expression and the PD-1 checkpoint pathway in cancer are promising processes that involve crucial targets, such as EGFR, PI3K, AKT and mTOR. The current understanding of immunotherapy in MPEM is limited by the small number of patients treated in clinical studies. A possible mechanism of pembrolizumab treatment for MPEM is summarized in Fig. 4. The anti-PD-1 agent pembrolizumab could reactivate T cells, enhancing their anti-tumor immune activity and exerting a strong anti-tumor effect. According to pathological data, PD-L1 is expressed in ~40-60% of mesotheliomas (24-26). A high frequency of PD-L1 expression is associated with more aggressive tumor biology and is also a biomarker for patients with MPEM that may benefit from immunotherapy (27-30). In the patient of the present study, immunotherapy may have been a priority, since PD-L1 expression was 60%. Finally, surprisingly, the patient of the present study benefited greatly from the therapy regimen covered by the insurance. Of note, the patient's fever and other unpleasant symptoms disappeared. Furthermore, an abdominal lump shrinkage was observed. The patient achieved maintained SD for up to 10 months and a long-term survival benefit of 26.2 months. In addition, this case sets a new record in the OS data for MPEM with paraneoplastic syndromes. This finding is encouraging in rare disease settings in which treatment options are limited.

However, individual factors cannot be ignored. The latest NCCN guidelines for MPEM published on December 22nd,

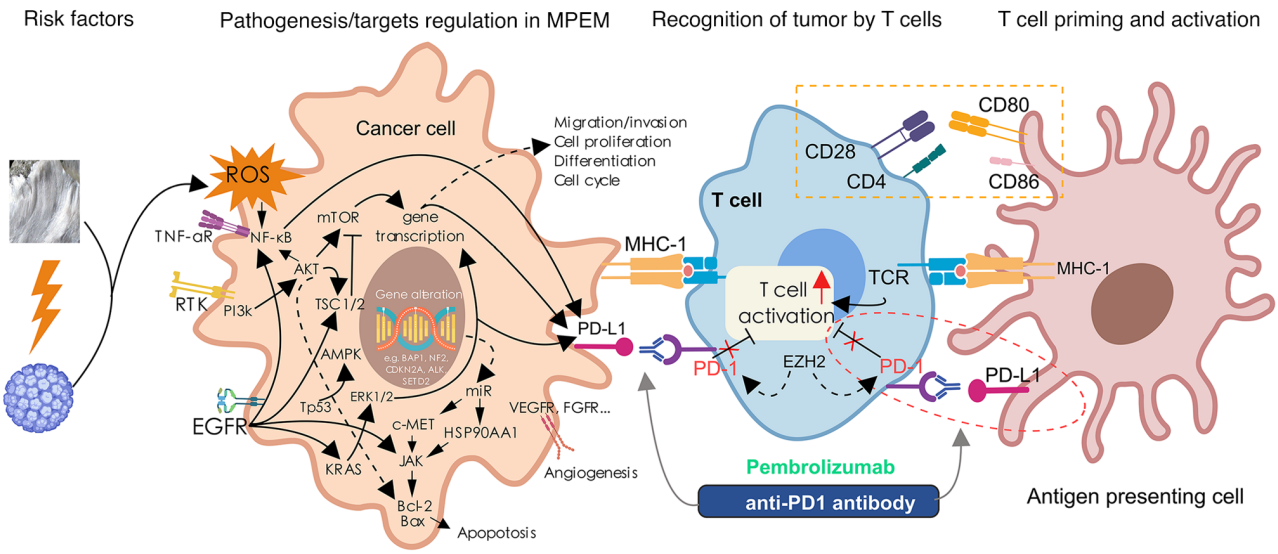

Figure 4. Pathogenesis/targets regulation in MPEM and the mechanism of Pembrolizumab. ROS, reactive oxygen species; MHC-1, major histocompatibility complex-1; TCR, T cell receptor; TNF-αR, tumor necrosis factor α receptor; RTK, receptor tyrosine kinase; EGFR, epidermal growth factor receptor; VEGFR, vascular endothelial growth factor receptor; FGFR, fibroblast growth factor receptors. This figure was created using MedPeer.

2021, recommended combination chemotherapy regimens of pemetrexed plus cisplatin/carboplatin, with a median PFS of 7.3 months; as well as pemetrexed and cisplatin/carboplatin plus bevacizumab, with a median PFS of 9.2 months (31), or immunotherapy regimens (nivolumab plus ipilimumab; median PFS, 6.8 months) (32) as first-line treatment. Although pembrolizumab may be a new first-line treatment option, the best treatment for MPEM requires verification in more clinical cases. Further multicenter, large-sample RCTs are essential to establish standard MPEM treatment strategies.

In conclusion, pembrolizumab may be an effective and well-tolerated method for treating MPEM. More proof is needed from further extensive clinical trials, resulting in better individualized treatment plans and outcomes for such patients.

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Figure 4 was created using MedPeer (https://www.medpeer.cn/).

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

CX, ZD and KT participated in the study design and wrote the original manuscript; CX, JZ and HC analyzed pathological images and made the diagnosis; ZD, XZ and YY obtained medical images and analyzed patient data; HC, JZ and SW were involved in drafting the manuscript, revising it critically for important intellectual content, and were responsible for managing this research project; SW contributed to the follow-up; JZ and SW provided grant support; CX and ZD confirm the authenticity of all the raw data. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional Review Board approval is not required at our institution for case-report studies.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of potentially identifiable images and data included in this case report.

Competing interests

The authors declare that they have no competing interests.

References

1. Kim J, Bhagwandin S and Labow DM: Malignant peritoneal mesothelioma: A review. Ann Transl Med 5: 236, 2017.
2. Moolgavkar SH, Meza R and Turim J: Pleural and peritoneal mesotheliomas in SEER: Age effects and temporal trends, 1973-2005. Cancer Causes Control 20: 935-944, 2009.
3. Boffetta P: Epidemiology of peritoneal mesothelioma: A review. Ann Oncol 18: 985-990, 2007.
4. Gray SG and Mutti L: Immunotherapy for mesothelioma: A critical review of current clinical trials and future perspectives. Transl Lung Cancer Res 9 (Suppl 1): S100-S119, 2020.
5. Jacquet P and Sugarbaker PH: Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res 82: 359-374, 1996.

6. Seymour L, Bogaerts J, Perrone A, Ford R, Schwartz LH, Mandrekar S, Lin NU, Litière S, Dancey J, Chen A, *et al*: iRECIST: Guidelines for response criteria for use in trials testing immunotherapeutics. Lancet Oncol 18: e143-e152, 2017.
7. Shavelle R, Vavra-Musser K, Lee J and Brooks J: Life expectancy in pleural and peritoneal mesothelioma. Lung Cancer Int 2017: 2782590, 2017.
8. Acherman YI, Welch LS, Bromley CM and Sugarbaker PH: Clinical presentation of peritoneal mesothelioma. Tumori 89: 269-273, 2003.
9. Su Y, Liu G, Du X and Li Y: Diffuse malignant peritoneal mesothelioma with paraneoplastic syndrome: A case report and literature review. Cancer Res Prev Treat 49: 246-250, 2022.
10. Kusamura S, Torres Mesa PA, Cabras A, Baratti D and Deraco M: The role of Ki-67 and pre-cytoreduction parameters in selecting diffuse malignant peritoneal mesothelioma (DMPM) patients for cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Ann Surg Oncol 23: 1468-1473, 2016.
11. Liu Y, Zheng G, Yang D, Guo X, Tian L, Song H and Liang Y: Osteopontin, GLUT1 and Ki-67 expression in malignant peritoneal mesothelioma: Prognostic implications. Intern Med J 51: 896-904, 2021.
12. Rizzolo A, Ah-Lan KC, Nu TNT and Alcindor T: Response to ipilimumab and nivolumab in a patient with malignant peritoneal mesothelioma. Clin Colorectal Cancer 21: 371-374, 2022.
13. Tang LK, Li ZK, Xiang YL, Ma DY and Du GB: Metachronous double primary malignant tumors with nasopharyngeal carcinoma and diffuse malignant peritoneal mesothelioma accompanied with paraneoplastic syndromes treated with nivolumab: A case report. Medicine (Baltimore) 102: e34349, 2023.
14. Deng M, Zhang X, Xu C, Luo R, Chen L, Zhou Y and Hou Y: Clinical and pathological observation of conversion therapy for malignant peritoneal mesothelioma: A case report and literature review. Pathol Oncol Res 29: 1611577, 2024.
15. Hung YP, Dong F, Watkins JC, Nardi V, Bueno R, Dal Cin P, Godleski JJ, Crum CP and Chirieac LR: Identification of ALK rearrangements in malignant peritoneal mesothelioma. JAMA Oncol 4: 235-238, 2018.
16. Chapel DB, Stewart R, Furtado LV, Husain AN, Krausz T and Deftereos G: Tumor PD-L1 expression in malignant pleural and peritoneal mesothelioma by Dako PD-L1 22C3 pharmDx and Dako PD-L1 28-8 pharmDx assays. Hum Pathol 87: 11-17, 2019.
17. Bairos Menezes M, Pedroso de Lima R, Dunões I, Inácio M and Dinis R: A complete response to pembrolizumab in malignant peritoneal mesothelioma: A case report. Cureus 16: e52716, 2024.
18. Mensi C, Mendola M, Dallari B, Sokooti M, Tabibi R, Riboldi L and Consonni D: Differences between peritoneal and pleural mesothelioma in Lombardy, Italy. Cancer Epidemiol 51: 68-73, 2017.
19. Borczuk AC, Cappellini GC, Kim HK, Hesdorffer M, Taub RN and Powell CA: Molecular profiling of malignant peritoneal mesothelioma identifies the ubiquitin-proteasome pathway as a therapeutic target in poor prognosis tumors. Oncogene 26: 610-617, 2007.
20. López-Ríos F, Chuai S, Flores R, Shimizu S, Ohno T, Wakahara K, Illei PB, Hussain S, Krug L, Zakowski MF, *et al*: Global gene expression profiling of pleural mesotheliomas: overexpression of aurora kinases and P16/CDKN2A deletion as prognostic factors and critical evaluation of microarray-based prognostic prediction. Cancer Res 66: 2970-2979, 2006.
21. Wang Q, Xu C, Wang W, Zhang Y, Li Z, Song Z, Wang J, Yu J, Liu J, Zhang S, *et al*: Chinese expert consensus on the diagnosis and treatment of malignant pleural mesothelioma. Thorac Cancer 14: 2715-2731, 2023.
22. National Comprehensive Cancer Network (NCCN). Mesothelioma: Peritoneal, Version 1. NCCN, Plymouth Meeting, PA, 2021.
23. Marmarelis ME, Wang X, Roshkovan L, Walker S, McNulty S, Ciunci CA, Muira J, Katz SI, Cengel KA, Karakousis G and Langer CJ: Real-world outcomes of pembrolizumab in peritoneal mesothelioma. J Clin Oncol 38 (15-suppl): e21094, 2020.
24. Tanaka T, Miyamoto Y, Sakai A and Fujimoto N: Nivolumab for malignant peritoneal mesothelioma. BMJ Case Rep 13: e237721, 2020.
25. Khanna S, Thomas A, Abate-Daga D, Zhang J, Morrow B, Steinberg SM, Orlandi A, Ferroni P, Schlom J, Guadagni F and Hassan R: Malignant mesothelioma effusions are infiltrated by CD3+ T cells highly expressing PD-L1 and the PD-L1+ tumor cells within these effusions are susceptible to ADCC by the Anti-PD-L1 antibody avelumab. J Thorac Oncol 11: 1993-2005, 2016.
26. Mansfield AS, Roden AC, Peikert T, Sheinin YM, Harrington SM, Krco CJ, Dong H and Kwon ED: B7-H1 expression in malignant pleural mesothelioma is associated with sarcomatoid histology and poor prognosis. J Thorac Oncol 9: 1036-1040, 2014.
27. Marmarelis ME, Wang X, Roshkovan L, Grady CB, Miura JT, Ginsberg MS, Ciunci CA, Egger J, Walker S, Cercek A, *et al*: Clinical outcomes associated with pembrolizumab monotherapy among adults with diffuse malignant peritoneal mesothelioma. JAMA Netw Open 6: e232526, 2023.
28. Gazivoda VP, Kangas-Dick AW, Greenbaum AA, Roshal J, Chen C, Moore DF, Langan RC, Kennedy TJ, Minerowicz C and Alexander HR: Expression of PD-L1 in patients with malignant peritoneal mesothelioma: A pilot study. J Surg Res 277: 131-137, 2022.
29. Valmary-Degano S, Colpart P, Villeneuve L, Monnien F, M'Hamdi L, Lang Averous G, Capovilla M, Bibeau F, Laverriere MH, Verriele-Beurrier V, *et al*: Immunohistochemical evaluation of two antibodies against PD-L1 and prognostic significance of PD-L1 expression in epithelioid peritoneal malignant mesothelioma: A RENAPE study. Eur J Surg Oncol 43: 1915-1923, 2017.
30. White MG, Schulte JJ, Xue L, Berger Y, Schuitevoerder D, Vining CC, Kindler HL, Husain A, Turaga KK and Eng OS: Heterogeneity in PD-L1 expression in malignant peritoneal mesothelioma with systemic or intraperitoneal chemotherapy. Br J Cancer 124: 564-566, 2021.
31. Zalcman G, Mazieres J, Margery J, Greillier L, Audigier-Valette C, Moro-Sibilot D, Molinier O, Corre R, Monnet I, Gounant V, *et al*: Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin cisplatin pemetrexed study (MAPS): A randomised, controlled, open-label, phase 3 trial. Lancet 387: 1405-1414, 2016.
32. Baas P, Scherpereel A, Nowak AK, Fujimoto N, Peters S, Tsao AS, Mansfield AS, Popat S, Jahan T, Antonia S, *et al*: First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): A multicentre, randomised, open-label, phase 3 trial. Lancet 397: 375-386, 2021.
33. Selleslag DL, Geraghty RJ, Ganesan TS, Slevin ML, Wrigley PF and Brown R: Autoimmune haemolytic anaemia associated with malignant peritoneal mesothelioma. Acta Clin Belg 44: 199-201, 1989.
34. Kimura N, Ogasawara T, Asonuma S, Hama H, Sawai T and Toyota T: Granulocyte-colony stimulating factor- and interleukin 6-producing diffuse deciduoid peritoneal mesothelioma. Mod Pathol 18: 446-450, 2005.
35. Banayan S, Hot A, Janier M, Ninet J, Zurlinden O and Billotey C: Malignant mesothelioma of the peritoneum as the cause of a paraneoplastic syndrome: Detection by 18F-FDG PET. Eur J Nucl Med Mol Imaging 33: 751, 2006.
36. Socola F, Loaiza-Bonilla A, Bustinza-Linares E, Correa R and Rosenblatt JD: Recurrent thrombotic thrombocytopenic purpura-like syndrome as a paraneoplastic phenomenon in malignant peritoneal mesothelioma: A case report and review of the literature. Case Rep Oncol Med 2012: 619348, 2012.
37. Thakral B and Loghavi S: Marked paraneoplastic leukemoid reaction in a patient with mesothelioma mimicking a myeloid neoplasm. Blood 135: 457, 2020.
38. Chen LY, Huang LX, Wang J, Qian Y and Fang LZ: Malignant peritoneal mesothelioma presenting with persistent high fever. J Zhejiang Univ Sci B 12: 381-384, 2011.
39. Hermann J, Bajko G, Stajgis M, Szmeja J, Kościński T and Drews M: Fever of unknown origin: A clinical mask of malignant peritoneal mesothelioma. Contemp Oncol (Pozn) 16: 596-599, 2012.
40. Ishizuka K, Uehara T, Arai M, Ikeda J, Hirose Y and Ikusaka M: Medical-type peritoneal mesothelioma leading to death two months after onset of fever of unknown origin. Radiol Case Rep 17: 540-543, 2022.
41. Calabrò L, Morra A, Fonsatti E, Cutaia O, Amato G, Giannarelli D, Di Giacomo AM, Danielli R, Altomonte M, Mutti L and Maio M: Tremelimumab for patients with chemotherapy-resistant advanced malignant mesothelioma: An open-label, single-arm, phase 2 trial. Lancet Oncol 14: 1104-1111, 2013.
42. Calabrò L, Morra A, Fonsatti E, Cutaia O, Fazio C, Annesi D, Lenoci M, Amato G, Danielli R, Altomonte M, *et al*: Efficacy and safety of an intensified schedule of tremelimumab for chemotherapy-resistant malignant mesothelioma: an open-label, single-arm, phase 2 study. Lancet Respir Med 3: 301-309, 2015.
43. Maio M, Scherpereel A, Calabrò L, Aerts J, Perez SC, Bearz A, Nackaerts K, Fennell DA, Kowalski D, Tsao AS, *et al*: Tremelimumab as second-line or third-line treatment in relapsed malignant mesothelioma (DETERMINE): A multicentre, international, randomised, double-blind, placebo-controlled phase 2b trial. Lancet Oncol 18: 1261-1273, 2017.

44. Desai A, Karrison T, Rose B, Pemberton E, Hill B, Straus CM, Tan YHC, Seiwert TY, Kindler HL: Phase II trial of pembrolizumab (P) in patients (pts) with previously-treated mesothelioma (MM). J Clin Oncol 36 (15-suppl): S8565, 2018.
45. Hassan R, Thomas A, Nemunaitis JJ, Patel MR, Bennouna J, Chen FL, Delord JP, Dowlati A, Kochuparambil ST, Taylor MH, *et al*: Efficacy and safety of avelumab treatment in patients with advanced unresectable mesothelioma: Phase 1b results from the JAVELIN solid tumor trial. JAMA Oncol 5: 351-357, 2019.
46. Calabrò L, Rossi G, Morra A, Rosati C, Cutaia O, Daffinà MG, Altomonte M, Di Giacomo AM, Casula M, Fazio C, *et al*: Tremelimumab plus durvalumab retreatment and 4-year outcomes in patients with mesothelioma: A follow-up of the open label, non-randomised, phase 2 NIBIT-MESO-1 study. Lancet Respir Med 9: 969-976, 2021.
47. Ikushima H, Sakatani T, Ohara S, Takeshima H, Horiuchi H, Morikawa T and Usui K: Cisplatin plus pemetrexed therapy and subsequent immune checkpoint inhibitor administration for malignant peritoneal mesothelioma without pleural lesions: Case report. Medicine (Baltimore) 99: e19956, 2020.
48. Kitadai R, Shimoi T, Sudo K, Noguchi E, Nagata Y, Sawada R, Takashima A, Boku N and Yonemori K: Efficacy of second-line treatment and prognostic factors in patients with advanced malignant peritoneal mesothelioma: A retrospective study. BMC Cancer 21: 294, 2021.
49. Raghav K, Liu S, Overman MJ, Willett AF, Knafl M, Fu SC, Malpica A, Prasad S, Royal RE, Scally CP, *et al*: Efficacy, safety, and biomarker analysis of combined PD-L1 (Atezolizumab) and VEGF (Bevacizumab) blockade in advanced malignant peritoneal mesothelioma. Cancer Discov 11: 2738-2747, 2021.
50. Raghav K, Liu S, Overman M, Morani A, Willette A, Fournier K and Varadhachary G: Clinical efficacy of immune checkpoint inhibitors in patients with advanced malignant peritoneal mesothelioma. JAMA Netw Open 4: e2119934, 2021.
51. Fennell DA, Ewings S, Ottensmeier C, Califano R, Hanna GG, Hill K, Danson S, Steele N, Nye M, Johnson L, *et al*: Nivolumab versus placebo in patients with relapsed malignant mesothelioma (CONFIRM): A multicentre, double-blind, randomised, phase 3 trial. Lancet Oncol 22: 1530-1540, 2021.
52. Huang X, Hong Y, Xie SY, Liao HL, Huang HM, Liu JH and Long WJ: Malignant peritoneal mesothelioma with massive ascites as the first symptom: A case report. World J Clin Cases 10: 10317-10325, 2022.
53. Fujiwara Y, Takahashi Y, Okada M, Kishimoto T, Kondo S, Fujikawa K, Hayama M, Sugeno M, Ueda S, Komuro K, *et al*: Phase I study of tremelimumab monotherapy or in combination with durvalumab in japanese patients with advanced solid tumors or malignant mesothelioma. Oncologist 27: e703-e722, 2022.
54. Peng XD, You ZY, He LX and Deng Q: Zimberelimab plus chemotherapy as the first-line treatment of malignant peritoneal mesothelioma: A case report and review of literature. World J Clin Cases 11: 5296-5302, 2023.
55. Sugarbaker PH: Response to Nivolumab followed by complete cytoreductive surgery with HIPEC resulted in long-term survival in a patient with sarcomatoid-predominant biphasic peritoneal mesothelioma. A case report. Int J Surg Case Rep 107: 108359, 2023.
56. Lal D, Misiura M, Adeel W and Tariq R: Brain metastases with malignant peritoneal mesothelioma: Never reported before. Cureus 15: e43744, 2023.