Obliterative bronchiolitis in fibreglass workers: a new occupational disease?

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ABSTRACT

Rationale and objectives Obliterative bronchiolitis (OB) is a rare disease with a small number of established occupational aetiologies. We describe a case series of severe OB in workers making glass-reinforced plastics.

Methods Workplace exposures were the likely cause after the independent diagnosis of OB in two workers laying up the fibreglass hulls of yachts; the second worker took over the job of the first after he left following a lung transplant. Presentation of these two cases at international meetings led to others identifying similar workers.

Main results We identified six workers with good evidence of OB. All were involved in preparing fibreglass with styrene resins, five as boat builders laying up fibreglass hulls and one during cooling-tower fabrication. The disease came on rapidly without unusual acute exposures. Two patients had lung transplants, while another died while waiting for one. Histology confirmed OB in the four with biopsies/post-mortem examinations or explanted lungs.

Conclusions A rare, potentially fatal disease occurring in six workers laying up fibreglass with styrene resins from five different worksites suggests that work exposures were the cause of their OB. The precise agent responsible awaits identification.

What this paper adds

- Obliterative bronchiolitis is a rare disease with few established aetiologies.
- These case reports suggest that work with glass-reinforced plastics may be a newly identified cause.
- Further epidemiological and toxicological work is needed to confirm this.

INTRODUCTION

Obliterative bronchiolitis (OB), a clinical term used to describe a disease process centred on the terminal and respiratory bronchioles, is a common response to bone marrow or lung transplantation, a less common consequence of respiratory infection (often viral) or drug ingestion, and an occasional complication of collagen-vascular and inflammatory bowel diseases. In the general population the disease is believed to be rare but, because its symptoms (cough and breathlessness) are not specific and because its diagnosis requires sophisticated investigation, its true frequency is probably underestimated.

Acute, high-dose inhalational exposures to several workplace agents have been reported to cause bronchiolitis. In this setting the disease is often severe, the bronchiolitis usually of obliterative (constrictive) histology and in some cases accompanied by alveolar extension ('organising pneumonia'). Recently, more chronic exposures at lower doses to a butter-flavouring used in the manufacture of some popcorns have been reported to cause a severe and sometimes fatal OB; the first cases of 'popcorn packer's lung' to be reported were three employees in two separate factories[1] at which stage the causative agent remained unidentified.

We report six cases of severe bronchiolitis in men working in the manufacture of glass-reinforced plastic.

METHODS

The cases were assembled unsystematically from the clinical experience of two of the authors (PC and PSB) and, in one instance, following the publication of their abstract from a scientific meeting.[2]

FINDINGS

The six patients, all male and five of them lifelong non-smokers, presented to different hospitals between 1987 and 2007 (table 1). None had any history of significant respiratory disease. Their average age at presentation was 34 years (range 25–51). Five had worked with fibreglass panels for 12 months or less before the onset of their symptoms, which in each case were characterised by marked breathlessness accompanied by cough. Spirometry at presentation confirmed severe airflow obstruction with gas trapping and evidence on flow-volume loops of small airways involvement.

Exposures

Five patients were employed directly in the manufacture of fibreglass-reinforced boats in the UK, two of them for the same company (case 3 took over the job of case 2 after the latter's transplant). The remaining patient (case 6) made fibreglass for a cooling tower manufacturer in Taiwan. While the exact processes are not known in each instance, they all involved the fabrication of glass-reinforced plastics using a resin mixed with styrene and an accelerating agent (in at least two cases known to include methylethyl ketone peroxide and dimethyl phthalate) laid on glass fibre. Other chemicals included (in some cases) acetone, butyl acetate, butanone, N,

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Table 1 Summary of cases

Case number	Presentation		Duration of employment prior to onset of dyspnoea (months)	Smoking (total pack-years)	Lung function at presentation			CT (chest)	Histology	Outcome
	Age	Year			FEV_1/FVC (ratio)	RV (% predicted)	kCO (% predicted)			
1	25	1987	5	7.5	0.7/2.85 (25%)	152	78	NA	OB (explant)	Heart lung transplant 1989; died from complications 2006
2	31	1996	7	0	0.88/2.65 (33%)	333	117	OB	OB (OLB)	Lung transplant 1997
3	42	1996	12	0	1.30/3.80 (34%)	171	95	ND	ND	Alive 1998
4	26	2007	12	0	1.25/4.44 (28%)	249	111	OB	OB (OLB)	Alive 2011
5	51	2003	48	0	1.81/4.66 (39%)	109	96	2006: bronchial wall thickening	ND	Improved away from work. 2009: FEV_1 2.32, FVC 4.58
6	26	2007	6	3	0.8/2.21 (36%)	196	50	Air trapping around the region of right upper lobe and right hilum; central bronchial dilatation	OB (autopsy)	Died from respiratory failure 2009

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; kCO, diffusing capacity/alveolar volume; NA, not available; ND, not done; OB, obliterative bronchiolitis; OLB, open lung biopsy; RV, residual volume.

N-diethylaniline, diethylene glycol and isophorone diisocyanate. Samples collected from the workplace of one patient (case 6) were analysed by gas chromatography–mass spectrometry and concentrations in air estimated using the near field model. The findings are summarised in online supplementary appendix 1; high concentrations of dimethyl phthalate and of styrene were estimated.

Pathology

Histology was available in four cases, two from open lung biopsy, one from explanted lung at transplant (case 1) and one at post-mortem (case 6), and in each instance was indicative of widespread constrictive bronchiolitis. Detailed examination of tissue from case 4 (see online supplementary appendix 2) showed diffuse chronic bronchiolitis with evidence of constriction. In addition, a focal foreign-body type granulomatous inflammation within the walls of narrowed airways suggested a localised response to an inhalation insult; there was no obvious fibrous or polarisable material but there was foreign pigmented granular debris within the macrophages in these areas. Two cases had neither histological nor radiological confirmation; in each, the diagnosis was made on the basis of clinical history and pulmonary function abnormalities.

Follow-up

Two patients (cases 1 and 2) underwent lung transplantation, one dying of late complications; a third (case 6) died of respiratory failure while awaiting a transplant. The remainder have survived, albeit in each case with severe airflow obstruction and significant respiratory disability.

DISCUSSION

Obliterative (constrictive) bronchiolitis is believed to be rare, although this may reflect the difficulties in its diagnosis and the readiness with which it can be confused with other, more common causes of airflow obstruction. We report six cases of what we believe to be severe bronchiolitis in men with similar exposures to fibreglass panel manufacture, five of them in boatyards. Three required lung transplantation; the remainder are left severely disabled. We cannot be definitive in attributing their disease to their work but note, in each case, the onset of symptoms after the start of such exposure, the absence of any other ready explanation for obstructive bronchiolitis and the several different locations, linked by the nature of the work and in two cases the same workplace. Without information on the size of the exposed populations, we cannot know the risk involved, but we suspect that in absolute terms it is small.

A causative agent(s) remains elusive at this stage. Given its aerodynamic properties and the absence of fibrous cellular inclusions on the available histology, we think it improbable that glass fibre is responsible. Several of the chemical agents involved are potential respiratory irritants and being insoluble are capable of penetration to the smaller airways after inhalation. They include dimethyl phthalate, which in the one case (case 6) where estimates are available may have been encountered at very high concentrations, and styrene which has similar properties although we do not have evidence of especially high exposures. OB has been reported in a man who burned polystyrene insulation and particle-board in his domestic wood burner.[3] The presumed exposures included nitrogen oxides from the particle board binders and styrene, formed by the thermal decomposition of polystyrene; the authors claim that styrene causes bronchial epithelial necrosis. Hypersensitivity pneumonitis has been described in a woman who worked with wet fibreglass in the

manufacture of yachts and was thus exposed to both dimethyl phthalate and styrene.[4]

Limited support for a causal relationship with the manufacture of glass-reinforced plastics is available from epidemiological studies of similar workforces, albeit with a focus on styrene exposure. Among a cohort of US workers employed between 1948 and 1977 in the reinforced plastics and composites industry,[5] a significant excess of deaths from "other, non-malignant respiratory disease" was observed during follow-up to 1989 (standardised mortality rate (SMR) 1.41, 95% CI 1.05 to 1.85). Increased SMRs from "bronchitis, emphysema or asthma" were also reported for those who were employed for more than 2 years in either open mould processing or mixing/closed mould processing. Similar findings were reported from a cohort of US fibreglass boat builders[6] employed between 1959 and 1978 and followed to 1998. In this population, the SMR from "pneumoconioses and other respiratory diseases" was, on the basis of 12 deaths, significantly raised (SMR 2.54, 95% CI 1.31 to 4.44) in those with high exposures to fibreglass manufacture and laminating. Interestingly, the increase in risk seemed to be confined to those workers with less than 1 year of employment, consistent with a disabling disease of short latency. In contrast, no increase in non-malignant respiratory mortality was observed in a cohort of over 50 000 Danish workers in the reinforced plastics industry.[7] Surveys of lung function in working populations have produced mixed findings. In 454 Polish men who had worked with both styrene and methylmethacrylate, almost half, irrespective of their smoking histories, had spirometric evidence of airways obstruction, a proportion about twice that in a referent group of unexposed factory workers.[8] In contrast, Lorimer and colleagues found no evidence of a relationship between cumulative styrene exposure and either respiratory symptoms or airways obstruction that could not be explained by age or smoking.[9]

The cases we describe did not report the exposure history characteristic of an acute inhalational injury but, rather, a more chronic exposure to the constituents of fibreglass manufacture. In this respect, and assuming a causative relationship between their disease and their work, their experience resembles that of flavouring-related bronchiolitis originally described in microwave popcorn packers. In that setting, the extent of the risk and the likely aetiological agent were established only through further epidemiological studies of employees in similar workplaces[10 11] or, importantly, making the same agent(s),[12] and through toxicological study of potential chemical causes. It is instructive that flavouring-related bronchiolitis came to light originally through the observations of an occupational physician and the work of a compensation lawyer, and that several cases were originally labelled as having "asthma", "bronchitis" or other forms of "COPD" (chronic obstructive lung disease).[11]

We suggest, on the basis of the case reports above, that OB may be aetiologically related to exposures encountered during the manufacture of glass-reinforced plastics (fibreglass) with, perhaps, a particular risk from boatbuilding. Further study of the issue will require epidemiological study of exposed workforces with high-quality spirometry and access to sensitive radiological investigations, notification of further cases to national surveillance schemes, and a detailed chemical and toxicological analysis of the several agents involved in the manufacturing process.

Contributors PC and PSB had the idea for the paper and wrote the manuscript for which they accept responsibility. CRMcG, AGN, TMM, TH, JB, AJNT, CHC, TSS and PJT originally identified the cases and/or took part in their clinical care. KK provided toxicological advice.

Competing interests None.

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