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Retrospective investigation on diagnostic process for benign asbestos pleural effusion (BAPE) using checklist

Takumi Kishimoto[1] | **Nobukazu Fujimoto**[1] | **Keiichi Mizuhashi**[2] | **Satoko Kozawa**[3] | **Motohiko Miura**[4]

[1]Research & Training Center for asbestos-related diseases, Okayama, Japan

[2]Toyama Rosai Hospital, Uozu, Japan

[3]Yokohama Rosai Hospital, Yokohama, Japan

[4]Tohoku Rosai Hospital, Sendai, Japan

Correspondence
Takumi Kishimoto, 1-10-25 Chikko Midorimachi, Minami-ku, Okayama 702-8055, Japan.
Email: nakisimt@okayamah.johas.go.jp

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Abstract

Objectives: In Japan, benign asbestos pleural effusion (BAPE) has been eligible for industrial accident compensation since 2003 as an asbestos-related disease despite the lack of good criteria. We compiled a criteria into a checklist of essential items and for excluding other diseases inducing pleural effusion as a diagnosis process.

Method: Thoracentesis was performed in order to confirm the presence of pleural effusion at the initial diagnosis, and 105 suspected BAPE patients were retrospectively examined. We complied a checklist comprising the following diagnostic items: (a) occupational asbestos exposure; (b) confirmation of exudate of pleural effusion; (c) exclusion of pleural effusion with malignant tumors based on negative results of CEA and hyaluronic acid, and cytology of pleural effusion; (d) exclusion of rheumatic, bacterial, and tuberculous pleuritis; (d) radiological findings for exclusion of malignancies; and (e) histopathological findings based on thoracoscopy that exclude malignancies (when thoracoscopy was not performed, there was confirmation that no malignancies were present during 3-month follow-up observation). Cases that satisfied all items were defined as BAPE.

Results: Among the 105 suspected cases, there were five cases that had no occupational asbestos exposure; six cases in which transudate of on pleural effusion; one case each of rheumatoid pleuritis and tuberculous pleuritis; and five cases of pleural mesothelioma based on chest radiography and histopathological findings within 3 months after initial diagnosis. Therefore, we excluded 18 cases from the 105 candidates and determined 87 cases of BAPE.

Conclusion: We consider that six items described above are suitable for diagnosing BAPE.

KEYWORDS

benign asbestos pleural effusion, exudative, occupational asbestos exposure, pleural mesothelioma, pleural plaques

1 | INTRODUCTION

Benign asbestos pleural effusion (BAPE) is a non-malignant pleural lesion induced by asbestos exposure, which is also known as asbestos pleuritis. Eisenstadt[1] reported BAPE as a new disease concept for the first time in 1964, and BAPE typically presents unilaterally and with a small volume of pleural effusion.

Epler et al[2] reported diagnostic criteria such as (a) asbestos exposure, (b) presence of pleural effusion by chest radiograph or thoracentesis, (c) no other causes except asbestos exposure, and (d) no appearance of malignancy during a period of 3 years from diagnosis. These criteria were generated for prospective epidemiological observation, and clinical follow-up for 3 years was set in order to exclude pleural mesothelioma. Hillerdal et al[3] showed that clinical follow-up for only 1 year is sufficient if precise checking is followed by diagnostic imaging such as chest computed tomography (CT) scanning in 1989. However, other new criteria have not been proposed since. Therefore, we cannot compare with standard data described the previous studies.

It is speculated that the pathogenic mechanism of BAPE is mechanical irritation of the visceral pleura by asbestos fibers, obstruction of the lymphatic drainage of the parietal pleura induced by pleural fibrosis,[4] or autoimmunity due to the adjuvant effect of asbestos fibers.[5] However, the true mechanism has not yet been established. It may be defined that the inflammation of visceral pleura induced by asbestos fibers induces BAPE.

In Japan, BAPE was approved in 2003 as an asbestos-related disease for industrial accident compensation. However, this compensation to BAPE patients was judged despite the lack of diagnosis criteria. It is suspected that some patients with BAPE have been overlooked because there are no diagnostic criteria for BAPE. Therefore, we examined retrospectively the diagnosis of BAPE based on occupational history, pleura, chest images, and laboratory data of pleural effusion together with data from reported BAPE patients.[6-8] We then established a diagnosis manual for BAPE, and report the findings.

2 | MATERIALS AND METHODS

From 2012 to December in 2019, 105 patients who were diagnosed with BAPE at the initial diagnosis at the Okayama Rosai Hospital, Toyama Rosai Hospital, Yokohama Rosai Hospital, and Tohoku Rosai Hospital in Japan, were examined retrospectively, and the validity of the diagnosis was investigated. These cases were diagnosed as BAPE at the initial diagnosis based on data from laboratory and radiological findings. However, we reinvestigated these cases based on a checklist of proposed new criteria, and some cases were deemed to be diagnosed incorrectly. Therefore, the remaining cases were diagnosed definitely as BAPE. It was made clear that BAPE should be diagnosed based on these procedures containing these exclusion items.

We complied a checklist for diagnosing BAPE as given in Figure 1, and judged retrospectively the validity of the diagnosis depending on this checklist for the 105 cases who were diagnosed as BAPE at the initial diagnosis. The checklist was basically complied based on (a) the presence of occupational asbestos exposure for confirmation of asbestos exposure, (b) pleural effusion findings with thoracentesis and exclusion of other diseases in the criteria defined by Epler et al[2] in 1982.

1. In order to confirm asbestos exposure, we inquired concerning occupational asbestos exposure. In the cases with confirmed asbestos exposure, we inquired concerning the age at first exposure, exposure term, and job duty, and investigated the latent period from the first exposure to the onset of BAPE. We designated cases as questionable exposure to asbestos where pleural plaques appeared in radiographs without confirmation of occupational asbestos exposure. We, therefore, excluded these cases.
2. In order to exclude other diseases that might induce pleural effusion, we checked the past history and present illness. There were 15 cases with heart disease, two cases with kidney disease, and one case with prostate cancer. However, none of these cases were excluded because these diseases were assessed not to cause pleural effusion. In the next step, we examined the pleural fluid. Since pleural fluid results from inflammatory disease with asbestos fibers, the fluid was confirmed to be exudative based on Light's criteria.[9]
3. (a) For exclusion of cases with malignant pleural effusion, cytopathological examination of the pleural effusion as well as assay of carcinoembryonic antigen (CEA) and hyaluronic acid in the pleural effusion were performed. (b) To exclude rheumatoid pleuritis, rheumatoid factors (RFs) in the serum and effusion were examined. (c) For exclusion of bacterial pleuritis, a bacterial check of the pleural effusion was performed and we confirmed that lymphocytes were more than half in the leukocytes of the pleural effusion. (d) Furthermore, to exclude tuberculous pleuritis, adenosine deaminase (ADA) was checked, and a bacterial smear and culture for tuberculosis were performed in addition to polymerase chain reaction for Mycobacterium tuberculosis (Tbc-PCR).
4. At chest imaging, the absence of irregular pleural thickening and no tumorous mass were confirmed in order to exclude pleural mesothelioma.[10]
5. To exclude the early stages for pleural mesothelioma, macroscopic findings based on thoracoscopy and biopsy of the parietal pleura were checked. Histopathological examination had not been performed in some of the cases,

Checklist for diagnosis of benign asbestos pleural effusion

1	Name		Date of birth	MM/DD/YYYY / /	Age	years
2	Occupational asbestos exposure		☐ Yes [ ] Occupational asbestos histories Exposure term [ ]			☐ Unknown
3	Pleural effusion		☐ Yes [☐ bloody ☐ others ( )]			☐ None
4	Past history and present illness		☐ Heart disease ☐ Kidney D ☐ Collagen D ☐ Malignanc ☐ None ☐ Thoracic surgery within 6 months ☐ Others ( )			
5	Pleural effusion		※Light's criteria 1. Effusion TP/Serum TP＞0.5 2. Effusion LDH/Serum LDH>0.6 3. Effusion LDH>Serum LDH 2/3			
	Exudate ☐ Yes ☐ No		Effusion: ☐ T-protein ( ) g/dL ☐ LDH ( ) U/L Serum: ☐ T-protein ( ) g/dL ☐ LDH ( ) U/L			
	Cytological result in PE		☐ Class Ⅰ ☐ Ⅱ ☐ Ⅲ ☐ Negative			☐ None
	CEA in PE less than 5.0 ng/ml		☐ Yes CEA ( )ng/mL			☐ None
	HA in PE less than 100,000 ng/ml		☐ Yes HA ( )ng/mL			☐ None
	Rule out rheumatism and other collagen disease		☐ Yes Effusion RF( )IU/mL , Serum RF( )IU/mL Others( )			☐ None
	ADA in PE less than 40IU/L		☐ Yes Effusion ADA ( )IU/L			☐ None
	Lymphocytes in PE (%)		☐ Yes Lymphocyte ( )%			☐ None
	Bacterial examination in PE	Bacteria	☐ Positive [☐ − ☐ ± ☐ 1+ ☐ 2+ ☐ 3+]			☐ Negative
		Mycobacteria: Smear	☐ Positive			☐ Negative
		Mycobacteria: Culture	☐ Positive			☐ Negative
		Mycobacteria: PCR	☐ Positive			☐ Negative
6	Chest radiological examination					
	Malignant signs by chest CT		☐ None			☐ Yes
	Pleural plaques		☐ Yes [ ]			☐ None
7	Thoracoscopic examination		☐ Yes [☐ Pleural plaques ☐ Susp of malignant chages]			☐ None
	Pleural biopsy		☐ Yes [☐ Malignant findings] Pathological exam [ ]			☐ None
BAPE			☐ OK ☐ NO ☐ Pending			
Registration date			MM/DD/YYYY / /		Confirmer	

HA : Hyaluronic acid , PE : Pleural effusion

FIGURE 1 Checklist for diagnosis of benign asbestos pleural effusion

and no malignant tumor was confirmed in follow-up observation during a period of at least 3 months.

3 | RESULTS

All 105 cases suspected as BAPE at the initial diagnosis were male and aged 60 to 96 years with the median age of 79 years at diagnosis.

1. One hundred cases (95.2%) were confirmed to have occupational history of asbestos exposure and four cases were suspected to have asbestos exposure with pleural plaque imaging without definite occupational asbestos exposure. One case was not confirmed to have occupational asbestos exposure and pleural plaques as indicated in Figure 2.
2. Differential diagnosis of pleural effusion was performed according to the Diagnostic Approach to Pleural Effusion.[11] Thoracentesis was performed on all 105 cases and 79% proved to be bloody effusion.
3. Pleural fluids of 99 cases (94.3%) were proven to be exudative. Among these, 55% satisfied all three items of Light's criteria, 22% satisfied two items, and 17% satisfied one item. Six cases (6%) that did not satisfy any item were determined as transudative, and were excluded at this stage.
4. (a) Only one case showed more than 5 ng/mL of CEA, and the malignant marker threshold was 6.5 ng/mL, but its malignancy was denied. Two point four percent of cases exhibited hyaluronic acid exceeding the 100 000 ng/mL threshold, but did not exceed 120 000 ng/mL, and pleural mesothelioma was denied. For cytology, with regard to Class III diagnosis, 4.9% of cases were Class III, but they were mild (Class IIIa) and malignant tumors such as mesothelioma were not observed during follow-up (Table 1). (b) One case with high levels of serum and effusion RFs was later proven to be rheumatoid arthritis. This case was diagnosed previously with rheumatoid pleuritis. (c) One case with an ADA level in the pleural effusion of 60.5 U/L was proven to be tuberculous pleuritis with detection of *Mycrobacterium tuberculosis* (M. tb) after 2 weeks culture, despite negative results with Tbc-PCR and interferon-γ releasing assay (T-SPOT) as given in Figure 2. (d) In regard to bacterial pleuritis, all cases presented negative in the bacterial test. The majority of cases (97.5%) had more than 50% of lymphocytes among the leukocytes in pleural effusion, and 3.5% increased in eosinophils, but no case increased in neutrophils (Figure 2).
5. For radiological examination, 97.5% of cases presented with pleural plaques, but no pulmonary asbestosis. No tumorous thickening of the pleura was detected at the initial diagnosis; however, three cases exhibited irregular pleural thickening in 1-3 months of follow-up. Figure 3 shows one of these three cases without positive findings in all sites containing the left pleura except pleural effusion on the left side with PET-CT. After 3 months, the left pleura exhibited slight irregular thickening, and distinct narrowing of the left thorax was present as shown in Figure 4. We suspected left pleural mesothelioma and was diagnosed definitively based on thoracoscopy as given in Figure 2.

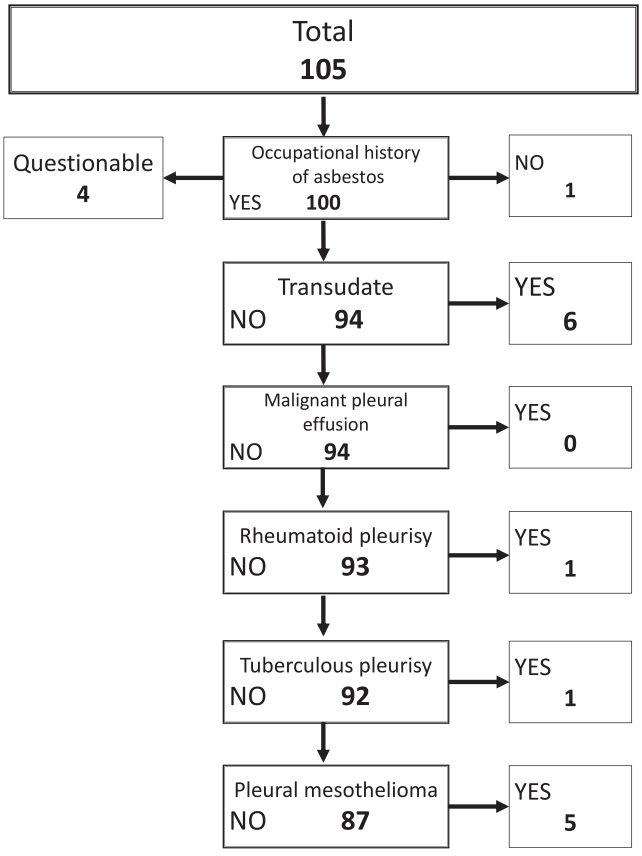

FIGURE 2 Differential diagnosis of BAPE from other diseases

TABLE 1 Laboratory findings in pleural effusion

CEA in PE less than 5.0 ng/mL		Lymphocytes dominant in PE	
YES	98.8%	YES	96.5%
NO	1.2%	NO	3.5%
HA in PE less than 100,000 ng/mL		Exclusion of RA pleuritis	
YES	97.6%	YES	96.4%
NO	2.4%	NO	3.6%
Cytology in PE		ADA in PE less than 40 IU/L	
Class I	30.5%	YES	98.8%
Class II	64.6%	NO	1.2%
Class III	4.9%		

Abbreviations: HA, hyaluronic acid; PE, pleural effusion.

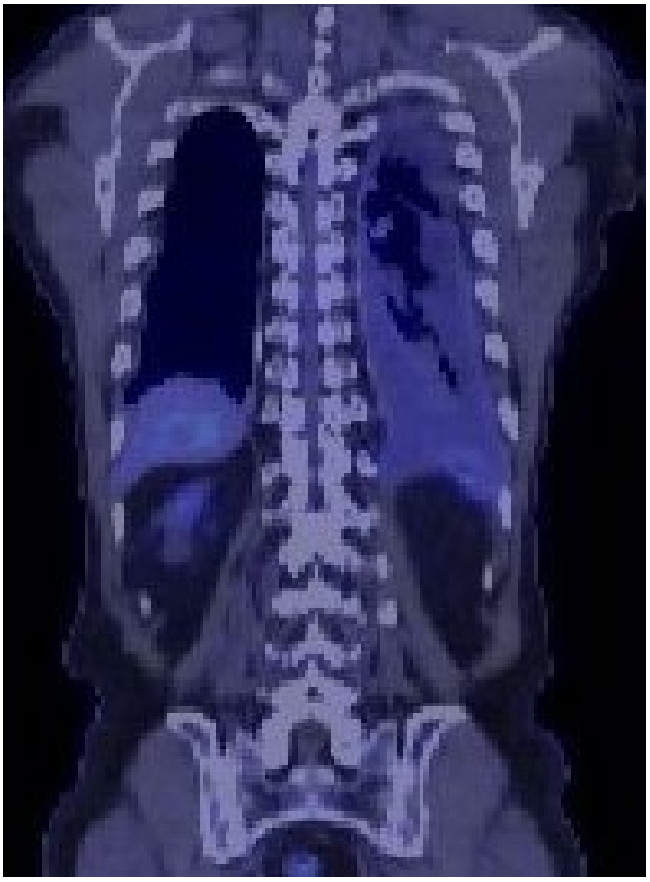

FIGURE 3 PET-CT shows no positive lesions in the left thorax with pleural effusion

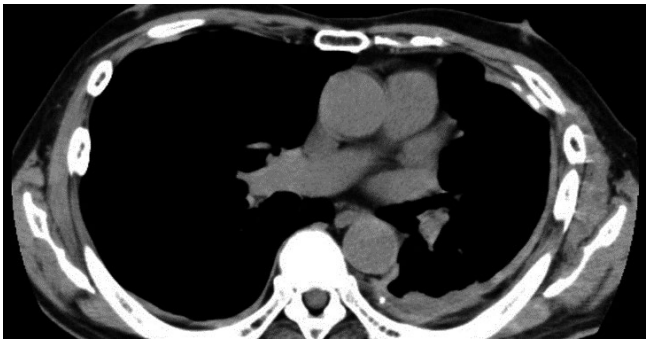

FIGURE 4 Chest CT that was taken 6 mo after first visit shows irregular pleural thickening in the left pleura. The left thorax becomes smaller than the right thorax suggesting left pleural mesothelioma

6. Just after the initial diagnosis, thoracoscopy in three cases among these five cases was performed but biopsy results were negative. However, tumorous pleural thickening appeared during the 3-month follow-up period, and subsequent biopsy proved to be sarcomatoid pleural mesothelioma. The other two cases complained of persistent severe chest pain as a subjective symptom although there were negative radiological findings. Pleural biopsy with thoracoscopy was performed and these cases were proved to be the epithelioid type of pleural mesothelioma. Therefore, we assessed the necessity of more than 3 months of follow-up after thoracentesis for the diagnosis of BAPE.

Based on the exclusion criteria, we determined BAPE induced by occupational asbestos exposure for 87 cases. All of the final defined 87 cases were male and aged 60 to 93 years with the median age of 79 years. In terms of the occupational history, the main occupation was shipbuilder followed by construction worker as indicated in Figure 5. The asbestos exposure term ranged from 2 to 55 years with the median of 38 years. The latency period ranged from 18 to 73 years with the median of 53.5 years.

4 | DISCUSSION

Pleural effusion comprises transudate occurring from impairment of the flow of body fluid such as heart failure or nephrotic syndrome, and exudate induced by local inflammation extending to the pleura or by malignancies. BAPE is visceral pleural pleuritis induced by asbestos fibers penetrating the pleural cavity, and has been considered to be an asbestos-related disease since the 1960s.[1] No new criteria for BAPE have been determined, since Epler et al[2] described criteria in 1982. In Japan in 2003, BAPE was added to the list of asbestos-related diseases for which patients were able to receive industrial accident compensation. Although no new criteria were identified, compensation for this disease was determined. Therefore, we present a new checklist to use as a reference in diagnosing BAPE based on a retrospective reinvestigation of the cases diagnosed as BAPE at the initial diagnosis that screens out the misdiagnosed cases.

Although asbestos exposure history is a criterion reported by Epler, we propose occupational history of asbestos exposure in order to ensure asbestos exposure. For this reason, there are no reports of BAPE induced by environmental asbestos exposure. Almost all cases were induced by occupational asbestos exposure. Based on the checklist, we excluded five cases including four cases whose occupational history of asbestos exposure was unclear from the 105 cases under investigation. Although almost all cases (97.5%) presented with pleural plaques, pleural plaques were considered as a reference item only and occupational asbestos exposure was considered more important.

By confirming the exudate as inflammatory pleural effusion using Light's criteria classification,[9] six cases with transudate were excluded. Ninety-three percent to 96% of cases meeting this criterion were reported to have exudate. Furthermore, the cases that did not satisfy this criterion were determined to be transudative.

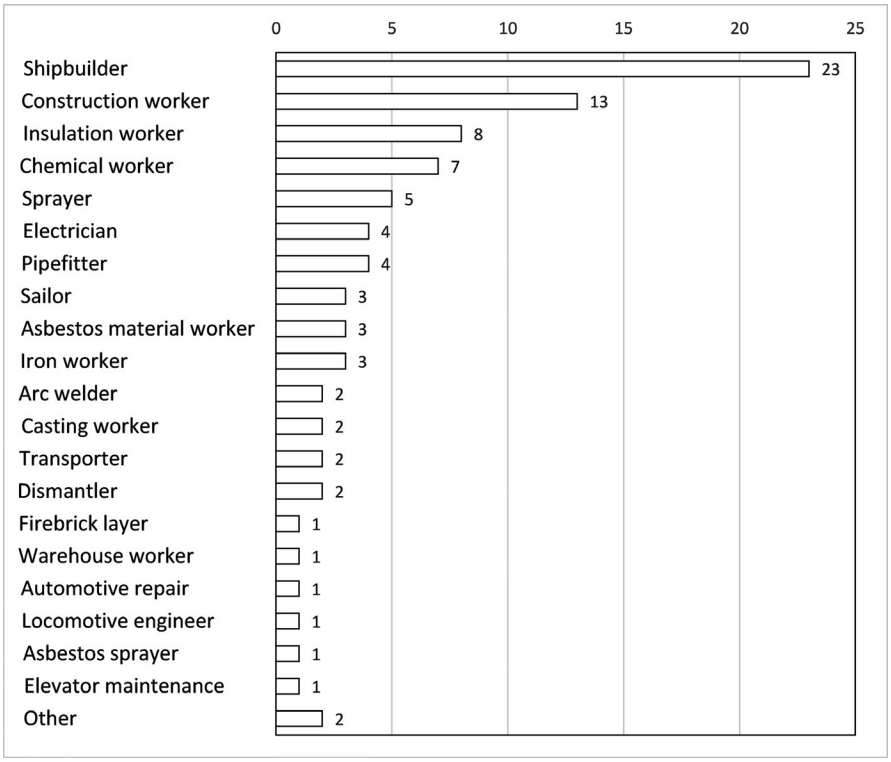

FIGURE 5 This figure shows the number of occupational histories for 87 confirmed BAPE cases. Shipbuilder and construction workers are main components for BAPE cases as reported for asbestos-related lung cancer or mesothelioma cases

For differential diagnosis to exclude malignant tumors, we considered CEA, hyaluronic acid, and cytology data. The CEA concentration in pleural effusion was reported to be less than 1.8 ng/mL for BAPE[12] and useful in identifying BAPE. However, for mesothelioma, CEA is not helpful in distinguishing from pleural mesothelioma because almost all pleural mesothelioma cases were within normal limits. The majority of pleural mesothelioma cases exhibited hyaluronic acid concentrations of greater than 100 000 ng/mL; however, almost all BAPE cases exhibited concentrations of less than 100 000 ng/mL.[6] Fujimoto reported that three cases among 87 cases with BAPE exceeded the concentration of 100 000 ng/mL, but those were less than 120 000 ng/mL.[7] Our results regarding hyaluronic acid in pleural effusion were consistent with this report and we assumed that there were no cases that suggested mesothelioma. It is relatively easy to differentiate malignant effusion using cytological examination. Five cases showed Class III, which was difficult to judge, and these were Class IIIa. We denied malignancies from clinical course. From these results, we judged that there were no cases with findings suggestive of a malignant tumor.

At the next step, differential diagnosis of collagen disease such as rheumatic pleuritis was performed. There was no case affected by these diseases based on past history and present illness. One case presented with high RFs in serum and pleural effusion, and was examined carefully at a later date. This was likely rheumatic pleuritis from diagnosis of rheumatoid arthritis,[13] and was excluded. In addition, to exclude bacterial pleuritis, we performed bacterial examination and assayed the differential count of leukocytes in the pleural effusion. There were no abnormal cases. Although the percentage of lymphocytes in leucocytes in the pleural effusion was greater than 50% in most cases, three cases presented with eosinophilia. BAPE cases with eosinophilia were reported,[14] and these results did not affect this diagnosis.

To exclude tuberculous pleuritis, which presents with many lymphocytes in pleural effusion, we performed ADA assay and bacterial examination. Only one case showed a concentration of greater than 40 U/L (60.5 U/L) of ADA. It has been reported that cases with ADA of greater than 40 U/L are suspected to suffer from tuberculosis.[15] This case presented negative for Tbc-PCR in effusion and serum T-SPOT tests, but culture of pleural effusion proved M. tb positive. We determined that this was tuberculous pleuritis. We excluded 13 cases due to the results so far.

Finally, it is difficult to differentiate diagnosis between BAPE and early stage pleural mesothelioma. Kato et al[10] focused on the thickening of the mediastinal pleura for one of the features of pleural mesothelioma, but no positive cases presented with this indicator in 92 cases examined. Although clinical symptoms during 3 months of follow-up presented only as pleural effusion, two cases complained of severe chest pain and three cases exhibited irregular pleural thickening and narrowing of the affected thorax. In three cases among them pleural biopsy was performed under thoracoscopy. Visual change in the tumors was not observed in these cases, and they were diagnosed with fibrinous pleuritis based on biopsy. However, after manifestation of irregular pleural thickening, the second pleural biopsy indicated pleural mesothelioma. The reason for this discrepancy was that

the biopsied sites were thought not to be suitable for definite diagnosis. Two other cases had no positive radiological abnormality but indicated persistent chest pain. We again performed thoracoscopic biopsy and made a definite diagnosis of epithelioid mesothelioma. The diagnosis of these five cases changed during the 3 months of follow-up, and we assessed the necessity for a 3-month of follow-up observation period after administering a pleural effusion test.

From the report by Metintas et al,[16] in the 287 cases that underwent thoracoscopy, 101 cases diagnosed with fibrinous pleuritis by biopsy were examined more closely, and the rate of false negatives was 18%. All of these cases presented as malignant pleural diseases. Of the 142 cases exhibiting exudate as pleural effusion, 30% to 40% could not be diagnosed based on histopathological data using thoracoscopy. Of that group 8% to 12% were found to have malignant pleural lesions and almost all cases were diagnosed with pleural mesothelioma. The other 25% to 91% were classified as non-specific pleuritis and were treated as idiopathic pleuritis. If a definite diagnosis is reported to be determined, greater accuracy using invasive biopsy is required.[17] For determining BAPE as a diagnosis by exclusion, we consider that a 3-month follow-up period is necessary. Nevertheless, a part of pleuritis in which definite diagnosis is not determined after thoracoscopic biopsy is thought to be grouped as BAPE. Using these criteria, we diagnosed 87 cases as BAPE.

Thus, when BAPE was diagnosed with (a) a history of occupational asbestos exposure and (b) the presence of exudate based on a pleural effusion test as the required main items; and (c) negative results of CEA and hyaluronic acid in pleural effusion, and cytology of pleural effusion for exclusion of malignancy; (d) exclusion of rheumatic, bacterial and tuberculous pleuritis; (e) exclusion of malignancy using radiological images; and (f) exclusion of histopathological malignancy using thoracoscopy (when thoracoscopy was not performed, no malignant tumor was confirmed in follow-up observation during at least 3 months) as required sub-items, BAPE could be determined with a more than 95% if cytology was class III. If some of these six sub-items are no, we should carefully make a differential diagnosis.

The age of BAPE onset induced by asbestos exposure has pointed out the relationship to the volume of asbestos to which the patient was exposed. The number of incidences increases and latency becomes short, if the exposure volume of asbestos increases.[18] The median age of BAPE onset was 66 years at our previous report,[8] but increased to 79 years at this report. Similar to previous reports, the history of occupational asbestos exposure is approximately the same such as No. 1 is shipbuilder and No. 2 is construction worker as shown in Figure 5, and asbestos exposure in these types of work was classified as moderate. The median exposure term was 38 years and the latency from the first exposure was 53.5 years, which was longer than that shown by previous data.[6,8,12] As a reason for this, considered together with many cases of advanced-age patients, it was suggested that the exposure dose was low when they worked with asbestos exposure. Workers were likely affected with BAPE after a long latency period with a low dose of past asbestos exposure.

On the other hand, five cases among those diagnosed as BAPE at the initial diagnosis were determined as pleural mesothelioma in their clinical course. The term of clinical observation was between 1 and 3 months. The reason why we did not confirm pleural mesothelioma was not that pleural mesothelioma changed from BAPE, but that we failed to make a definite diagnosis of pleural mesothelioma at the initial diagnosis due to the presence of only pleural effusion without malignant findings such as tumorous pleural thickening by chest CT and that definite diagnosis could be performed during the progression of the disease. Although we observed parietal pleura in three of the five cases using thoracoscopy and performed a pleural biopsy under thoracoscopy at the initial diagnosis, we failed to reach a definite diagnosis.

If we do not detect malignant findings that suggest mesothelioma based on chest CT, we should pursue more precise observation through thoracoscopy and perform a biopsy at the proper site. In particular, in cases presenting with persistent chest pain, we need to consider early stage pleural mesothelioma based on Positron Emission Tomography-Computed Tomography (PET-CT) scanning and perform biopsy at suitable sites for final diagnosis.

As mentioned above, we are convinced that the presented criteria such as occupational asbestos exposure, exudative pleural effusion, tumor marker in pleural effusion, bacterial test results, radiological findings and histopathological findings are suitable for diagnosing BAPE, and it is valid that cases that satisfied these criteria during the 3 months of follow-up be diagnosed as BAPE.

DISCLOSURE

Approval of the research protocol: N/A. *Informed consent:* All participants provided written informed consent before inclusion in the study. *Registry and the registration no. of the study/trial:* N/A. *Animal studies:* N/A. *Conflict of interest:* N/A.

AUTHOR CONTRIBUTIONS

Takumi Kishimoto was involved in data analysis and writing manuscript. Nobukazu Fujimoto, Keiichi Mizuhashi, Satoko Kozawa, and Motohiko Miura were involved in accumulation of patients for BAPE.

ETHICAL APPROVAL

This study was approved by the 11th research ethics committee of the Japan Organization of Occupational Health and Safety on June 18, 2018 (No. 9).

ORCID

Takumi Kishimoto https://orcid.org/0000-0003-2718-1713
Nobukazu Fujimoto https://orcid.org/0000-0002-4516-0433

REFERENCES

1. Eisenstadt HB. Asbestos pleurisy. *Dis Chest*. 1964;46:78-81.
2. Epler GR, McLoud TC, Gaensler EA. Prevalence and incidence of benign asbestos pleural effusions in a working population. *J Am Med Assoc*. 1982;247(5):617-622.
3. Hillerdal G, Ozesmi M. Benign asbestos pleural effusion. 73 exudates in 60 patients. *Eur J Respir Dis*. 1987;71(2):113-121.
4. Lees PSJ, Breysse PN, McArthur BB, et al. End user exposure to man-made vitreous fibers: I Installation of residual insulation products. *Appl Occup Environ Hyg*. 1993;8:1022-1030.
5. Warheit DB, Chang LY, Hill LH, et al. Pulmonary macrophage accumulation and asbestos induced lesions at sites of fiber deposition. *Am Rev Respir Dis*. 1984;129(2):301-310.
6. Kishimoto T, Gemba K, Aoe K, et al. Asbestos pleural effusion. *Res Physician*. 2010;17:374-379.
7. Fujimoto N, Gemba K, Asano M, et al. Hyaluronic acid in the pleural fluid of patients with malignant pleural mesothelioma. *Respir Investig*. 2013;51(2):92-97.
8. Kishimoto T, Okahara M, Chikamori K, et al. Clinical evaluation of benign asbestos pleural effusion. *Jap J Thorac Dis*. 1998;36(1):18-22.
9. Light RW, Macgregor MI, Luchsinger PC, et al. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med*. 1972;77(4):507-513.
10. Kato K, Gemba K, Fujimoto N, et al. Pleural irregularities and mediastinal pleural involvement in early stages of malignant pleural mesothelioma and benign asbestos pleural effusion. *Eur J Radiol*. 2016;85(9):1594-1600.
11. Saguil A, Wyrick K, Hallgren J. Diagnostic approach to pleural effusion. *Am Fam Physician*. 2014;15:90(2):99–104.
12. Fujimoto N, Gemba K, Aoe K, et al. Clinical investigation of benign asbestos pleural effusion. *Pul Med*. 2015;2015:1-6.
13. Walker WC, Wright V. Rheumatoid pleuritis. *Ann Rheum Dis*. 1967;26(6):467-474.
14. Robinson BW, Musk AW. Benign asbestos pleural effusion: diagnosis and course. *Thorax*. 1981;36(12):896-900.
15. Porcel JM. Tuberculous pleural effusion. *Lung*. 2009;187(5):263-270.
16. Metintas M, Ak G, Cadirci O, et al. Outcome of patients diagnosed with fibrinous pleuritis after medical thoracoscopy. *Respir Med*. 2012;106(8):1177-1183.
17. Wrightson JM, Davies HE. Outcome of patients with non-specific pleuritis at thoracoscopy. *Curr Opin Pulm Med*. 2011;17(4):242-246.
18. Peacock C, Copley SJ, Hansell DM. Asbestos-related benign pleural disease. *Clin Radiol*. 2000;55(6):422-432.

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