Journal of Nippon Medical School

Case reports

Cytological assessment of desmoplastic malignant pleural mesothelioma in an autopsy case

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Acknowledgement

The authors thank Prof. Kazuki Nabeshima, Department of Pathology, Fukuoka University School, for his support in diagnosing the case.

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Abstract

Introduction: Desmoplastic malignant pleural mesothelioma (DMPM) is a sarcoma type mesothelioma, comprising about 5% of malignant pleural mesotheliomas. Although effusion cytology is commonly used as the primary diagnostic approach for mesothelioma, this may not be useful for DMPM due to its desmoplastic nature and bland cellular atypia. We hereby report a case of DMPM diagnosed through autopsy along with its cytological features that have not been described previously.

Case Presentation: A male in his 60s with a history of occupational asbestos exposure was referred to our hospital with right chest pain. Chest computed tomography scan showed right pleural effusion. Thirteen months later, the patient died of respiratory failure. In autopsy, the scrape-imprint smear and the pleural effusions cytology were performed. The scrape-imprint smear samples exhibited spindle cells with mild nuclear atypia and grooves with fibrous stroma. In the pleural effusion cytology, spindle cells having mild nuclear atypia and grooves with loose epithelial connections were observed. Histological examination of the right pleura showed spindle cells proliferating with dense collagen fibers, as seen in cytological samples, thus rendering the diagnosis of DMPM. Diagnosis was confirmed by fluorescence *in situ* hybridization.

Conclusion: Cytological procedures, such as pleural effusion cytology and scrape-imprinting method, may be useful as an ancillary tool in the diagnosis of rare tumors such as DMPM.

Keywords: Fluorescence *in situ* hybridization (FISH), autopsy, cytology, desmoplastic malignant pleural mesothelioma (DMPM), immunohistochemistry (IHC).

Introduction

Desmoplastic malignant pleural mesothelioma (DMPM) is a sarcoma type of malignant pleural mesothelioma (MPM). DMPM is a rare tumor accounting for only 5% of MPM in Japan. Prognosis is poor with a median survival time of 3.8 months¹. Effusion cytology is the primary diagnostic approach for MPM since most patients with MPM initially present with pleural effusion. However, cytological diagnosis of DMPM is challenging because tumor cells scarcely exfoliate into pleural effusion due to its desmoplastic nature. Furthermore, histological diagnosis of DMPM is also difficult due to bland nuclear atypia mimicking fibrous pleurisy.

Autopsy cytology is a rapid and inexpensive diagnostic tool at the time of autopsy, prospectively guiding pathologists, clinicians, and the patient's family. Autopsy cytology can play an ancillary role in the diagnosis of rare diseases with ambiguous histological features, and can also be used for educational purposes. We hereby report a case of DMPM, for which final diagnosis was established by autopsy, aided by post-mortem cytology. Cytological features of DMPM characterized by spindle cells with mild atypia and nuclear grooves are described here for the first time, and have not been reported in previous literature.

Case Report/Case Presentation

Clinical history

A male in his 60s was presented to our hospital due to right chest pain. He was a retired carpenter with a history of asbestos exposure. Chest computed tomography (CT) showed right pleural effusion (shown in Fig. 1), and the concentration of the hyaluronic acid (HA) in the pleural fluid was 58,405 mg/ml. A right thoracoscopy revealed that the parietal pleura was speckled with white nodules. Cytology of the pleural effusion showed only a small number of atypical cells with pale cytoplasm in the inflamed background. Significant findings suggesting neoplasms including mesothelioma were not observed. The patient received a video-assisted thoracoscopic surgery (VATS) biopsy for diagnosis. The parietal pleural biopsy revealed increased collagen fibers with inflammatory cells, predominantly comprising lymphocytes. However, these were judged as "indeterminate" without apparent

mesothelioma cells being identified. Cause of the patient's refractory pleural effusion was considered to be pleurodesis, and only supportive care was provided to maintain respiratory function. Thirteen months after the first presentation, the patient died from respiratory failure. Under family consent, an autopsy was performed.

Autopsy findings

From the autopsy, right parietal pleural thickening and adherence to the surrounding tissue was observed (shown in Fig. 2). No findings were indicative of lymph node metastases or distant metastases. Two samples of 15x7 mm and 10x10 mm in size were collected from the disseminated lesion in the right pleura, and the scrape-imprint smear was made by scraping a cut surface of the samples. Smear samples were fixed immediately in 95% ethanol for 30 minutes and then subjected to Papanicolaou staining. The scrape-imprint smear samples consisted of spindle cells with fibrous stroma. The cells had spindle or round nuclei with mild atypia (shown in Fig. 3a), and some exhibited nuclear grooves (Fig. 3b). According to pleural effusion cytology, there were loosely connected cells with thick, light green cytoplasm (Fig. 3c) and round or spindle nuclei and nuclear grooves (Fig. 3d). Based on these autopsy cytological features the possibility of mesothelioma was considered, and DMPM was hypothesized as one differential diagnosis.

Histological samples of 3 cm and 2 cm in size were obtained from the right pleura, independently from the samples for the scrape-imprint smear. Histological analysis revealed spindle cells proliferating in a short storiform pattern with dense collagen fibers. The spindle cells accounted for more than 50% of the tumor (Fig. 3e), and some exhibited nuclear grooves (Fig. 3f) as seen in the cytological samples. Asbestos bodies were not found in the parietal pleura or the lung. Upon immunohistochemical (IHC) analysis (Table 1)²⁻¹⁸, the tumor cells were positive for cytokeratin AE1/AE3 (Fig. 3g), α -smooth muscle actin (α -SMA) (Fig. 3h), vimentin (Fig. 3i), CAM5.2, calretinin, glucose transporter 1 (GLUT1), and developmental protein with EGF like domains (HEG1). The tumor cells were negative for S-100, CD34, myogenin, desmin, carcinoembryonic antigen (CEA), thyroid transcription factor 1 (TTF-1), Napsin A, epithelial cell adhesion molecule antibody clone number Ber-EP4

(BerEP4), anti-epithelial cell adhesion molecule monoclonal antibody, clone number-31 (MOC31), p63, and p40. In the fluorescence *in situ* hybridization (FISH) analysis, homozygous loss of the cyclin-dependent kinase inhibitor 2A (*CDKN2A*)/*p16* gene was observed in 50.4% of the cells (shown in Fig. 4). In consideration of all cyto-histological and IHC findings, diagnosis of DMPM was established.

Discussion/Conclusion

DMPM is a rare tumor accounting for 5% of malignant pleural mesothelioma. Due to its rarity and desmoplastic nature, only histological findings have been reported up to now, and cytological characteristics remained unclear. In this case, scrape-imprint smear from the right pleura showed many atypical spindle cells with nuclear grooves with fibrous stroma. Similar findings were also seen in the tumor cells of the right pleural tissue. Histological examination revealed that the spindle cells accounted for more than 50% of the tumor in the dense collagen fibers, rendering the diagnosis of DMPM. Diagnosis was further confirmed by FISH, in which the homozygous loss of *CDKN2A/p16* gene was detected. To the best of our knowledge, this is the first report describing the cytological features of DMPM.

High concentrations of HA in MPM have been reported. With a cutoff value of 100,000mg/ml for HA in the pleural fluid, the sensitivity is 73-93%, and the specificity is 90-100%^{19, 20}. However, aggressive, sarcomatoid type MPM shows lower concentrations of HA^{20, 21}. In the present case, the concentration of the HA in the pleural fluid was 58,405 mg/ml, which was difficult for the precise diagnosis of MPM.

The cytologic identification of MPM and its subtypes in effusions can be challenging due to the lack of well-established definite cytological criteria. The epithelioid type appears to be very cellular, with multiple atypical mesothelial cells arranged in three-dimensional structures with molurae and/or papillae. The abundant cytoplasm is eosinophilic, and the peripheral is fuzzy, which is due to the action of the hyaluronic acid on the microvilli. In addition, the cytoplasm of the engulfed cells exhibits a hump-like cytoplasmic structure²². The sarcomatoid type shows lower cellularity than the epithelial type. The tumor cells appear solitary with moderate or marked nuclear pleomorphism, with irregular chromatin

and prominent nucleoli. The desmoplastic type scarcely appears in the pleural effusion, but discohesive, spindle cells can be noted. A surrounding fibrous stroma can also be present. The nuclear atypia is less than in sarcomatoid types, and the nucleoli are less prominent. The comparison of the cytological features between the MPM subtypes are summarized in Table 2. During hospitalization, pleural effusion cytology was carried out to assess any tumor cells which may have exfoliated into the effusion. However, there was not enough obtained sample to provide any significant information. This may have been a result of DMPM cells rarely appearing in the pleural effusion due to their desmoplastic nature. At autopsy, clusters of atypical spindle cells with a reduced connection and high nuclear-cytoplasmic ratio in the pleural effusion could be identified. Notably, these tumor cells exhibited many nuclear grooves. These cytological characteristics are not particularly unique to DMPM as previous reports have also described nuclear grooves in other types of MPM, such as microcystic types and adenomatoid types^{23, 24}. Although these are not specific characteristics of the DMPM, they support the diagnosis.

In this case, the pleural scrape-imprint smear cytology from the autopsy was a diagnostic key. Autopsy cytology is a rapid and inexpensive diagnostic tool on the day of autopsy, providing quick guidance to pathologists and the family of the deceased patient. For instance, this technique can provide a tentative diagnosis before final histological diagnosis, and can also be used for educational purposes. The scrape-imprint cytology is a combination of the scrape and imprint methods. The scraping method allows for the collection of many tumor cells, especially from stroma-rich tumors. The imprint method enables visualization of cytological features in detail. Because of these factors, we believe that a combination of scrape and imprint methods can be useful in the cytological diagnosis of stroma-rich tumors, such as DMPM.

p16 FISH is a useful assay in the diagnosis of several types of mesotheliomas. For instance, homozygous deletion of *p16* is found in up to 80% of patients, and in 90-100% of the DMPM patients²⁵⁻²⁷. Particularly, detection of homozygous deletion of *p16* in the effusion smears or pleural tissue using FISH is a confirmatory test for MPM diagnosis, with a positive predictive value of 100%^{26, 28}. If enough cells can be collected from effusion samples, FISH should be performed to confirm the histological diagnosis of DMPM.

169 Currently, cytological diagnosis alone is not recommended for the diagnosis. However,
170 as the disease progresses and the pleura thickens, usually the clinicians perform a pleural
171 biopsy. At the same time, scrape-imprint cytology is useful to confirm the appearance of
172 tumor cells, and a presumptive diagnosis can be made. If DMPM is highly suspected due to
173 the cytological features, IHC and/or FISH are highly recommended. Reviewing the current
174 case, as many cells as possible cells should be collected by centrifuging all the fluid for the
175 further analysis. Even if it is not possible to collect cells from the tumor itself, collecting cells
176 from pleural and ascitic fluid can predict the histological type, and cell block-IHC and FISH
177 can be performed. Even if a definitive diagnosis is difficult to make, it is possible to obtain a
178 variety of information that will be useful for subsequent treatment strategies.

179 In conclusion, this is considered to be the first report on rare cytology findings of
180 DMPM in an autopsy. Scrape-imprint smear and pleural effusion cytology exhibited spindle
181 cells with mild nuclear atypia and grooves with fibrous stroma. Cytological procedures
182 during autopsy can be a rapid and convenient tool in the diagnosis of rare tumors such as
183 DMPM.

184

Statements

Statement of Ethics

Written informed consent was obtained from the patient and his family. All procedures performed in studies involving human participants were in accordance with ethical insitutional standards and with the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Y.K., S.Kure., H.K., S.Kunugi, and M.O. conceived of the presented idea. Y.K., K.K., and K.T. made and screened the cytological specimen, and all authors assessed the cytological and histological findings. N.M. and R.O. supervised the work. Y.K. and S.Kure drafted the manuscript. All authors discussed the results and contributed to the final manuscript.

References

- 198 1. Hashimoto K, Okuma Y, Hosomi Y, Hishima T. Malignant mesothelioma of the pleura with
 199 desmoplastic histology: a case series and literature review. *BMC Cancer*. 2016 Sep 6;16:718.
 200 Available from: <https://www.ncbi.nlm.nih.gov/pubmed/27599565>.
- 201 2. Kushitani K, Takeshima Y, Amatya VJ, Furonaka O, Sakatani A, Inai K. Differential diagnosis of
 202 sarcomatoid mesothelioma from true sarcoma and sarcomatoid carcinoma using
 203 immunohistochemistry. *Pathol Int*. 2008 Feb;58(2):75-83. Available from:
 204 <https://www.ncbi.nlm.nih.gov/pubmed/18199156>.
- 205 3. Tsuji S, Washimi K, Kageyama T, et al. HEG1 is a novel mucin-like membrane protein that
 206 serves as a diagnostic and therapeutic target for malignant mesothelioma. *Sci Rep*. 2017 Mar
 207 31;7:45768. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28361969>.
- 208 4. Husain AN, Mirza MK, Gibbs A, et al. How useful is GLUT-1 in differentiating mesothelial
 209 hyperplasia and fibrosing pleuritis from epithelioid and sarcomatoid mesotheliomas? An
 210 international collaborative study. *Lung Cancer*. 2014 Mar;83(3):324-8. Available from:
 211 <https://www.ncbi.nlm.nih.gov/pubmed/24440278>.
- 212 5. Minato H, Kurose N, Fukushima M, et al. Comparative immunohistochemical analysis of
 213 IMP3, GLUT1, EMA, CD146, and desmin for distinguishing malignant mesothelioma from
 214 reactive mesothelial cells. *Am J Clin Pathol*. 2014 Jan;141(1):85-93. Available from:
 215 <https://www.ncbi.nlm.nih.gov/pubmed/24343741>.
- 216 6. Carbone M, Shimizu D, Napolitano A, et al. Positive nuclear BAP1 immunostaining helps
 217 differentiate non-small cell lung carcinomas from malignant mesothelioma. *Oncotarget*.
 218 2016 Sep 13;7(37):59314-21. Available from:
 219 <https://www.ncbi.nlm.nih.gov/pubmed/27447750>.
- 220 7. Amatya VJ, Kushitani K, Mawas AS, et al. MUC4, a novel immunohistochemical marker
 221 identified by gene expression profiling, differentiates pleural sarcomatoid mesothelioma

from lung sarcomatoid carcinoma. *Mod Pathol*. 2017 May;30(5):672-81. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28128276>.

8. Venkatachala S, Shivakumar S, Prabhu M, Padilu R. Histomorphological and Immunohistochemical Analysis of Pleural Neoplasms. *Iran J Pathol*. 2018 Spring;13(2):196-204. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30697290>.

9. Tandon RT, Jimenez-Cortez Y, Taub R, Borczuk AC. Immunohistochemistry in Peritoneal Mesothelioma: A Single-Center Experience of 244 Cases. *Arch Pathol Lab Med*. 2018 Feb;142(2):236-42. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29048219>.

10. Mawas AS, Amatya VJ, Kushitani K, et al. MUC4 immunohistochemistry is useful in distinguishing epithelioid mesothelioma from adenocarcinoma and squamous cell carcinoma of the lung. *Sci Rep*. 2018 Jan 9;8(1):134. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29317712>.

11. Truong LD, Maccato ML, Awalt H, Cagle PT, Schwartz MR, Kaplan AL. Serous surface carcinoma of the peritoneum: a clinicopathologic study of 22 cases. *Hum Pathol*. 1990 Jan;21(1):99-110. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/1688545>.

12. Comin CE, Dini S, Novelli L, Santi R, Asirelli G, Messerini L. h-Caldesmon, a useful positive marker in the diagnosis of pleural malignant mesothelioma, epithelioid type. *Am J Surg Pathol*. 2006 Apr;30(4):463-9. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/16625092>.

13. Khalidi HS, Medeiros LJ, Battifora H. Lymphohistiocytoid mesothelioma. An often misdiagnosed variant of sarcomatoid malignant mesothelioma. *Am J Clin Pathol*. 2000 May;113(5):649-54. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/10800396>.

14. Kinoshita Y, Takasu K, Yuri T, et al. Two cases of malignant peritoneal mesothelioma without asbestos exposure: cytologic and immunohistochemical features. *Ann Diagn Pathol*. 2013 Feb;17(1):99-103. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/22784439>.

- 247 15. Hasteh F, Lin GY, Weidner N, Michael CW. The use of immunohistochemistry to distinguish
248 reactive mesothelial cells from malignant mesothelioma in cytologic effusions. *Cancer*
249 *Cytopathol.* 2010 Apr 25;118(2):90-6. Available from:
250 <https://www.ncbi.nlm.nih.gov/pubmed/20209622>.
- 251 16. Chapel DB, Churg A, Santoni-Rugiu E, Tsujimura T, Hiroshima K, Husain AN. Molecular
252 pathways and diagnosis in malignant mesothelioma: A review of the 14th International
253 Conference of the International Mesothelioma Interest Group. *Lung Cancer.* 2019
254 Jan;127:69-75. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30642555>.
- 255 17. Bishop JA, Sharma R, Illei PB. Napsin A and thyroid transcription factor-1 expression in
256 carcinomas of the lung, breast, pancreas, colon, kidney, thyroid, and malignant
257 mesothelioma. *Hum Pathol.* 2010 Jan;41(1):20-5. Available from:
258 <https://www.ncbi.nlm.nih.gov/pubmed/19740516>.
- 259 18. Gumurdulu D, Zeren EH, Cagle PT, et al. Specificity of MOC-31 and HBME-1
260 immunohistochemistry in the differential diagnosis of adenocarcinoma and malignant
261 mesothelioma: a study on environmental malignant mesothelioma cases from Turkish
262 villages. *Pathol Oncol Res.* 2002;8(3):188-93. Available from:
263 <https://www.ncbi.nlm.nih.gov/pubmed/12515999>.
- 264 19. Pettersson T, Froseth B, Riska H, Klockars M. Concentration of hyaluronic acid in pleural fluid
265 as a diagnostic aid for malignant mesothelioma. *Chest.* 1988 Nov;94(5):1037-9. Available
266 from: <https://www.ncbi.nlm.nih.gov/pubmed/3180855>.
- 267 20. Fujimoto N, Gemba K, Asano M, et al. Hyaluronic acid in the pleural fluid of patients with
268 malignant pleural mesothelioma. *Respir Investig.* 2013 Jun;51(2):92-7. Available from:
269 <https://www.ncbi.nlm.nih.gov/pubmed/23790737>.

- 270 21. Creaney J, Dick IM, Segal A, Musk AW, Robinson BW. Pleural effusion hyaluronic acid as a
271 prognostic marker in pleural malignant mesothelioma. *Lung Cancer*. 2013 Dec;82(3):491-8.
272 Available from: <https://www.ncbi.nlm.nih.gov/pubmed/24161718>.
- 273 22. Matsumoto S, Nabeshima K, Kamei T, et al. Morphology of 9p21 homozygous deletion-
274 positive pleural mesothelioma cells analyzed using fluorescence in situ hybridization and
275 virtual microscope system in effusion cytology. *Cancer Cytopathol*. 2013 Aug;121(8):415-22.
276 Available from: <https://www.ncbi.nlm.nih.gov/pubmed/23450849>.
- 277 23. Ko HM, Kamil ZS, Geddie WR. Microcystic variant malignant mesothelioma presenting as a
278 localized paraspinal mass. *CytoJournal*. 2014;11:16. eng.
- 279 24. Kawai T, Kawashima K, Serizawa H, Miura H, Kyeongil K. Adenomatoid mesothelioma with
280 intranuclear inclusion bodies: a case report with cytological and histological findings. *Diagn*
281 *Cytopathol*. 2014 May;42(5):436-40. Available from:
282 <https://www.ncbi.nlm.nih.gov/pubmed/23166110>.
- 283 25. Wu D, Hiroshima K, Matsumoto S, et al. Diagnostic Usefulness of p16/CDKN2A FISH in
284 Distinguishing Between Sarcomatoid Mesothelioma and Fibrous Pleuritis. *Am J Clin Pathol*.
285 2013 Jan;139(1):39-46. Available from: <Go to ISI>://WOS:000312678900005 English.
- 286 26. Hida T, Matsumoto S, Hamasaki M, et al. Deletion status of p16 in effusion smear
287 preparation correlates with that of underlying malignant pleural mesothelioma tissue.
288 *Cancer science*. 2015 Nov;106(11):1635-41. eng.
- 289 27. Tochigi N, Attanoos R, Chirieac LR, Allen TC, Cagle PT, Dacic S. p16 Deletion in Sarcomatoid
290 Tumors of the Lung and Pleura. *Archives of Pathology & Laboratory Medicine*. 2013
291 May;137(5):632-6. Available from: <Go to ISI>://WOS:000319778400008 English.
- 292 28. Illei PB, Ladanyi M, Rusch VW, Zakowski MF. The use of CDKN2A deletion as a diagnostic
293 marker for malignant mesothelioma in body cavity effusions. *Cancer*. 2003 Feb 25;99(1):51-
294 6. eng.

Figure Legends

Fig. 1. Chest computed tomography on admission. Thickening of the right pleura with effusion was observed (arrow).

Fig. 2. Macroscopic findings of the right lung at autopsy. Right parietal pleura was thickened (arrow).

Fig. 3. Cytological and histological findings of DMPM in scrape-imprint smear (a,b), pleural effusion (c,d), and histological sections (e,f). (a) Cytological findings of the right pleural scrape-imprint smear. Spindle cells with mild nuclear atypia proliferating with fibrous stroma, stained with Papanicolaou stain (Pap), x200. (b) A few cells exhibited nuclear grooves (arrow), x400. Inset: Higher magnification of the nuclear grooves. (c) Cytological findings of the patient's pleural effusion. Atypical spindle cells formed rough epithelioid clusters stained with Pap, x200. (d) Many cells exhibited nuclear grooves and green cytoplasm (arrowhead), x400. Inset: Higher magnification of the nuclear grooves. (e) Histological findings of the right pleural tissue. DMPM cells comprise more than 50% of the tumor in the dense collagen fibers. Hematoxylin and eosin stain (H&E), x200. (f) Some cells exhibit nuclear grooves (arrowheads), x400. Inset: Higher magnification of the nuclear grooves.

On immunohistochemistry, the tumor cells were positive for cytokeratin AE1/AE3 (g), α -smooth muscle actin (α -SMA) (h), and vimentin (i). X600.

Fig. 4. Fluorescence *in situ* hybridization (FISH) of the *CDKN2A/p16* gene. Homozygous loss of the *CDKN2A/p16* gene is observed in 50.4% of the tumor cells.

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Table 1. Immunohistochemical profile of mesothelioma [2-18] in comparison with the current case.

	Epithelioid type		Sarcomatoid type (including DMPM)	Current case
	Pleural mesothelioma	Peritoneal mesothelioma		
Calretinin	+	+	-/+	+
WT-1	+	+	-/+	-
D2-40	+	+	-/+	-
EMA	+	+	-/+	-
GLUT-1	+	-/+	-/+	+
HEG1	+	+	-/+	+
IMP3	+	+	-/+	-
CD146	+	+	-/+	-
AE1/AE3	+	+	+	+
CAM5.2	+	+	+	+
Vimentin	-/+	+	+	+
α-SMA	-	-	+	+
S-100	-	-	-	-
CD34	-	-	-	-
Myogenin	-	-	-	-
Desmin	-	-	-	-
BerEP4	-	-	-	-
MOC31	-/+	-	-	-
p63	-	-	-	-
p40	-	-	-	-
CEA	-	-	-	-
TTF-1	-	-	-	-
Napsin A	-	-	-	-

α-SMA, α-smooth muscle actin; BerEP4, epithelial cell adhesion molecule antibody, clone BerEP4; CEA, carcinoembryonic antigen; DMPM, desmoplastic malignant pleural mesothelioma; EMA, epithelial membrane antigen; GLUT1, glucose transporter 1; HEG1, heart development protein with EGF like domains 1; IMP3, insulin-like growth factor II mRNA-binding protein-3; MOC31, Anti-epithelial cell adhesion molecule monoclonal antibody, clone number-31; TTF-1, thyroid transcription factor 1; WT-1, Wilms' tumor 1.

Table 2. The comparison of the cytological features between the MPM subtypes.

	Epithelioid	Sarcomatoid	DMPM
Cellularity	++	+	+/-~-
Cytoplasm	++	+/-~-	+/-~-
Microvilli	++	-	-
Nuclear atypia	+	++	+/-

MPM, malignant pleural mesothelioma; DMPM, desmoplastic malignant pleural mesothelioma.