Pain Medicine

Pain Medicine 2011; 12: 1303–1308
Wiley Periodicals, Inc.

ORIGINAL RESEARCH ARTICLE

A Retrospective Study of Chest Pain in Benign Asbestos Pleural Disease

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Conflict of Interest
Professors Roger K. A. Allen and Tess Cramond have acted as expert witnesses to the courts for over 20 years. Professor Allen now acts as a Thoracic Physician for the General Medical Assessment Tribunal—Thoracic, for The Workers' Compensation Regulatory Authority (Q-Comp). Emeritus Professor Tess Cramond retired in March 2009. They derived no financial benefit from this study which was done *pro bono*. Slater and Gordon had no input into the conduct of this study, the analysis of its data, or its results.

Abstract

Purpose. The aims of this review were to ascertain the incidence of asbestos-related chest pain at presentation in two groups of patients referred with asbestos diseases and the demographics, comorbidities, and chest computed tomography findings associated with chest pain.

Methods. Medical charts of patients presenting 1995–2008, audited for quality assurance, were chosen at random by data managers. Patients with mesothelioma, lung cancer, and angina were excluded. Rigorous attempts had been taken by the authors to exclude other causes of chest pain.

Results. There were 167 patients who were medicolegal referrals (Group 1) and 115 clinical referrals (Group 2). Although the patients in Group 1 had more severe disease generally than Group 2, the proportion with pain was not significantly different (45.5% and 55.7%, mean duration 4.8 years, range 1–22 years). Group 1 had more severe disease as a rule. However, the proportion with pain in Groups 1 and 2, respectively, was as follows: diffuse pleural thickening (50.8% and 67.6%, $P = 0.072$), pleural plaques (47.0% and 59.7%, $P = 0.076$), folded atelectasis (70.6% and 83.3%, $P = 1.000$), and asbestosis (43.6% and 53.3%, $P = 0.346$). Of all those with folded atelectasis, 73.9% had pain.

Conclusion. Chest pain appears to be much more common in patients with benign asbestos diseases than is currently recognized, particularly in those with folded atelectasis and is not restricted to litigants. Improved recognition of this entity is needed along with practical management guidelines for the general practitioner. Further studies are envisaged by the authors.

Key Words. Benign Asbestos Diseases; Chest Pain; Retrospective Study

Introduction

For over 20 years, the first two authors have each examined approximately 10,000 patients with asbestos-related diseases both as clinicians and, for medicolegal reports, as expert witnesses in both federal and state jurisdictions. Over this period, they have commonly seen patients with benign asbestos diseases complaining of chest pain. However, this problem has been poorly documented in the literature resulting in incorrect diagnoses or, worse still, no diagnosis at all. A recent review article on asbestos diseases by the Dust Diseases Board of New South Wales makes no mention of benign asbestos chest pain [1].

The only population study in the literature was by Mukherjee et al. in Western Australia who studied chest pain in

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1,280 asbestos-exposed individuals with the Wittenoom crocidolite mine. They administered a pain questionnaire and related their responses to the abnormalities on plain chest radiographs. They found a significant proportion with either "anginal" or "non-anginal" pain as the Rose Questionnaire had been validated to distinguish these types of pain [2]. However, the study did not include a clinical examination, lung function tests, or computed tomography (CT) scanning. Chest pain was found in 43% of patients, and 12% were considered to have "angina." As their proportion with chest pain supported our own clinical experience, it was decided to corroborate this by a retrospective sample of our own patients as we had a considerable amount of detailed clinical and radiographic material available.

The aim of our study was two-fold: to ascertain the proportion with asbestos-related chest pain at presentation in two distinct groups of patients referred with asbestos diseases and to ascertain if any of their chest CT findings were associated with pain. As we were aware that the study could be seen as biased in favor of litigants, we decided to include a "control" group of non-litigants, that is, those referred by their general practitioners for assessment of asbestos diseases.

Methods

The study was conducted under the auspices of the Asbestos Research Group, Wesley Research Institute, and with the approval of the Wesley Hospital Medical Ethics Committee. Prior to the study, all patients had signed consent to any future chart audits and for the confidential use of their data for medical research studies. Patient confidentiality was respected, and the data file for each patient was given an accession number.

Data Collection

Data managers were instructed that benign asbestos pleural pain was a diagnosis of exclusion but with specific characteristics: a chronic dull aching pain usually located in the anterior chest, often parasternal, or in the posterior chest wall along the paravertebral gutters, with sharp exacerbations often induced by movement or exercise. It often had neuropathic features, sometimes with allodynia and was not relieved by nitrates or antacids and usually only partially responsive to simple analgesics. Data managers were also instructed before coding on the characteristics and causes of other causes of chest pain including angina, cervical and thoracic spinal pain, hiatus hernia, gastro-oesophageal reflux, costochondritis, shoulder pain, and shingles. As all the patients had been examined in detail by the first author and the cause of the chest pain made only after detailed investigations, data managers had to identify and code expressions such as "benign asbestos chest pain," "plaque pain," "pain due to benign asbestos pleuritis," etc. As a diagnosis of the cause of pain was clearly stated in the medical records, data managers were not expected to deduce a diagnosis of benign asbestos chest pain by other means.

Medical charts of patients presenting between 1995 and 2008 were chosen at random in alphabetical order by data managers. The charts of all patients in the study had been filed separately as "medicolegal" and "non-medicolegal" in alphabetical order of the first letter of the surname. Charts were chosen in order, one at a time by letter of the alphabet and then repeated (from A to Z) until the required number was reached. In some cases, there were no letters represented, for example, X as it was a largely Anglo-Saxon population. Only the presenting data was collated. The sample size was the maximum possible for the funding resources available. As the proportion with asbestos chest pain was not known precisely, it was considered that approximately 200–300 patients would be required to obtain meaningful results. Stratification into two groups was done as it was expected that the medicolegal group would have more severe asbestos diseases in general than those referred by general practitioners, and thus would be more likely to have chest pain.

Group 1 comprised patients referred with asbestos diseases for medicolegal assessments, while Group 2 had been referred by general practitioners for clinical assessment of suspected asbestos diseases. As a rule, most in Group 1 had already undergone detailed investigation by thoracic and other specialists for management of their asbestos diseases and were referred to the authors for medicolegal reports, usually by the plaintiffs' lawyers. These reports usually requested a detailed diagnosis, estimate of impairment, prognosis, and future costs. Group 2 were referred by general practitioners for investigation and management of their asbestos-related diseases often with other conditions discovered by the first author, for example, sleep apnea. None of these patients were litigants. Patients with mesothelioma and lung cancer were initially included in the sample selection to ascertain the relative proportion of malignant conditions to benign asbestos diseases as there is little information available about this in literature. However, these were excluded at the completion of data collection phase.

All patients underwent a general and occupational history, a physical examination, lung function in a body plethysmograph with diffusing capacity, and a high-resolution CT chest with prone lung windows. Particular care was taken to palpate the chest and to elicit localized bony or cartilaginous tenderness, for example, costosternal junction pain. The CT chest scans were reported by Dr. R. Slaughter, Senior Radiologist, who is an experienced expert witness in asbestos-related diseases. The first author, also expert in diagnosing asbestos diseases by CT chest radiography, examined the radiographic material. Where appropriate, other tests included stress echocardiography, coronary angiography, barium swallow with provocative posturing, upper endoscopy, CT scan and magnetic resonance imaging (MRI) of the thoracic spine, and radionuclide bone scanning. Thus, the diagnosis of asbestos-pleural pain was reached only after detailed investigation of other potential causes of chest pain and was clearly stated in the charts. Regrettably, when these patients presented to the first author, no specific pain questionnaire was in use.

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Table 1 Demographic variables by group

	Group 1 n/N (%)	Group 2 n/N (%)	*P* value
Male	163/167 (97.6)	109/115 (94.8)	0.208
Age (years), mean ± SD	66.7 ± 8.2	65.0 ± 9.5	0.945
Current smoker	14/165 (8.5)	5/113 (4.4)	0.231*
Former smoker	126/167 (75.4)	90/115 (78.3)	0.584
Work type			
Blue collar	139/167 (83.2)	89/114 (78.1)	0.277
Maritime	20/167 (12.0)	14/114 (12.3)	0.939
White collar	6/167 (3.6)	4/114 (3.5)	1.000*

* Based on Fisher's exact test.
Group 1 = medicolegal patients; Group 2 = referred by their general practitioner.
SD = standard deviation.

Statistical Analysis

An independent data auditor assessed the quality of data collection in a random sample of patients. All data managers had tertiary qualifications. In no case was the diagnosis of chest pain incorrectly coded, although there were some minor irregularities found, for example, postcode and date of birth. All coders and independent data auditors had English as their first language. Statistical analysis was done in consultation with a qualified statistician. Differences in two means were assessed using Student's *t*-test. Proportions were compared using a *z*-test or Fisher's exact test. The 95% confidence intervals (CIs) were calculated using Wilson's confidence limits. Statistical significance is set at the conventional level of 0.05. The software packages used for data analysis were PASW 17 (SPSS Inc., Chicago, IL, USA) and R (R Development Core Team, 2011, R Foundation for Statistical Computing, Vienna, Austria).

Results

Subjects

After exclusion of the 15 patients with mesothelioma, Group 1 consisted of 167 "medicolegal" patients and Group 2 had 115 patients. In both groups, the overwhelming majority of subjects are male (97.6% and 94.8%). Table 1 displays a summary of subject characteristics by group, with the final column showing *P* values for tests of equality of either proportions or means. There were no significant differences between groups with respect to proportion of males, average age, smoking status, or work type. The proportion still smoking was lower than expected (8.5% and 4.4%, respectively). The majority of subjects were blue collar or maritime workers.

Comorbidities by group are summarized in Table 2. Of note, the proportion of patients with ischemic heart disease was relatively high (37.7% and 38.3%, respectively). Sleep apnea was also common, and there was a significant difference in the proportion of subjects with this comorbidity (15.0% vs 31.3%, $P = 0.001$). The proportion of subjects with chronic obstructive pulmonary disease (COPD) was higher in Group 1 (38.9% vs 27.8%), although this failed to achieve statistical significance ($P = 0.054$). There were no other significant differences. Depression was being treated in 4.8% (8/167) of Group 1 and 4.3% (5/115) in Group 2. Asbestos diseases from spousal exposure to asbestos (mostly in women) accounted for 5.6% and 5.0%, respectively.

In most subjects, the type of asbestos could not be clearly identified. Chrysotile (white asbestos) was the predominant fiber type, with some amosite and only a minority exposed to crocidolite (blue asbestos). The types of asbestos diseases were coded as four types: pleural plaques, diffuse pleural thickening (DPT), folded atelectasis, and asbestosis. There was no separate code for

Table 2 Comorbidities by group

Comorbidity	Group 1 (N = 167) n (%)	Group 2 (N = 115) n (%)	*P* value
None	28 (16.8)	22 (19.1)	0.609
IHD	63 (37.7)	44 (38.3)	0.927
Prior cancer	23 (13.8)	16 (13.9)	0.973
COPD	65 (38.9)	32 (27.8)	0.054
Chronic renal failure	3 (1.8)	0 (0.0)	0.273*
Obesity (BMI > 30 kg/m^2)	33 (19.8)	22 (19.1)	0.896
CVA	8 (4.8)	4 (3.5)	0.767*
Diabetes	24 (14.4)	13 (11.3)	0.453
Sleep apnea	25 (15.0)	36 (31.3)	0.001
Other	17 (10.2)	9 (7.8)	0.502

* Based on Fisher's exact test.
Group 1 = medicolegal patients; Group 2 = referred by their general practitioner.
IHD = ischemic heart disease; COPD = chronic obstructive pulmonary disease; BMI = body mass index; CVA = cerebrovascular accident.

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Table 3 High-resolution CT chest findings by group

	Group 1			Group 2			
CT chest diagnosis	n/N	%	95% CI	n/N	%	95% CI	*P* value
Pleural plaques	149/167	89.2	(83.6, 93.1)	72/115	62.6	(53.5, 70.9)	<0.001
Diffuse pleural thickening	126/167	75.4	(68.4, 81.4)	37/115	32.2	(24.3, 41.2)	<0.001
Folded atelectasis	17/167	10.2	(6.5, 15.7)	6/115	5.2	(2.4, 10.9)	0.135
Asbestosis	101/161	62.7	(55.0, 69.8)	30/86	34.9	(25.7, 45.4)	<0.001

Group 1: medicolegal patients, Group 2: referred by their general practitioner.
CI = confidence interval; CT = computed tomography.

benign asbestos pleural effusions as these were included in the DPT. Table 3 shows the findings of high-resolution CT scans of the chest, with 95% CIs for percentages. A higher proportion of patients in Group 1 had more severe disease. The more serious condition, asbestosis was significantly more prevalent in the medicolegal patients compared with those referred by general practitioners (62.7% vs 34.9%, $P < 0.001$). Similarly, pleural plaques and DPT were significantly more common in medicolegal patients ($P < 0.001$ in both cases). The radiographic features of asbestosis were graded as mild, moderate and severe. Mild disease had thickened subpleural septal lines and dot-like opacites (mild), moderate had ground-glass opacification and or reticulation with small subpleural thick-walled cysts (moderate), while severe constituted of honeycomb lung. Parenchymal bands alone did not constitute asbestosis. Finger clubbing was found in (10%) of the medicolegal patients and in only (2%) of the physician-referred group and only in patients with severe asbestosis.

Chest Pain

The proportion of subjects with chest pain for each radiographic diagnosis is shown in Table 4. Results include 95% CIs for percentages. There was no significant difference in the proportion with chest pain in the two groups overall ($P = 0.094$). Within Group 1, 45.5% (76/167, 95% CI: 38.1–53.1) had chest pain, while the figures were 55.7% (64/115, 95% CI: 46.5–64.4) for Group 2. When stratified into disease subtypes, the general practitioner referred patients in general had more chest pain (Table 4); however, the differences failed to achieve statistical significance. Of all those with folded atelectasis, 17/23 (73.9%) had chest pain. Of all patients with asbestosis, 60/131 (45.8%) had chest pain, although all had some form of pleural disease. Of those with pain in Group 1, in only 18% was it possible to grade the severity of the pain with any accuracy. However, over half (57%) of these rated their pain at or above 5/10 in severity (0 = no pain, 10 = unbearable). The mean duration of pain was 4.8 years (standard deviation 4.5 years, range 1–22 years). At the time of presentation and before the institution of analgesics by the authors, chest pain had not been treated at all in 69% or with simple analgesics in 16% with the remainder by opioids and anti-neuropathic medications. Most were self-medicating with only a few being treated by multidisciplinary pain clinics. The proportion of patients with pain over the study period was not significantly different, although the absolute numbers of patients rose, with a peak in 2004. Chest pain did not correlate significantly with age, gender, body mass index, occupation, or comorbidities.

Discussion

Ours is the first population study in 10 years to corroborate the findings of Mukherjee et al. [2] who showed that benign asbestos disease commonly causes chest pain. They acknowledge the possibility of observer bias by the

Table 4 Chest pain prevalence by radiographic diagnosis and group

	Group 1			Group 2			
CT chest diagnosis	n/N	%	95% CI	n/N	%	95% CI	*P* value
Pleural plaques	70/149	47.0	(39.1, 55.0)	43/72	59.7	(48.2, 70.3)	0.076
Diffuse pleural thickening	64/126	50.8	(42.2, 59.4)	25/37	67.6	(51.5, 80.4)	0.072
Folded atelectasis	12/17	70.6	(46.9, 86.7)	5/6	83.3	(43.6, 97.0)	1.000*
Asbestosis	44/101	43.6	(34.3, 53.3)	16/30	53.3	(36.1, 69.8)	0.346
Total	76/167	45.5	(38.1, 53.1)	64/115	55.7	(46.5, 64.4)	0.094

* Based on Fisher's exact test.
Group 1 = medicolegal patients; Group 2 = referred by their general practitioner.
CI = confidence interval; CT = computed tomography.

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clinicians in the study. However, as there was lack of an increased proportion of litigants with pain and the stable proportion with pain for over a decade suggests that any bias was at least consistent.

The higher proportion of chest pain in those with folded atelectasis and DPT is not surprising as these processes are due to inflammation of the pleura and in the case of folded atelectasis, the pleura drawn into the lung parenchyma by fibrotic contraction. However, even pleural plaques were associated with chest pain. It was not possible to isolate asbestosis as a cause of chest pain as all patients with asbestosis had asbestos pleural disease in various forms. Indeed, asbestosis in the absence of benign asbestos pleural disease is a rarity. As there were numerous combinations of the four main entities of asbestos diseases, the subgroups became too small to be statistically valid. The higher proportion of general practitioner referred patients with chest pain may be explained by the "squeaky wheel" phenomenon. These patients' complaints of chest pain may sometimes have been the cause of the referral.

Although several case reports have described chest pain in benign asbestos pleural disease, detailed knowledge of this condition is lacking. Indeed, at the recent 13th World Congress on Pain in Montreal in 2010, ours was the only article on this subject out of approximately 2,000 presented [3]. In addition, the preoccupation with mesothelioma in "asbestos" research by drug companies may have unwittingly resulted in a lack of cell biological studies into the far more common benign asbestos pleural disease such as by immunohistochemistry and associated cell biological research into the precise mechanism of pain induction. The fact that asbestos pleural disease is generally progressive should dispel the common notion that pleural plaques and pleural thickening are somehow inert.

With regard to DPT, Chapman et al. state, "*Exertional breathlessness and chest pain (which can be chronic and severe) are relatively common symptoms of DPT*" [4]. A recent review of asbestos diseases in the British Medical Journal states, ". . . *pleural plaques have been associated with anginal pain*" [5], citing the article by Mukherjee et al. [2]. In an open access review of the benign asbestos diseases, Miles et al. from the New South Wales Dust Diseases Board state, "*Chronic chest pain may be a feature of DPT, although this is usually mild. Mild to moderate chest pain was noted in over half of the patients with moderate to severe DPT in a study of more severe cases*." [6]. They cited the original findings of Yates et al. from the UK who found 56% of patients with DPT had chest pain [7].

However, the Official Statement of the American Thoracic Society states, "*Chronic severe pleuritic pain is rare in patients with asbestos pleural disease. Vague discomfort appears to be more frequent. Studies examining the frequency of atypical chest pain in asbestos-exposed patients have not been performed. In the few cases described, it was present for many years, disabling and often bilateral*" [8].

Only two papers were cited in their Official Statement. The first was a US case report of four patients with intractable pleural pain from asbestos pleural disease [9]. The second paper was a case study from Australia of four patients treated by pleurectomy for intractable pleural pain for benign asbestos pleural disease [10]. The procedure was only partially effective and totally ineffective in two patients whose intractable neuropathic pain persisted, one of whom later had a cervical cordotomy. Three of these patients had diffuse parietal pleural thickening, and one had multiple large pleural plaques raging from 5- to 8-mm thick. Pleural adhesions were present for three of the four subjects. This article is unique as it attests to the lack of success of pleurectomy where the pain has a significant neuropathic component. Thus, the Official Statement is based on only eight patients.

With regard to the possible impact of benign asbestos chest pain in Australia, our sample initially included 297 patients but those with mesothelioma were then excluded after the sample was done and no cases of lung cancer were found in the sample. Between 1986 and 2000, there were 5,176 cases of malignant mesothelioma reported in Australia with a projected peak occurring between 2010 or as late as 2014 and with a projected compensation cost of $A5 billion [1]. On the assumption that the proportion of mesothelioma patients to benign asbestos cases is about 1:25 (and it may be much less), the number of patients in Australia with benign asbestos diseases over a similar period, 1986–2000, should be in excess of 100,000 people. Unfortunately, there is no national register kept to verify this. As these conditions are chronic, the overall prevalence in the population with these conditions may be much higher. If even half suffer from benign asbestos chest pain, management guidelines are clearly needed for the medical community to manage this growing cohort cost-effectively.

As we have observed that the pain is often located over the paravertebral gutter or parasternally, it may be caused by irritation of the intercostal nerves where they lie unprotected by the internal intercostal muscles. This is supported by our own observations and those of others that there is a neuropathic quality to the pain that explains why it responds fairly well to gabapentin and pregabalin and only partially to opioid analgesics.

Greater awareness of this increasingly common condition is needed by both the medical profession and asbestos support groups. Until we develop better diagnostic tools, it will remain a diagnosis of exclusion. Prospective studies into the natural history of asbestos-related chest pain and some basic immunohistochemical research are clearly needed.

Acknowledgments

This study was supported by a grant from the legal firm, Slater and Gordon, under the aegis of the Asbestos Research Group, Wesley Research Institute, Wesley Hospital, Auchenflower, Brisbane chaired by Professor Julie

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Campbell. We wish to thank Dr. Richard Slaughter, Radiologist, The Prince Charles Hospital, Brisbane for his assistance with the radiology.

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