Peer Review File

Article information: https://dx.doi.org/10.21037/acr-22-102

1. Abstract

(1) The authors was suggested to further highlight the unique point of the case in the Abstract-Background as in the discussion-"To our knowledge, this is the first case of co-existing pericardial and pleural MM treated with nedaplatin and pemetrexed and responding well".

(2) Case Description: Please provide the detailed information in this subsection, including the patient's symptom (dyspnea and chest tightness for six days), main history (history of occupational exposure to asbestos), and the received therapy drugs of antituberculosis treatment.

Reply 1: Thank you for your meticulous reminder. We have modified our abstract as advised. (See page 2, line 7-9) (See page 2, line 10-14)

Changes in the text: A 33-year-old woman, who had worked in a kiln for more than 10 years, suffered from dyspnea and chest tightness for six days. Chest computed tomography (CT) showed a massive pericardial effusion. She was diagnosed tuberculous pericarditis and received six months antituberculosis treatment (Rifampicin, Isoniazide, Pyrazinamide, Ethambutol). (See page 3, line 1-5)

2. Introduction

(1) Page 3, lines 7-12: Each claim and reference to previous work should be cited. Please cite references for the sentences "The current first-line chemotherapy for advanced MM…be a more appropriate choice".

Reply 2 (1): Thank you for your meticulous reminder. We are very sorry for unintentionally missing out the citation of this sentence, and we have cited the references. (See page 11-12)

Changes in the text:

References

3. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III Study of Pemetrexed in

Combination With Cisplatin Versus Cisplatin Alone in Patients With Malignant Pleural Mesothelioma. J Clin Oncol 2023; 41(12):2125-33

4. Ziolkowska B, Cybulska-Stopa B, Papantoniou D, et al. Systemic treatment in patients with malignant pleural mesothelioma - real life experience. BMC Cancer 2022; 22(1):432

(2) It's better to clearly clarify the serious adverse effects when used cisplatin (e.g., severe gastrointestinal responses, renal toxic effects and so on).

(3) Besides, provide detailed claim instead of using vague statement "lower toxicity", like "Nedaplatin, a second-generation platinum-based antitumor agent, has antitumor mechanisms and effectiveness similar to cisplatin and was designed to decrease the adverse events, such as nephrotoxic and gastrointestinal toxic effects, seen with cisplatin". A brief description about the therapy effect of nedaplatin in various malignant tumors, is necessary.

(4) We suggest the authors add the statement-"To our knowledge, there is no report of co-existing pericardial and pleural MM treated with nedaplatin and pemetrexed", before stating the aim of the study "Here, we report a patient diagnosed… and pemetrexed"..

Reply 2 (2-4): Thank you very much. We have modified our introduction according to your suggestions. (See page 3, line 9-22)

Changes in the text: The current first-line chemotherapy for advanced MM is a combination with cisplatin and pemetrexed (3, 4). However, cisplatin may cause some serious adverse effects, such as severe gastrointestinal side effects, renal toxic effects and so on, which always force patients to discontinue chemotherapy (5-7). Several clinical trials have found out that Nedaplatin, a second-generation platinum-based antitumor agent, has the similar therapeutic effects as cisplatin but higher water solubility and lower toxicity (lower gastrointestinal toxicity and nephrotoxicity compared with cisplatin), which may be a more appropriate choice and used increasingly in chemotherapy of lung cancer (7, 8). Moreover, the same clinical findings could be also confirmed in other carcinoma like nasopharyngeal carcinoma

and esophageal cancer, in comparison between nedaplatin-based and cisplatin-based chemotherapy (9, 10). To our knowledge, there is no report of co-existing pericardial and pleural MM treated with nedaplatin and pemetrexed. Here, we report a 33-year-old woman diagnosed with co-existing pericardial and pleural MM is responding well to chemotherapy with nedaplatin and pemetrexed.

3. Case presentation

(1) Please clearly clarify the received treatment for suspected tuberculous pericarditis, including the drugs, dosage, strength, duration.

Reply 3 (1): Thank you for your meticulous reminder. We have modified as advised. (See page 6, line 1-4)

Changes in the text: Thus, the patient was treated for suspected tuberculous pericarditis and received six months antituberculosis treatment (Rifampicin 450mg QD, Isoniazide 300mg QD, Pyrazinamide 500mg TID, Ethambutol 750mg QD).

(2) Page 4, lines 15-16: "LDH was found to be elevated in both fluids , 5372 U/L in pleural fluid and 1818 U/L in pericardial fluid respectively". Please confirm the accuracy of the data. The LDH was 6954 U/L in pericardial fluid in March 2020.

Reply 3 (2): We confirm that the data of LDH were all accurate in pleural and pericardial fluids. Because of its significant high value, we paid special attention and suspected the possibility of tumors in pleura and pericardium.

(3) Page 5, line 7: Please provide the stage information instead of using "advanced carcinoma".

Reply 3 (3): Thank you for your meticulous reminder. We have staged malignant mesothelioma as T4N2Mx stage IV, according to International Mesothelioma Interest Group (IMIG) staging system. (See page 7, line 1-10)

Changes in the text: Malignant mesothelioma (T4N2Mx, grade IV) in pericardium and pleural was diagnosed according to International Mesothelioma Interest Group (IMIG) staging system, based on the summarized results: (1) a long history of occupational exposure to asbestos; (2) Clinical manifestation: cough, expectoration,

dyspnea and chest tightness; (3) Imaging results: recurrent pleural and pericardial effusion, pleural thickening; (4) Laboratory results: exudative effusion with significantly elevated LDH and marked mesothelial proliferation; high level of CYFRA 21-1 and CA125 but not CEA. (5) Immunohistochemical results: positive for Calretinin, HBME-1, CK(pan), CK5/6, but negative for TTF-1, GLUT-1, Desmin, S100, Myogenin, CD34, BcL-2 and stat-6.

(4) If available, the authors should add the CT results to provide evidence for the "the malignancy had been improved gradually".

Reply 3 (4): Thanks for your suggestion. We have added another two chest CT images at Apr 17, 2021 (maintained clinical stabilization after 8 cycles of pemetrexed and nedaplatin) and at Jul 20, 2021(malignancy improved after 3 cycles of pemetrexed). Moreover, we merged the whole chest CT imaging with Mediastinal window and pulmonary Window at different-time points in the timeline to show the dynamic changes. (See Figure 1 and page 13, line 2-5)

Changes in the text:

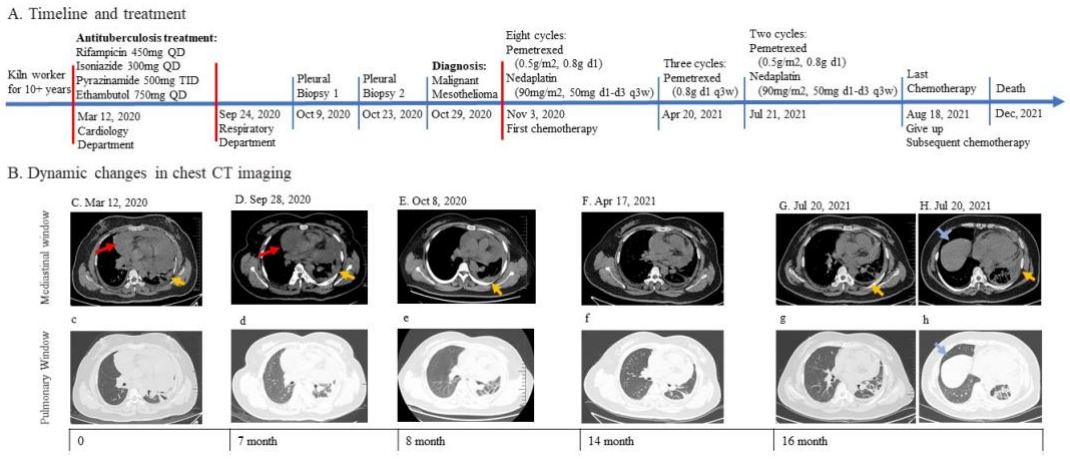

Figure 1. Treatment timeline. (A) Timeline and treatment. Illustration of the treatment received by the patient. (B) Dynamic changes in chest computed tomography (CT) imaging at different time-points. Yellow arrow: pleura; Red arrow: pericardium; Blue arrow: liver.

(5) Please also add a statement about whether the symptom (e.g., cough and

expectoration) was alleviated after the chemotherapy?

Reply 3 (5): Thank you for your meticulous reminder. We have added a statement about the clinical manifestation in case report section. (See page 7, line 12-13)

Changes in the text: the clinical manifestations such as cough, expectoration, dyspnea and chest tightness were alleviated significantly

4. Timeline

Please consider drawing a timeline to visualize the whole case. The authors are encouraged to merge the existing figures in the timeline too. Please see some examples from our sister journals:

Reply 4: Thank you for your suggestion. We have added Figure 1 to show the timeline to visualize the whole case. (See Figure 1 and page 13, line 2-5)

Changes in the text:

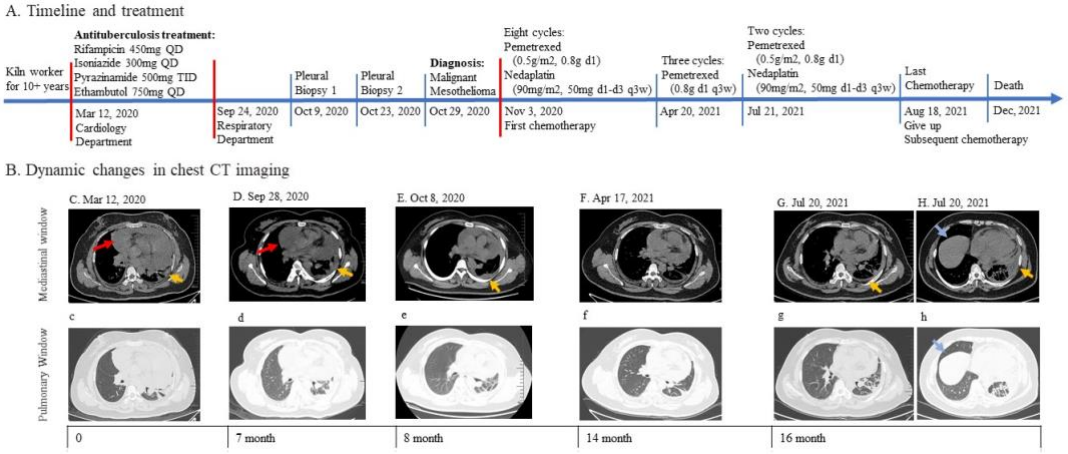

Figure 1. Treatment timeline. (A) Timeline and treatment. Illustration of the treatment received by the patient. (B) Dynamic changes in chest computed tomography (CT) imaging at different time-points. Yellow arrow: pleura; Red arrow: pericardium; Blue arrow: liver.

5. Discussion

(1) Page 6, lines 4-8: Please summarize the diagnostic presentation of malignant pericardial mesothelioma and malignant pleural mesothelioma under different diagnostic methods. The current claim is too little and just the comment on diagnostic

methods. For the authors' reference, "CT is the main imaging method for MPM. The typical presentation is a limited or diffuse thickening of the peritoneum, which can be combined with multiple large nodules of varying size, and is often accompanied by moderate to massive ascites. Meanwhile, immunohistochemistry (IHC) is very helpful to increase the accuracy of diagnosis. For example, calretinin and WT1 are the most sensitive and specific IHC markers for mesothelioma…".

Reply 2: Thank you for your meticulous reminder. We have summarized the diagnostic presentation in case report section. (See page 7, line 1-10)

Changes in the text: Malignant mesothelioma (T4N2Mx, grade IV) in pericardium and pleural was diagnosed according to International Mesothelioma Interest Group (IMIG) staging system, based on the summarized results: (1) a long history of occupational exposure to asbestos; (2) Clinical manifestation: cough, expectoration, dyspnea and chest tightness; (3) Imaging results: recurrent pleural and pericardial effusion, pleural thickening; (4) Laboratory results: exudative effusion with significantly elevated LDH and marked mesothelial proliferation; high level of CYFRA 21-1 and CA125 but not CEA. (5) Immunohistochemical results: positive for Calretinin, HBME-1, CK(pan), CK5/6, but negative for TTF-1, GLUT-1, Desmin, S100, Myogenin, CD34, BcL-2 and stat-6.