Introduction

Malignant mesothelioma is a mesothelial cell originating tumor, which is strongly associated with asbestos exposure and carries a very poor prognosis (1). Well-differentiated papillary mesothelioma (WDPM) is a distinct subtype of mesothelioma that demonstrates a papillary architecture arising in the peritoneum of women of reproductive age without a history of asbestos exposure (2,3). WDPM is usually incidentally detected during surgery for other indications and

Objectives

Well-differentiated papillary mesothelioma is an uncommon subtype of mesothelioma with a frequently indolent course, although it occasionally manifests in a more aggressive form. To establish a treatment strategy for this rare disease, we report the clinical characteristics and outcomes of 15 patients with well-differentiated papillary mesothelioma.

Methods

All pathologically diagnosed well-differentiated papillary mesothelioma cases were reviewed between 1998 and 2012.

Results

Of the 15 cases, 8 and 7 presented with single and multiple lesions, respectively. All cases with single lesions were asymptomatic, while 4 out of the 7 cases with multiple lesions were symptomatic. After tumor excision, none of the eight single-lesion cases experienced tumor recurrence. Among the other seven cases with multiple lesions, only one patient with disseminated lesions died due to disease burden. Five patients with multiple lesions received cisplatin-based intravenous or intraperitoneal chemotherapy, with a mix of complete \((n = 2)\) and partial \((n = 2)\) responses observed. Of particular note, one patient receiving cisplatin and pemetrexed combination chemotherapy experienced complete tumor resolution without any serious toxicity.

Conclusions

We recommend different treatment strategies based on the disease status. If the tumor is completely resectable, an excisional biopsy seems to be sufficient. If complete resection is unavailable for the asymptomatic patient with a localized tumor extent, close follow-up is an appropriate option. When the tumor is extensive or accompanied by symptoms, chemotherapy should be strongly considered.

Key words: well-differentiated papillary mesothelioma – peritoneum – chemotherapy – cisplatin – pemetrexed – therapeutic strategy
is known to behave in a benign or indolent fashion in many cases (2,4–6). In our experience, WDPM demonstrates a wide spectrum of clinical behavior, ranging from indolent course to disseminated disease resulting in death. Because of its rarity, only a few series have been reported, mostly emphasizing the pathologic features of WDPM, and the clinical features and treatment outcomes are poorly defined (2–6). Some WDPM patients underwent various local and systemic treatments, while other patients were only regularly followed without any treatment (3,5,6). Therefore, an extensive review of the clinic- al features with a relatively large sample size is warranted.

In this study, we describe the clinical features and treatment outcomes of 15 cases of peritoneal WDPM. Based on our previous experience, we established prognostic factors for clinical outcomes in this disease. We also analyzed detailed chemotherapy regimens and their responses to find a promising treatment option.

MATERIALS AND METHODS

Between 1998 and 2012, a total of 15 cases of newly diagnosed WDPM at two institutions in Korea were retrospectively reviewed. The inclusion criteria were: (i) pathologically confirmed diagnosis of WDPM; (ii) complete clinical information which was defined by patient demographics, primary tumor site, disease extent, treatment record and survival follow-up. Follow-up data included tumor recurrence with local or distant metastasis, and details of vital status, including whether the patient is alive without disease, alive with disease, dead of other cause or dead as a result of WDPM or WDPM treatment. Treatment response was evaluated by response evaluation criteria in solid tumors.

RESULTS

PATIENT CHARACTERISTICS

The clinical characteristics of the 15 cases included in the analysis are provided in Table 1. Nine patients (60%) were women with a median age of 53 years (range 23–76 years). In terms of multiplicity of lesions, eight and seven patients presented with single and multiple lesions, respectively. Among the 11 asymptomatic cases, 9 were incidentally diagnosed during abdominal surgery, 1 was diagnosed during a health check-up and 1 with Von-Hippel–Landau disease was diagnosed during routine screening for renal cell carcinoma. The other four patients were initially symptomatic, of which two presented with abdominal pain and two had abdominal distension. Most asymptomatic cases demonstrated only a single lesion (8 out of 11), while all symptomatic cases were diagnosed with multiple lesions. Four out of seven patients with multiple lesions had tumors disseminating throughout the peritoneum, while the tumors of three patients arose from focal peritoneal lesions. Information on tumor size was available in 11 cases, and this ranged from 0.4 to 7.1 cm (median 1.2 cm). A detailed history of asbestos exposure was available in 12 cases and no patients worked in occupations with a high likelihood of asbestos exposure.

TREATMENT MODALITIES AND SURVIVAL OUTCOME

Detailed treatment and follow-up information is summarized in Table 1. The overall follow-up period ranged from 6 to 146 months. For the eight patients with a single WDPM lesion (Cases 1–8), complete tumor excision was performed, including excisional biopsy (n = 7) and right salpingo-oophorectomy (n = 1). Adjunctive treatment was performed for four of these patients with 5-fluorouracil (5-FU)-based chemotherapy. None of the patients experienced tumor recurrence, and six patients are alive while two died of other causes (one occurred rectal cancer and the other an uncertain cause).

For the seven cases presenting with multiple lesions, one patient with seven lesions on the peritoneum (Case 9) underwent excisional biopsies for two of the seven lesions, and another patient with numerous omental lesions (Case 10) did not receive any surgery, except for initial laparoscopic biopsy. Both of these patients received no adjuvant therapy for their residual tumors, and are still alive with disease. The other five patients with multiple lesions (Cases 11–15) underwent chemotherapy at some time in their disease course. Among the four evaluable patients, two complete responses (CRs) and two partial responses (PRs) were observed. One patient (Case 11) received aggressive surgical resection with total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, infracolic omentectomy and multiple peritoneal biopsies. After three cycles of adjuvant paclitaxel and cisplatin chemotherapy, she obtained a PR and is alive without disease after 4 years. One patient (Case 12) had synchronous WDPM with B-viral hepatocellular carcinoma and he received 12 cycles of 5-FU and cisplatin combination chemotherapy. A CR was confirmed by positron emission tomography–computed tomography (PET–CT), and he is alive without WDPM recurrence after 8 years. One patient who presented with low abdominal pain (Case 13) received two cycles of adriamycin and cisplatin combination chemotherapy. Although the response data were not identified, she is alive after >12 years. One patient with massive ascites and a pleural effusion (Case 14) received three cycles of intra-peritoneal (IP) chemotherapy. A PR was initially obtained, but he died of tumor progression 9 years after the initial diagnosis.

Of particular interest, one patient was initially diagnosed with significant ascites and a pleural effusion attributed to a disseminated tumor burden (Case 12). A surgical biopsy of the omentum was performed during laparoscopy. Biopsy tissue contained part of the tumor, which was characterized by papillae consisting of stout fibrovascular cores covered by a single layer of relatively uniform bland-looking cuboidal mesothelial cells (Fig. 1A and B). Immunohistochemically, tumor cells were positive for D2–40 and calretinin (Fig. 1C and D). She received pemetrexed and cisplatin combination chemotherapy. After eight courses of chemotherapy, the
| Case | Age (year) | Sex | Presentation | Tumor number and extension | Largest tumor size (cm) | Surgical treatment | Residual tumor | Chemotherapy | Response | Follow-up |
|------|------------|-----|--------------|---------------------------|------------------------|--------------------|----------------|--------------|----------|-----------|-----------|
| 1    | 23         | F   | Incidental for RCC screening | Single | 3.5 | Excisional biopsy | No | No |               | N/E | NED 20 months |
| 2    | 62         | F   | Incidental finding | Single | 1.2 | Excisional biopsy | No | Adjuvant FOLFOX4, 12 cycles | N/E | NED 48 months |
| 3    | 66         | F   | Incidental finding | Single | 0.4 | Excisional biopsy | No | No |               | N/E | DOC 6 months |
| 4    | 53         | M   | Incidental finding | Single | 0.5 | Excisional biopsy | No | No |               | N/E | NED 22 months |
| 5    | 45         | M   | Incidental finding | Single | INA | Excisional biopsy | No | Adjuvant 5-FU-based chemotherapy | N/E | NED 146 months |
| 6    | 59         | M   | Incidental finding | Single | 1.2 | Excisional biopsy | No | Adjuvant 5-FU-based chemotherapy | N/E | DOC 47 months (reoccurred rectal cancer) |
| 7    | 62         | M   | Incidental finding | Single | INA | Excisional biopsy | No | Adjuvant oral 5-FU | N/E | NED 12 months |
| 8    | 43         | F   | Incidental finding | Single | 6 | RSO | No | No |               | N/E | NED 49 months |
| 9    | 47         | F   | Incidental finding | Multiple, localized | 0.5 | Excisional biopsy | Yes | No |               | N/E | AWD 42 months |
| 10   | 52         | F   | Lower abdominal pain | Multiple, localized | 1.2 | No | Yes | No |               | N/E | AWD 62 months |
| 11   | 64         | F   | Incidental finding | Multiple, localized | 1.0 | TAH-BSO | Yes | Paclitaxel/cisplatin, 3 cycles | PR | AWD 48 months |
| 12   | 58         | M   | Incidental finding | Multiple, disseminated | 0.5 | No | Yes | 5-FU/cisplatin, 12 cycles | CR | NED 96 months |
| 13   | 36         | F   | Lower abdominal pain | Multiple, disseminated | 7.1 | No | Yes | Adriamycin/cisplatin, 2 cycles | INA | AWD 145 months |
| 14   | 76         | M   | Ascites and pleural effusion | Multiple, disseminated | 3.7 | No | Yes | Cisplatin + mytomycin, 3 times (IP) | PR | DOD 110 months |
| 15   | 49         | F   | Ascites and pleural effusion | Multiple, disseminated | 0.5 | No | Yes | Pemetrexed/cisplatin, 8 cycles | CR | NED 18 months |

RCC, renal cell carcinoma; RSO, right salpingo-oophorectomy; TAH-BSO, total abdominal hysterectomy with bilateral salpingo-oophorectomy; CCRT, combined chemoradiation therapy; IP, intraperitoneal; N/A, not applicable; PR, partial response; CR, complete response; INA, information not available; NED, no evidence of disease; DOC, dead of other cause; AWD, alive with disease; DOD, dead of disease; WDPM, well-differentiated papillary mesothelioma.

*Oxaliplatin 85 mg/m² Day 1, leucovorin 200 mg/m² Days 1–2, 5-FU 400 mg/m² Days 1–2, 5-FU 600 mg/m² Days 1–2.
*Paclitaxel 175 mg/m² Day 1, cisplatin: 70 mg/m² Day 2.
*5-FU 1000 mg/m² Days 1–5, cisplatin 80 mg/m² Day 2.
*Adriamycin 45 mg/m² Day 1, cisplatin 70 mg/m² Day 1.
*First: cisplatin 30 mg, second: cisplatin 50 mg and mytomycin 10 mg, third: cisplatin 50 mg.
*Pemetrexed 500 mg/m² Day 1, cisplatin 75 mg/m² Day 1.
pleural effusion and ascites resolved (Fig. 2A and B) and PET–
CT imaging showed no signs of abnormal fluorodeoxyglucose
uptake (Fig. 2C and D). In addition, no serious toxicity was
demonstrated, and she completed the chemotherapy without
dose reduction or treatment delay. She is alive without tumor
recurrence 12 months after treatment completion.

Figure 2. (A) Computed tomography (CT) images at the time of initial diagnosis show ascites (red arrow) and a pleural effusion (blue arrow). (B) After eight cycles of pemetrexed and cisplatin chemotherapy, ascites and pleural effusion resolved (red and blue arrows). (C) Positron emission tomography–computed
tomography (PET–CT) image of initial diagnosis showed an abnormally increased fluorodeoxyglucose (FDG) uptake of omentum (green arrow). (D) After eight
cycles of treatment, FDG uptake was resolved (green arrow).
DISCUSSION

In contrast to the malignant mesothelioma, WDPM is much rarer and has a relatively indolent course and carries a good prognosis (3,6). In addition, female cases are more frequently reported and the majority of patients are between 20 and 50 years (2,3,6,7). WDPM is primarily seen in the peritoneum, but it is sometimes detected in the pleura, pericardium, tunica vaginalis and epididymis (2,4,6–8). Though the association with asbestos is rarely reported, pleural WDPM is often associated with asbestos exposure (4–6). Diagnosis is usually made incidentally during surgery for other indications (6,7). However, it presents with symptoms of abdominal pain, abdominal distension, menorrhagia, haematospermia and dyspnea (2–9). Although many reports show WDPM with an indolent clinical course, some cases describe more aggressive features resulting in tumor-related deaths (4,5,10–13).

Because of its rarity, no standardized treatment has been established. In previous studies, some patients received no additional treatment but remained in stable condition and showed little or no disease progression (2–6). A debulking surgery was performed for some patients (3,6,7,14). Medical treatment was also sometimes performed, including intravenous (IV) or IP chemotherapy, radiation therapy, immunotherapy, sclerosing therapy and combinations thereof, but the benefit of these treatments has not been clearly demonstrated (3,5,7,14). In particular, one author reported 26 patients with WDPM who underwent complete resection without adjuvant therapy for WDPM, and only one patient experienced recurrence, which was surgically curable (6). Thus, some authors suggest simply removing bulky masses when present and following the patient with close observation (2,3,6). However, some patients who experience disease progression and deaths attributed to disease burden have been reported (4,5,10–13). Therefore, it is worthwhile to consider WDPM as a disease with malignant potential, which requires active treatment. In addition, further work is needed to determine how to identify the high-risk patients who need aggressive treatment. In this study, we describe the various clinical courses of WDPM patients and suggest a treatment strategy based on identifiable risk factors. To our knowledge, this is the first study which depicts the clinical characteristics and suggests a treatment strategy for this rare disease. Considering its rarity, 15 cases of WDPM is likely to be helpful in outlining clinical outcomes.

Only a few studies have previously reported chemotherapy treatment for WDPM (2,4,5,7,9,11,14–16). Most of the cases described here presented with peritoneal involvement, and various kinds of chemotherapy were administered as shown in Table 2 (2,4,7,9,11,15,16). Seven cases were treated with IV chemotherapy, four cases with IP chemotherapy and two cases with combined systemic and local treatment. Among those cases, two patients received complete tumor excision followed by either IP hyperthermic chemoperfusion of mitomycin C with 5-FU (case I) or cisplatin with doxorubicin (Case K) (11,16). The former patient was alive without recurrence 6 months later, while the latter patient experienced recurrence within 15 months. The direct response to chemotherapy could be assessed in only one case (Case L) (9). She presented with extensively disseminated peritoneal nodules accompanied by ascites and pleural effusion. An aggressive debulking surgery was performed and residual ascites and pleural effusion totally resolved after additional IP, intrapleural and IV carboplatin administration. She is alive without disease after 4 years. Another symptomatic patient (Case M) was also treated with aggressive surgery followed by extensive IV and IP chemotherapy (7). Although the detailed response to chemotherapy was not described, she is alive with disease after >20 years. Therefore, optimal cytoreductive surgery and combined chemotherapy seem to be an appropriate treatment strategy when a poor prognosis is predicted.

In our study, we identified some interesting trends in patient outcomes. Tumor size does not seem to have a clear effect on symptoms or prognosis of WDPM, especially when the tumor can be excised. Two patients with a large mass did not experience any symptoms at the time of diagnosis, or recurrences after tumor removal (Cases 1 and 8). Patients with multiple lesions, however, were more likely to be symptomatic than those with a single lesion. The eight patients with single lesions (Cases 1–8) did not experience any symptoms at the time of diagnosis. However, four out of seven patients with multiple disseminated tumors presented with disease-related symptoms (Cases 10 and 13–15). In particular, three out of those four symptomatic patients showed massive tumor involvement throughout the peritoneum. This finding is consistent with previous reports, in which most symptomatic patients had multiple lesions (2,4,6,7,9). In addition, the prognosis of WDPM is likely to be correlated with disease extent. Most WDPM cases were discovered incidentally prior to developing symptoms according to the previous studies (6). However, among the seven patients from previous studies who died due to WDPM, all of four evaluable patients showed multiple lesions at diagnosis and presented with symptoms at diagnosis or shortly after diagnosis (4,5,10–13). This finding is compatible with our study. Among our patients only one died of disease progression (Case 11). He had extensive disease with a large volume of ascites at diagnosis. These findings suggest that disseminated tumor extent causes symptoms and results in a poor prognosis. Therefore, these factors should be carefully considered when deciding on a treatment strategy for WDPM.

Based on our study, we could evaluate potential therapeutic strategies for this rare disease. When WDPM tumors were completely excised, recurrence was rare even without adjuvant therapy (Cases 1–8). If complete excision is not available, platinum-based chemotherapy seems to be effective. All of our four evaluable patients who received cisplatin demonstrated a favorable tumor response in our study (Cases 8, 9, 11 and 12). Furthermore, two patients who underwent cisplatin-based IV chemotherapy showed complete resolution. These findings are consistent with previous studies, in which surgical resection followed by chemotherapy demonstrated favorable survival outcomes (2,4,7,9,11,15,16). However, the efficacy
Table 2. Clinical feature of 13 WDPM of peritoneum patients who received chemotherapy reported in the literature

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Presentation</th>
<th>Tumor number and extension</th>
<th>Surgery</th>
<th>Residual tumor</th>
<th>Chemotherapy: regimen (type)</th>
<th>Response</th>
<th>Other therapy</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>46</td>
<td>M</td>
<td>Constipation</td>
<td>INA</td>
<td>Done</td>
<td>INA</td>
<td>Cisplatin and doxorubicin (IV)</td>
<td>INA</td>
<td>No</td>
<td>NED, 3 years</td>
</tr>
<tr>
<td>B</td>
<td>38</td>
<td>M</td>
<td>Abdominal pain</td>
<td>Multiple, disseminated</td>
<td>Done</td>
<td>INA</td>
<td>Cisplatin and doxorubicin (IV)</td>
<td>INA</td>
<td>No</td>
<td>DOD, 3 years</td>
</tr>
<tr>
<td>C</td>
<td>32</td>
<td>F</td>
<td>Ascites</td>
<td>INA</td>
<td>Done</td>
<td>INA</td>
<td>Ranpirnase (IV)</td>
<td>INA</td>
<td>No</td>
<td>AWD, unknown period</td>
</tr>
<tr>
<td>D</td>
<td>11</td>
<td>F</td>
<td>Abdominal pain</td>
<td>Multiple, disseminated</td>
<td>RSO and omentectomy</td>
<td>Yes</td>
<td>Cisplatin/cyclophosphamide (IV, as neoadjuvant therapy)</td>
<td>INA</td>
<td>Luprolide</td>
<td>AWD, 11 months</td>
</tr>
<tr>
<td>E</td>
<td>69</td>
<td>F</td>
<td>Incidental finding during TAH-BSO</td>
<td>Multiple, localized</td>
<td>TAH-BSO</td>
<td>INA</td>
<td>INA (IV)</td>
<td>INA</td>
<td>No</td>
<td>Alive, 2 years</td>
</tr>
<tr>
<td>F</td>
<td>25</td>
<td>F</td>
<td>Ascites and left pelvic mass</td>
<td>INA</td>
<td>TAH-BSO and omentectomy</td>
<td>INA</td>
<td>INA (IV)</td>
<td>Radiotherapy</td>
<td>Death, uncertain cause, 7 years</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>31</td>
<td>F</td>
<td>Incidental finding during left oophorectomy</td>
<td>Multiple, localized</td>
<td>Left oophorectomy</td>
<td>INA</td>
<td>INA (IV)</td>
<td>Radiotherapy</td>
<td>Death, uncertain cause, 2 years</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>48</td>
<td>F</td>
<td>Ascites</td>
<td>Multiple, disseminated</td>
<td>No</td>
<td>Yes</td>
<td>Thiotepa (IP)</td>
<td>INA</td>
<td>Radiotherapy</td>
<td>AWD, 4 years</td>
</tr>
<tr>
<td>I</td>
<td>55</td>
<td>F</td>
<td>Incidental finding during LAR</td>
<td>Multiple, disseminated</td>
<td>LAR, omentectomy and peritonectomy</td>
<td>No</td>
<td>Mitomycin/fluorouracil (IPHC)</td>
<td>N/A</td>
<td>No</td>
<td>NED, 6 months</td>
</tr>
<tr>
<td>J</td>
<td>48</td>
<td>F</td>
<td>INA</td>
<td>INA</td>
<td>Cytoreductive surgery</td>
<td>Yes</td>
<td>Cisplatin/mytomycin (IPHC)</td>
<td>INA</td>
<td>No</td>
<td>DOD, 13 months</td>
</tr>
<tr>
<td>K</td>
<td>47</td>
<td>F</td>
<td>INA</td>
<td>INA</td>
<td>Cytoreductive surgery</td>
<td>No</td>
<td>Cisplatin/doxorubicin (IPHC)</td>
<td>N/A</td>
<td>No</td>
<td>AWD, 15 months (Recurrence)</td>
</tr>
<tr>
<td>L</td>
<td>56</td>
<td>F</td>
<td>Ascites and right pleural effusion</td>
<td>Multiple, disseminated</td>
<td>TAH-BSO and omentectomy</td>
<td>Yes</td>
<td>Carboplatin (IP, intrapleural and IV)</td>
<td>CR</td>
<td>No</td>
<td>NED, 4 years</td>
</tr>
<tr>
<td>M</td>
<td>36</td>
<td>F</td>
<td>Abdominal pain</td>
<td>Multiple, disseminated</td>
<td>TAH-BSO</td>
<td>Yes</td>
<td>Sixth lines of chemotherapy (IV + IP)</td>
<td>INA</td>
<td>Tamoxifen and megace</td>
<td>AWD, 24 years</td>
</tr>
</tbody>
</table>

LAR, low anterior resection; IV, intravenous; IPHC, intraperitoneal hyperthermic chemoperfusion.
of radical surgery which exceeds simple tumor excision is debatable. One patient still had a residual tumor even after undergoing radical debulking surgery before chemotherapy (Case 8). In contrast, two patients with a complete response to chemotherapy did not receive surgery (Cases 9 and 12).

If the tumor is completely resectable, regardless of whether it presents as a single or multiple lesions, complete excision is an acceptable treatment. In these cases, adjuvant therapy is generally not necessary and regular follow-up seems to be sufficient, considering the rarity of recurrence after complete resection (6). If the tumor is multifocal and unresectable, chemotherapy should be considered. If the patient is asymptomatic and disease extent is localized, then close follow-up might be sufficient considering the indolent nature of WDPM and the potential complications of aggressive treatment. However, chemotherapy should be more strongly considered if the tumor is extensive or accompanied by symptoms such as abdominal pain or distension, because these findings appear to be associated with a poor prognosis. Cytoreductive surgery and adjuvant chemotherapy might be an option, but radical surgery exceeding simple tumor resection may not be beneficial.

To determine the most effective chemotherapy regimen for WDPM, we can apply some information known about malignant mesothelioma, which can be considered as a malignant counterpart to WDPM. Platinum-based combination regimens demonstrated superior outcomes compared with single-agent regimens or non-platinum-based combinations (17,18). Currently, the cisplatin and pemetrexed doublet therapy has been established as the effective first-line chemotherapy for advanced malignant mesothelioma (1,18–20). The combination of cisplatin and pemetrexed showed far greater activity than cisplatin alone (19). Though peritoneal mesothelioma is rarer than mesothelioma of the pleura, one subgroup analysis indicated acceptable activity and safety for peritoneal mesothelioma (21). However, cisplatin and pemetrexed combination has not been previously used for peritoneal WDPM. One WDPM patient with pleural involvement was treated with three courses of neoadjuvant cisplatin and pemetrexed combination followed by extrapleural pneumonectomy, but the response to chemotherapy was not described in the study (14). Cisplatin-based chemotherapy appeared to be effective among the cases described here, and one patient in particular was successfully treated with eight courses of cisplatin and pemetrexed regimen without any significant toxicity. Although she was diagnosed with massive ascites and pleural effusion secondary to WDPM, she experienced complete disease remission via chemotherapy alone (Case 12). Therefore, cisplatin and pemetrexed doublet therapy may be a promising treatment option for extensive or symptomatic WDPM.

It is obvious that there is a room for debate on the optimal treatment of WDPM. Although WDPM usually shows low malignant potential and an indolent clinical course, more aggressive therapies are needed for patients at higher risk of malignant transformation. We have extensively reviewed previous literature and analyzed clinical courses according to the patient characteristics. We recommend different treatment strategies based on the disease status. In addition, pemetrexed and cisplatin combination could be a promising therapeutic option for WDPM. To our knowledge, this is the first study which extensively reviewed the clinical aspects of WDPM. We also suggest risk-based treatment strategies with newer chemotherapeutic agents. Further studies with a larger sample size will help elucidate the most effective and safe therapeutic strategies.

Conflict of interest statement
None declared.

References

18. Ellis P, Davies AM, Evans WK, Haynes AE, Lloyd NS. The use of chemotherapy in patients with advanced malignant pleural
mesothelioma: a systematic review and practice guideline. 


