# Asbestos Exposure: A Potential Cause of Retroperitoneal Fibrosis

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The etiology of retroperitoneal fibrosis is unknown in 70% of the cases. The aim of our study was to examine the possible association between occupational asbestos exposure and retroperitoneal fibrosis; only two cases have been reported in the literature. We gathered all the cases of retroperitoneal fibrosis diagnosed in the Tampere University Hospital between 1987 and 1995. We examined their hospital records to evaluate the possible etiology of the disease. We also sent a structured questionnaire to all living patients (10/13) to obtain information on their asbestos exposure. The chest radiographs of the patients were re-read to evaluate possible changes resulting from asbestos exposure.

We found 13 cases of idiopathic retroperitoneal fibrosis. Seven patients (all male) had been exposed to asbestos in the past. The chest radiographs of the four most-exposed patients showed characteristic asbestos-related abnormalities, including bilateral pleural plaques, round atelectasis and small irregular lung opacities. In our study, we found that asbestos exposure and asbestos-induced changes in the lung and pleura were common among male retroperitoneal fibrosis patients. We suggest that occupational exposure to asbestos may be an important etiological factor for retroperitoneal fibrosis. Am. J. Ind. Med. 33:418–421, 1998. © 1998 Wiley-Liss, Inc.

KEY WORDS: asbestos; retroperitoneal fibrosis; chest radiograph; occupational health

# **INTRODUCTION**

Retroperitoneal fibrosis is a rare syndrome causing a fibrous mass over the abdominal aorta and vena cava. Bilateral ureteral compression, causing anuria, is a common occurrence in this syndrome. Thus far, in 70% of the cases the etiology of retroperitoneal fibrosis remains unknown [Lepor and Walsh, 1979]. Malignant tumors, inflammatory processes around the abdominal aorta, radiation therapy, retroperitoneal hematomas, infection, and various medicines

have been suggested as causal agents [Buff et al., 1989; Maguire et al.,1991]. In only two case reports, describing three patients, has occupational asbestos exposure been associated with retroperitoneal fibrosis [Maguire et al.,1991; Boulard et al.,1995].

The aim of our study was to examine retrospectively the possible association between retroperitoneal fibrosis and occupational asbestos exposure.

### MATERIALS AND METHODS

In October 1996, we gathered all the cases of retroperitoneal fibrosis diagnosed between 1987 and 1995 in the Tampere University Hospital in southern Finland. The catchment area of the hospital is about one million people. The ICD-9 diagnostic classification [WHO,1977] was used in Finland in 1987-1995. The diagnosis code 5934A refers to "other ureteric obstruction" and includes idiopathic retroperitoneal fibrosis. Therefore, this code also includes occlusion of the ureter that may have specific etiologies recognized by

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**TABLE I.** Patients with Retroperitoneal Fibrosis, their Occupations, Age, Asbestos Exposure and Radiographic Findings. Tampere, Finland 1987–1995

Pat. no	Occupation	Age at diagnosis	Asbestos exposure	Radiograph findings
1	Insulator	53	Repairing pipes and insulations 1958–85	Bilateral pleural plaques, diffuse irregular small lung opacities <sup>a</sup>
2	Carpentery machine operator	68	Sawing fire insulation plates some- times containing asbetsos 1941–78	Normal
3	Plumber, carpenter	50	Repairing pipes and insulations 1965–75, in construction work 1975–96	Bilateral pleural plaques, round atelectasis on both sides
4	Carpenter	67	In construction work 1970–85	Bilateral pleural plaques, round atelectasis on right side
5	Automobile engineer	63	Repairing brakes of cars 1957–60 and 4 summers	Normal
6	Automobile mechanic	48	Passive exposure, repairing engines of buses 1966–96	Unilateral pleural plaque
7	Paitner	51	Painting with asbestos-containing pigments 1965–75, 1 year in shipyard (1967)	Bilateral pleural plaques
8	Salesperson	39	Not known <sup>b</sup>	Normal
9	Farmer's wfe	79	Not known <sup>b</sup>	Normal
10	Farmer's wife	45	Not known <sup>b</sup>	Pleural effusion of unknown etiology
11	Farmer's wife	65	No	Normal
12	Owner of an upholstery business	54	No	Normal
13	Farmer's wife	62	No	Unilateral pleural plaque

<sup>&</sup>lt;sup>a</sup>Asbestosis diagnosed in 1994 on the basis of computerized tomography.

the diagnosing clinicians. Of 45 patients with the diagnosis code 5934A, 13 cases were diagnosed by the urology service as idiopathic retroperitoneal fibrosis. The remaining cases were recognized to have malformations, ureterolithiasis, or neoplasms. Consequently, patients with other presentations of retroperitoneal fibrosis than ureteral obstruction were not included in this study.

The hospital records of all 13 cases of retroperitoneal fibrosis were retrospectively examined. The criteria for including a retroperitoneal fibrosis case in our study was a diagnosis confirmed by laparotomy. The possible etiological factors that were recorded in each record were noted. The chest radiographs and computerized tomography (CT) images of the patients were reviewed and abnormalities consistent with asbestos exposure were identified. These abnormalities included bilateral pleural plaques, round atelectasis, and small irregular opacities. We also sent a structured questionnaire to all the living patients (10/13) to ascertain their exposure to asbestos. The questionnaire was similar to the one used in the national asbestos screening study in Finland in 1990-1992 [Koskinen et al.,1996]. It

contained detailed questions about different occupations and tasks in which asbestos exposure may occur. Finally, if needed, we interviewed the patients by telephone to acquire a complete occupational history. Two of 10 patients were interviewed during a health examination.

## **RESULTS**

All the patients had surgery for ureteral obstruction, and ureterolysis was performed. Ten of the 13 retroperitoneal fibrosis patients were still alive during the time of this study and three died. The mean age of the patients was 57 years when the disease was diagnosed; 6 were women and 7 were men.

The results of the questionnaire on the working history, the asbestos exposure of the patients, and the findings on the chest radiographs possibly resulting from asbestos exposure are shown in Table I.

Other possible risk factors for retroperitoneal fibrosis in the hospital records were aortic aneurysms, retroperitoneal hematoma, methysergide or analgesics, and retroperitoneal

<sup>&</sup>lt;sup>b</sup>Painter dead.

inflammation due to diverticulosis. None of the patients were given radiation therapy or had a malignancy. One patient had diabetes and another suffered from hypothyroidism.

## DISCUSSION

It has been suggested that retroperitoneal fibrosis may be part of an asbestos-induced fibrotic process similar to that causing pleural plaques or lung fibrosis [Maguire et al.,1991; Boulard et al.,1995]. Asbestos fibers may be transported from the gastrointestinal tract or via lymphatic drainage from the lung to the retroperitoneal space [Maguire et al.,1991]. This is supported by the finding of asbestos bodies in organs other than the lung, e.g., in such retroperitoneal organs as the kidney and adrenal glands [Auerbach et al.,1980]. It is also possible that an immunological response to asbestos plays a role in the fibrotic process [Kagan, 1981].

In our study, all seven male patients showed exposure to asbestos in their occupational history, whereas generally only 5% of the total labor force in Finland has been exposed to asbestos [Ministry of Labour, 1990]. The asbestos exposure was confirmed by the chest radiograph findings, which showed typical changes due to asbestos in four of the seven male patients exposed to asbestos (patients 1,3,4,7) and an additional patient had a suggestive radiographic finding, namely, unilateral plaque (patient 6). The rate of bilateral plaques among the male patients here is eight times more than that of the Finnish male population [Zitting, 1995]. These findings imply that both asbestos exposure and the radiographic abnormalities due to asbestos exposure are much more common among retroperitoneal fibrosis patients than among the general population.

It may be possible for retroperitoneal fibrosis to be associated with asbestos exposure in the absence of radiographic pulmonary abnormalities. Not all of our patients with previous exposure to asbestos had chest radiographs with bilateral pleural plaques or small lung opacities. The imperfect sensitivity of radiographs in detecting asbestos-related disease is well known [Kipen et al.,1987]. As such, asbestos exposure cannot be entirely excluded as an etiological factor for retroperitoneal fibrosis in these patients. The time course for the appearance of radiographic abnormalities due to asbestos exposure in the lungs varies. It is possible that the roentgenological changes in some patients develop later. It is also plausible that these patients have additional etiological factors other than being exposed to asbestos even if we were unable to recognize them all.

Three of the six female patients and one male patient had other risk factors for retroperitoneal fibrosis than asbestos exposure. Patients 2 and 11 had an aneurysm in the abdominal aorta. It has been suggested that retroperitoneal fibrosis may be a reaction to an antigen, ceroid, in aortic atheroma [Bullock, 1988]. Retroperitoneal hematoma is also

a possible etiology [Maguire et al., 1991] in patient number 2, because an aorto-iliac Y-prothesis had been placed some years before retroperitoneal fibrosis was diagnosed. In some reports, it has been estimated that malignancy accounts for 8-10% of all cases of retroperitoneal fibrosis [Koep and Zuidemu, 1977]. In our study, we excluded all the ureteral obstructions caused by a malignant tumor whose diagnosis was established during clinical evaluation of the patient.

In previous studies, drug-induced retroperitoneal fibrosis has been associated clearly with methysergide [Buff et al., 1989]. A case report also links methysergide use with parenchymal and pleural abnormalities [Malaquin et al.,1989]. One such case was found here (patient 8). The action and interaction of other drugs are also possible in this case, because the patient had used many different medications for treating migraine. Analgesic abuse has previously been suggested as one explanation of retroperitoneal fibrosis [Lewis et al.,1975; Finan and Finkbeiner, 1981].

In our study we found that a history of asbestos exposure and lung and pleura radiographic abnormalities consistent with asbestos exposure were much commoner among male patients with retroperitoneal fibrosis than among the general population. On the basis of this finding, we suggest that occupational exposure to asbestos may be an important aetiological factor for retroperitoneal fibrosis. Therefore, we encourage clinicians to take careful note of patients' work histories, with special attention to asbestos exposure, when evaluating patients with retroperitoneal fibrosis. We also encourage a formal epidemiological casecontrol study to confirm the association apparent between retroperitoneal fibrosis and asbestos exposure.

### REFERENCES

Auerbach O, Conston AS, Garfinkel L, Parks VR, Kaslow HD, Hammond EC (1980): Presence of asbestos bodies in organs other than the lung. Chest 77:133-137.

Boulard JC, Hanslik T, Moulonguet Doleris L, Prinseau J, Baglin A (1995): Asbestos and idiopathic retroperitoneal fibrosis. Lancet 345:1379.

Buff DD, Bogin MB, Faltz LL (1989): Retroperitoneal fibrosis: A report of selected cases and a review of the literature. NY State J Med 89:511-516.

Bullock N (1988): Idiopathic retroperitoneal fibrosis: Now known to be an allergic reaction to insoluble lipid leaking through arteries. BMJ 1:240-241.

Finan BF, Finkbeiner AE (1981): Renal papillary necrosis and retroperitoneal fibrosis secondary to analgesic abuse. J Urol 126:533-534.

Kagan E (1981): The alveolar macrophage: Immune derangement and asbestos-related malignancy. Semin Oncol 8:258-267.

Kipen HM, Lilis R, Suzuki Y, Valciukas JA, Selikoff IJ (1987): Pulmonary fibrosis in asbestos insulation workers with lung cancer: A radiological and histopathological evaluation. Br J Ind Med 44:96-100.

Koep L, Zuidemu G (1977): The clinical significance of retroperitoneal fibrosis. Surgery 81:250.

Koskinen K, Rinne JP, Zitting A, Tossavainen A, Kivekäs J, Reijula K, Roto P, Huuskonen MS (1996): Screening of asbestos-induced diseases in Finland. Am J Ind Med 30:241-251.

Lepor H, Walsh P (1979): Idiopathic retroperitoneal fibrosis. J Urol 122:1.

Lewis CT, Molland EA, Marshal VR, Tresidder GC, Blandy JP (1975): Analgesic abuse, ureteric obstruction, and retroperitoneal fibrosis. BMJ 2:76-78.

Maguire GP, Meggs LG, Addonizo J, Del Guercio LRM (1991): Association of asbestos exposure, retroperitoneal fibrosis, and acute renal failure. NY State J Med 91:357-359.

Malaquin F, Urban T, Ostinelli J, Ghedira H, Lacronique J (1989): Pleural and retroperitoneal fibrosis from dihydroergotamine [letter]. N Engl J Med 321:1760.

Ministry of Labour, State Asbestos Committee (1990):Final Report 66/1989. Ministry of Labour. Helsinki,104 p. In Finnish with English summary.

World Health Organization (WHO)(1977): "Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death," 9th rev, vol. 1. Geneva: WHO.

Zitting AJ (1995): Prevalence of radiographic small lung opacities and pleural abnormalities in a representative adult population sample. Chest 107:126-131.