Malignant pleural mesothelioma in situ

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Abstract

Although the diagnosis of malignant pleural mesothelioma at an in situ stage was traditionally challenging, it is now possible owing to advances in molecular biological methods such as P16 fluorescence in situ hybridization or BRCA1-associated protein 1 immunohistochemistry. Here, we report the first case, to our knowledge, of total parietal pleurectomy for mesothelioma in situ. Future follow-up and accumulation of cases are necessary to determine whether total parietal pleurectomy could be applied as a treatment for mesothelioma in situ or not.

Keywords: Malignant pleural mesothelioma • In situ • Pleurectomy

INTRODUCTION

Malignant pleural mesothelioma (MPM) is a fast-growing, fatal disease, and thus, detection and treatment at an early stage are important. Mesothelioma in situ (MesIS) represents an early stage before the mesothelioma invades the surrounding tissue. Although the existence of MesIS was proposed long ago [1], there have been no reports of a confirmed MesIS diagnosis until recently. This is mainly due to the histological difficulty in distinguishing mesothelioma at a pre-invasion stage from a benign reactive mesothelium. Recent studies indicated that malignant mesothelioma can be diagnosed based on the homozygous deletion of the P16 gene confirmed by fluorescence in situ hybridization (FISH) or loss of BRCA1-associated protein 1 (BAP1) expression confirmed by immunohistochemistry, in mesothelium-derived cells [2, 3]. These advances in molecular biology techniques led to more reports of MesIS cases [4]. Here, we report a case that was diagnosed as MesIS based on total parietal pleurectomy.

CASE REPORT

The patient was a 71-year-old man, who had worked at a shipyard where he had been exposed to asbestos. He had dyspnoea on exertion; chest X-ray revealed right pleural effusion. Cell block of the pleural effusion revealed multinucleated cells, a hump-like cytoplasmic process, and mutually including cells; MPM was therefore suspected (Fig. 1). Immunostaining of cell blocks was strongly positive for EMA, partially positive for D2-40, partially weakly positive for WT-1, partially positive for p53 and negative for calretinin, TTF-1, napsin A and Glut-1, leading to a suspected diagnosis of epithelial-type MPM. Homozygous deletion of the P16 gene by FISH was found in 52% of the cells in the cell block (Fig. 1); however, due to the lack of knowledge at the time, MPM could not be diagnosed. Chest contrast-enhanced computed tomography after puncturing pleural effusion showed only slight pleural effusion and mild pleural thickening, but no nodules (Fig. 2). A thoracoscopic pleural biopsy was performed (Video 1), showing no evidence of mesothelioma either macroscopically or histologically. Although no diagnosis of mesothelioma was made at this point, the possibility of mesothelioma existing somewhere could not be ruled out. After obtaining sufficient informed consent from the patient, we performed total parietal pleurectomy, including the diaphragmatic and mediastinal pleura. We did not resect the visceral pleura. The resected specimen was completely divided and observed histologically, but no evidence of tumour invasion into the adipose tissue was observed. However, based on more recent reports indicating that homozygous deletion of P16 detected by FISH should be diagnosed as MPM even without tumour invasion [2, 3], we revised the diagnosis to MesIS. BAP1 loss was not observed, although immunohistochemistry was performed after the MesIS diagnosis. Five years have passed since the operation, and the patient is being followed up with no recurrence based on computed tomography.
DISCUSSION

MesIS is the stage in which mesothelioma remains in the serosal membrane, before invading the adipose tissue. Recent reports have indicated that MPM can be distinguished from benign reactive mesothelium with 100% specificity if the mesothelium-derived cells show homozygous deletion of the $P16$ gene by FISH or loss of BAP1 in immunohistochemistry [2, 3]. Since then, MesIS cases have been reported.

Churg et al. [4] reported the largest study on MesIS conducted to date. Seven of the 10 cases progressed to advanced mesothelioma from MesIS, and the median period from biopsy to advanced mesothelioma was 60 months (interquartile range 12; 92). The authors concluded that MesIS may be a favourable stage for treatment because it is likely to develop into advanced mesothelioma and its progression takes a relatively long time.

To our knowledge, this is the first report of total parietal pleurectomy for MesIS. Since the visceral pleura was not resected in our case, the possibility that mesothelioma remains cannot be ruled out. However, we did not resect the visceral pleura because it was highly invasive. Future follow-up and accumulation of cases are required to determine whether total parietal pleurectomy is a useful treatment for MesIS.

Figure 1: Cell block of the pleural effusion showing (A) multinucleated cells, (B) a hump-like cytoplasmic process and (C) mutually including cells, suggesting malignant pleural mesothelioma (Papanicolaou stain, original magnification ×400). (D) Homozygous deletion of the $P16$ gene by fluorescence in situ hybridization was found in 52% of the cells.
Conflict of interest: none declared.

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