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Pleural irregularities and mediastinal pleural involvement in early stages of malignant pleural mesothelioma and benign asbestos pleural effusion

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ABSTRACT

Objective: To elucidate differences in the level and localization of pleural irregularities in early malignant pleural mesothelioma (eMPM) and benign asbestos pleural effusion (BAPE) using CT.
Study design: Retrospective assessment of CT findings of consecutive patients with BAPE at a single centre and patients with eMPM reported in Japanese vital statistics.
Methodology: Thirty-six patients with confirmed diagnoses of BAPE and sixty-six patients with confirmed diagnoses of eMPM (mesothelioma stages T1 or T2) were included. Informed consent, CT scans, and clinical and pathologic details were obtained for all patients and were reviewed by one radiologist, two pathologists, and two pulmonologists. Asbestosis, pleural plaque, rounded atelectasis, and diffuse pleural thickening were assessed in all patients.
Results: Prevalence of asbestosis, pleural plaque, rounded atelectasis, and diffuse pleural thickening was significantly higher in the BAPE group. Low-level irregularity was more common in the BAPE group ($p < 0.001$), whereas high-level irregularity, mediastinal localization, and interlobar fissure were more prevalent in the eMPM group ($p < 0.001$). Interlobar pleural irregularity was not observed in any patients in the BAPE group, although 55% of patients in the eMPM group showed interlobar pleural irregularity. Mediastinal pleural involvement was observed in 74% of patients in the eMPM group and had a positive predictive value of 89%.
Conclusion: This study demonstrates that the level and localization of plural irregularities significantly differed between patients with BAPE and eMPM. Large-scale prospective studies are needed to fully establish the diagnostic utility of such differences.

1. Introduction

Malignant pleural mesothelioma (MPM) is a neoplasm of mesodermal origin and is associated with exposure to asbestos [1]. MPM has a poor prognosis, but detection in early stages can significantly increase patient survival, as distant metastasis occurs at considerably later stages. Unfortunately, however, the diagnosis of MPM is often delayed, either because of nonspecific symptoms or the unreliability of radiological imaging and pleural biopsy techniques [2]. In particular, the variability of pleural findings makes features of anatomical imaging modalities complicated [3], leading to poor differential diagnosis with benign tumours and with other malignant tumours, such as sarcomas and adenocarcinomas [4–6].

Benign asbestos pleural effusion (BAPE) is a complication of chronic exposure to asbestos. It is generally classified as the accumulation of pleural fluid and may be asymptomatic or associated with pain, fever, and dyspnoea. Differentiation of BAPE from early stages of MPM is difficult, due to several overlapping radiological features [7,8]. Considerable work has been conducted to discern

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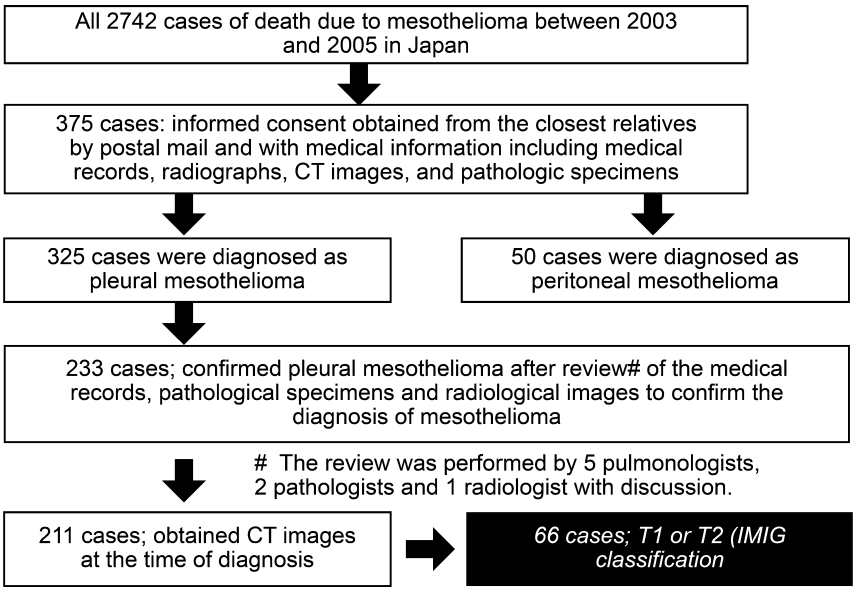

Fig. 1. Flow chart summarizing enrolment of patients in eMPM group.

distinct features of MPM and BAPE, using different diagnostic modalities including X-ray, PET, MRI, and CT [9–11]. However, confirmatory diagnoses of MPM mostly still depend on histopathologic evaluations of biopsy specimens, even though the procedure is associated with complications [12].

In Japan, the production and application of asbestos have been prohibited since 2004. However, since asbestos-related diseases have long latency periods, the number of mesothelioma patients has increased in recent years [13–15]. Evidence suggests that it takes 30–40 years of incubation to develop mesothelioma after exposure to asbestos. It has therefore been postulated that the number of MPM patients in Japan will peak in 2025. The trend is in line with other advanced countries, as in the past, asbestos was used extensively for construction and industrial products [16,17]. We researched the Vital Statistics survey carried out by the Japanese Ministry of Health, Labour, and Welfare and found more than 6000 mesothelioma cases [17]. These statistics, along with the diagnostic issues outlined above, clearly stress an immediate need for efficient strategies for the early diagnosis and management of MPM.

Computed tomography (CT) has been used as a non-invasive tool for diagnosing, staging, and following-up MPM. Asbestos exposure may lead to pleural effusion, pleural thickening, and pleural plaques, which can be effectively diagnosed using CT scans [18]. However, the differences between the CT features of benign and malignant pleural diseases are poorly understood [3,4,19]. The purpose of this study was to evaluate the differences between the CT findings of patients diagnosed with stage I and II MPM and patients diagnosed with BAPE. We also attempted to assess changes in the grade of pleural irregularity, localization of pleural irregularity, and changes in CT scan features during follow-up.

2. Subjects and methods

2.1. BAPE group

Thirty-six patients who were referred to the Okayama Rosai Hospital between Mar 1, 2005 and Apr 30, 2008 and who had a definitive diagnosis of BAPE were included. BAPE was indicated by symptoms including chronic cough, abnormal pulmonary function tests, chest pain, breathlessness, hoarseness of the voice, and CT scan results. All patients had a history of asbestos exposure. Pleural biopsy was performed in all cases. All pathologic specimens were reviewed by a pathologist, and the histological assessment of malignancy was made on the basis of standard cytological tests. BAPE was defined on the basis of four criteria: (a) history of asbestos exposure, (b) radiologic or thoracentesis confirmation of pleura, (c) absence of another cause for the pleural effusion, and (d) no malignant tumour developing within one year [20–22]. Follow-up was conducted through routine visits. Informed consent was obtained from all patients, and the Institutional Ethical Review Board of Okayama Rosai Hospital approved the study.

The CT scans were obtained using X-vigor in 6 cases and Aquilion^{TM}32 (Toshiba Medical Systems, Otawara, Tochigi, Japan) in 30 cases. Patients were screened in the supine position with or without injection of contrast media, depending on the radiologists' judgment; 9 cases were screened without contrast media, while 24 cases used it and 3 cases were screened both with and without contrast media. A slice thickness of 5 mm and mediastinal and lung parenchymal window settings were used. The window width was 1500 HU for parenchymal imaging and 350 HU for soft tissues. Parenchymal and soft tissue images were reconstructed with sharp and smooth filters, respectively. Intravenous iodinated contrast medium was used to determine lymph node enlargement and pleural irregularities. The CT scans and accompanying chest radiographs were reviewed by one radiologist and two pulmonologists (K. K., T. K., and N. F.) who were familiar with asbestos-related disease and who were members of the official pneumoconiosis examination committee for labourers in the Okayama prefecture. The observers were unaware of the pathologic diagnosis; a conclusion was reached by consensus.

2.2. Early MPM (eMPM) group

Sixty-six patients were included in the early MPM group. The subjects were selected from mesothelioma death cases in the Japanese Vital Statistics (2003–2005). The detailed method for patient selection and data collection has been described elsewhere [23]. In brief, we extracted all cases of death due to malignant mesothelioma in the Vital Statistics register in Japan (2003–2005). Informed consent was obtained from living relatives, and complete medical records, radiographs, and/or CT images were obtained from the respective medical institutions. We reviewed medical records and radiological images with clinically and pathologically confirmed diagnoses of malignant mesothelioma based on ICD CD46.