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Original Article

Confirmation of asbestos body by both a usual optic microscopy and an electron probe micro-analysis (EPMA) —three autopsied cancer cases of pulmonary asbestosis—

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Abstract

Background : Most simple and definitive diagnosis of asbestosis was established by light microscopic examination with Hematoxylin-Eosin stain (HE), and EPMA was regarded as one of the supplemental diagnostic methods. Our four cases of occupational pneumoconiosis were examined with microscopy and EPMA, and its effectiveness for diagnosis was discussed in this report. Cases : Three cases among these four occupational pneumoconiosis had malignancies : adenocarcinoma of lung, small cell carcinoma of lung, and diffuse mesothelioma. Formalin-fixed paraffin-embedded pulmonary specimens were searched for a presence of asbestos body by light microscopy and analyzed for physical constitutions of deposits. Two cases were diagnosed by both an occupational history and an EPMA analysis. The other two cases were amphibole asbestosis. Discussion : Asbestosis was microscopically confirmed in two constructional workers and also electron-microscopically in one brake-lining maker. EPMA was very valuable for a physical confirmation of asbestos character. Even if a use of asbestos becomes severely regulated legally, a lot of asbestosis or its complications are expected to occur as illness on-the-job for the next 40-50 years, and a detailed occupational history and clearer diagnostic methods as EPMA will be demanded.

Key Words : occupational exposure, X-ray microanalyzer, electron probe micro-analysis (EPMA), serpentine, amphibole, asbestosis, asbestos body

Background

Asbestos is superior in both a nonflammability and a plasticity and three types of asbestos are widely used in industries as a commercial asbestos ; e.g. chrysotile, crocidolite, and amosite (Fig. 1). An on-the-job accident related to asbestos exposure has been legally regulated according to both the second number and the seventh one in Table 1－2 related to Article 35 of the Constitution in Enforcement Regulations of Labor Standards Law from 1948 in Japan. A consumption of asbestos has been legally restricted and reduced after 1990s because asbestos induces asbestosis and other complications. Pathological or autopsied confirmation of occupational exposure of asbestos became very important to rescue the asbestosis-related patients.

Asbestos fibers consist mainly of silicon, iron, and magnesium and are classified into 6 materials (Fig. 2) (1－3).

It was suggested that an occupational exposure of asbestos induced several diseases, classified based on an exposure condition as follows : (i) an exposure of both high-dose and short-duration less than 20 years induced pulmonary asbestosis, beginning from lower lobes, (ii) both high-dose and long-duration between 20 and 40 years caused carcinoma of lung in 10-20% of asbestosis with 5 times risk rate by smoking, (iii) both low-dose and short-duration raised pleural plaque regardless of occupation or non-occupation, (iv) diffuse pleural thickening, (v) long-duration of 30 years induced benign asbestos pleural effusion or pleuritis, and (iv) either a low-dose and long-duration from 20 to 40 years or a 40-years-latent phase with 20-years-exposure induced diffuse malignant mesothelioma in pleura (80% in whole cases with mesothelioma), peritoneum, pericardium, and testicular vaginal peritoneum (Fig. 3) (1－3). In the Workmen's Compensation Law, a pathological decision of pneumoconiosis with an occupational history was very important for an identification of on-the-job disease.

As to asbestosis, counting asbestos number was also useful as well as an existence of asbestos body because its number also corresponded to a possibility of its exposure (Fig. 4) (1－3).

We experienced four autopsied cases suggested as occupational pneumoconiosis and reported in this article. Asbestosis was analyzed by both a usual optic microscopy and an EPMA, and their utility was discussed (1－4).

Cases

Four pneumoconiosis cases were listed with occupational histories, complications of cancer, light microscopic findings, EPMA analyses, and estimations of exposure materials (Fig. 6). Examined specimens from lungs con-

sisted of one or six tissues a pulmonary lobe, each one of which was at least accompanied with charcoal deposition and fibrosis.

In the first case an asbestoid body confirmed microscopically was regarded as an iron-related deposit, not true asbestos body, because there was no silicon element in spite of much content of iron in EPMA analysis. Other occupationally suspicious materials, carbonized silicon and aluminum oxide, were also confirmed by EPMA analysis. In the second case making brake-lining for 34 years, no asbestos could be confirmed in routine microscopic examination, but EPMA revealed much magnesium as well as silicon. Both much deposition of magnesium and an occupational history of brake-lining rich of asbestos suggested asbestosis. Asbestosis was induced by chrysotile asbestos because there was much magnesium in EPMA analysis and a microscopic absence of asbestos was thought to its soluble tendency in acid-sided fixative of fromalin (Fig. 2, 6). The third and the fourth cases were constructional workers. Asbestos body was derived from amphibole asbestos because it richly contained of both silicon and iron with a very small amount of magnesium (Fig. 2, 6).

Asbestos bodies were mainly found in lower pulmonary fields with anthracosis. There was no tendency between the number of asbestos bodies and the pleural predominance or scar formations.

Discussion

Asbestos was reported as a inducer of carcinoma of lung and mesothelioma as well as asbestosis (1-3).

The onset frequency correlated to not only its exposing dosage but also its exposing duration or smorking (1-3).

As to the routine microscopic analysis with HE stain for a confirmation of asbestos body in lungs, it was reported that the density of asbestos body in malignancy-complicated cases was slightly more than that in control asbestosis ones without malignancies. On the basis of the exposing degree, malignancy-complicated cases was classified into no asbestos body (1%), low density (73%), moderate density defined by 0.5-2 asbestos body fibers/cm 2 of specimen area (14%), and high density (12%) (2). On the other hand, control malignancy-uncomplicated cases consisted of no asbestos body (3%), low density (85%), moderate density (9%), and high density (3%) (2). These results required intensely microscopical analysis because any microscopic glass contained only few asbestos bodies and, furthermore, asbestos body of serpentine type was dissoluble in formalin fixative and disappeared. On searching asbestos body anthracosis and fibrotic foci became a hallmark in this study.

Asbestos body consisted mainly of silicon, iron, and magnesium. Furthermore, asbestos was differentiated into serpentine-type and amphibole-type based on a ratio of magnesium to iron. When a confirmation was very difficult in this study, physical analysis by EPMA was regarded as more suitable for the physical constitutional analysis of pulmonary deposits(4).

Acknowledgement :

I thank Hiroshi Kobayashi, a pathologist in Hamamatsu Seirei General Hospital and one of the most famous specialists in asbestos, for his advice as follows : asbestosis could be diagnosed only by routine light microscopic analysis in formalin-fixed paraffin-embedded HE stained sections if specimens could be sampled from anthracotic or fibrotic areas in lower lobes of lungs. But asbestos body used to be too small and various in shape microscopically, this brown-magic-stick-mimetic body may be easily overlooked with a poor attention. An additional microscopic examination after a few days will bring you around the magic stick.

I thank Masayoshi Kobayashi, the technologist in Room of EPMA (Electron Probe Micro-Analysis) analysis in Center for Instrumental Analysis Niigata University, for his physical analysis.

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和　文　抄　録

原著

通常光学顕微鏡検査とElectron Probe Micro-Analysis（EPMA）によるアスベスト体の確認―肺石綿症の3担癌剖検例―

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要約

背景：アスベスト（石綿）が石綿症、肺癌および中皮腫を誘発するので、アスベストの消費は法的に規制され、1990年代よりその輸入量は激減してきた。アスベストの職業的な曝露に関する病理学的または解剖学的確証は、石綿症関連の業務上の疾患症例の労災判定の為に非常に重要である。大部分の症例における最も簡単で決定的な診断手法は通常の光学顕微鏡検査によって確立され、そして、EPMA は補助的な診断法の１つであろう。症例報告：今回検討された職業性塵肺の４症例において、３例は悪性腫瘍（肺腺癌、小細胞性肺癌、瀰漫性胸膜中皮腫）を合併していた。ホルマリン固定パラフィン包埋肺組織の顕微鏡検査によるアスベスト小体の存在が検索され、また、沈着物の物理学的構成成分が分析された。２症例は職歴と EPMA 分析によって診断された。残りの２症例は角閃石系石綿症であった。考察：石綿症は、顕微鏡学的に２人の建築関係労働者で確認され、その上、EMPA により１人のブレーキライニング製造者で推定された。EPMA は、アスベストの物理学的成分分析上、非常に有効であった。たとえアスベスト使用が法的に厳格に管理されるとしても、多くの石綿症とその合併症が今後40–50年の間に発症することが予測され、労災認定上、詳細な職業上の曝露の確認と EPMA 分析が重要となるであろう。

キーワード：業務上の疾病、X 線マイクロアナライザー（EPMA）、蛇紋石、角閃石、石綿症、アスベスト小体

Fig 1．Using list of asbestos products

kinds of products		usage	substitution	legal control
building materials	pushed－out molding cement board	outer wall, partitioning wall	possible	prohibited
	slate for Making－up roof	maked－up slate－covered roof		
	cement board reinforced with fibers	roof, outer wall		
	siding in ceramics	decoration		
	asbestos cement cylinder	chimney		
non－building materials	glue	building materials, industrial product		
	friction materials	clutch－lining, clutch－facing, brake－pad, brake－lining		
	heat resistance, electric insulation board	switchboard	impossibility	restricted, managed
	joint－sheet	plumbing gasket		
	sheeling materials	filler for leak prevention of machinery joint		
	industrial product materials	asbestos cloth		

Fig 2．Characteristics of asbestos fibers

mineralogy	asbestos name	constitutional			charcteristics				legal control by the cabinet order of Industrial Safety and Health Law	
family		ideal formula	chief ingredients	ubsidiary ingredients	acid－resistnace	heat－resistant（℃）	consumption	oncogenesis	in 1995	in 2004
serpentine	chrysotile（white asbestos）	$Mg_3Si_2O_5(OH)_4$	Si, Mg		soluble in formalin	550－700	90% ＜			restricted
amphibole	crocidolite（blue a.）	$Na_2(Mg_{<2}Fe^{2+}_3Fe^{3+}_2)Si_8O_{22}(OH)_2$	Si, Fe, Na	Mg	resistant	400－600	＋	＋	prohibited	
	amosite（brown a.）	$(Mg_{<2}Fe^{2+})_7Si_8O_{22}(OH)_2$	Si, Fe	Mg	resistant	600－800	＋		prohibited	
	anthophylite	$(Mg_{>2}Fe^{2+})_7Si_8O_{22}(OH)_2$								restricted
	tremolite	$Ca_2(Mg_{>>2}Fe^{2+})_5Si_8O_{22}(OH)_2$								restricted
	actinolite	$Ca_2(Mg_{<2}Fe^{2+})_5Si_8O_{22}(OH)_2$								restricted

Fig 3．Vulnerable diseases on the basis of a relation between a dose and a duration of occupational asbestos exposure

dose	duration	
	short（＜20　years）	long（20－40　years）
high	asbestosis	carcinoma of lung
low	pleural thickening	mesothelioma

Fig 4．Diagnostic standards presented in an official notice（＃0919001）by the chief of Labour Standards Bureau, Ministry of Health, Labour and Welfare, on Sep 19th, in 2003.

diseases	criteria for workmen's compensation
pulmonary asbestosis	pneumoconiosis of the 4 th. stage in management classification or with any other complications
carcinoma of lung	(1) or (2), with occupational exposure for 10 years or more
	(1) pneumoconiosis on chest roentgenogram
	(2) pleural plaque or asbestos body
mesothelioma（pleural, peritoneal, testicular vaginal	(1) or (2), with occupational exposure for 1 year or more
	(1) pneumoconiosis on chest roentgenogram
	(2) pleural plaque or asbestos body
pleural thickening	related to asbestosis with marked respiratory disturbance

stage of management : based on Article 4 in Pneumoconiosis Law

Fig 5．Evaluation of an asbestos exposure level based on a asbestos body concentration in the pulmonary tissue

exposure levels	AB	
	AB/cm 2 in HE	ABx10E＋3／g（dried weight）
common inhabitant	＜1	＜1
occupational exposure, possible	1－2	1－5
occupational exposure, probable	2＜	5＜

10E＋3：x1000

AB : number of asbestos bodies

Fig 6. Summary of our autopsied cases

case number			case 1			case 2	case 3	case 4
autopsy number			SN99-009			SN02-003	SN02-013	SN02-026
age			57			53	69	78
occupation			grind (carbonized silicon, iron oxide, aluminum oxide)			brake-lining (car availability of traffic facilities part, during 34 years)	building dismantling, construction	wall-blowing
occupational diseases			pneumoconiosis of the 4 th. stage in management classification			adenocarcinoma of lung, pneumoconiosis (pleural thickening)	mesothelioma of pleura, pneumoconiosis (pleural thickening)	small cell carcinoma of lung, pneumoconiosis (pleural thickening)
Hematoxylin - Eosn stain	asbestoid (#/cm^2)		0.1			0	0	0
	asbestos	upper field (numbers/cm^2)	0			0	0.3	0.2
		lower field (numbers/cm^2)	0			0	1.8	2.2
	specific areas	subpleural %	0			0	0	19
	asscociated lesions	scar %	0			0	50	15
		anthracosis %	100			0	75	96
EPMA analysis	constitution %	Si	++			+	61	34
		Fe		++		+	23	40
		Mg				++	1	1
		Al			++	-	13	6.6
		Ca		++			4.3	4
		K	+				2.4	8.8
		Cr					2.3	
		S					1.3	1.1
		Ti						2.3
		P	+					2.2
		Cl						0.3
estimation			SiC	FexOy	Al 2 O 3	serpentine	amphibole	amphibole