Bullous Pulmonary Damage in Users of Intravenous Drugs*

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Among a large group of users of illicit intravenous drugs, the incidence of bullous pulmonary damage was noted to be 2 percent (6/387). Bullous damage was significantly different in the drug users than in those who did not use drugs. The drug users were significantly younger than the nonusers, their bullae were large and confined to the upper lobes, and α1-antitrypsin deficiency was very unlikely. These features strongly implicate intravenous drug abuse in the pathogenesis of these patients' bullous pulmonary damage.

Pulmonary disorders which result from intravenous drug abuse include pulmonary edema, septic emboli with or without infarction, pneumonia, pulmonary abscess, empyema, bronchiectasis, and talc granulomatosis. Recently, we found chest roentgenographic evidence of bilateral upper lobe bullous pulmonary damage in three known users of intravenous drugs. To determine whether the intravenous use of illicit drugs and bullous pulmonary damage were associated, we reviewed the charts and chest roentgenograms of all patients in the past 23 years with bullous emphysema who underwent pulmonary function tests at the Bronx Municipal Hospital Center. After identifying those patients with bullous pulmonary damage who were intravenous drug users, we compared them to those patients with bullous emphysema who did not use intravenous drugs. Additionally, we examined chest roentgenograms of patients being treated in a clinic for intravenous use of illicit drugs. The data support our belief that bullous pulmonary damage should be added to the list of pulmonary disorders associated with the intravenous use of illicit drugs.

Materials and Methods

All patients in this study had chest roentgenographic evidence of bullous pulmonary damage and were divided according to whether they additionally were users of intravenous drugs (group 1) or not (group 2). They were found in one of three ways. First, the three patients alluded to in the introductory paragraph were found to have bullous pulmonary damage after they were hospitalized for nonpulmonary problems (assigned to group 1). None of these patients had histories that suggested pulmonary disease. Second, all of the records of patients with bullous emphysema who were studied in the Pulmonary Function Laboratory of the Bronx Municipal Hospital Center between 1960 and 1983 were reviewed. Seventeen patients were identified and assigned to group 1 or group 2 according to their history of drug abuse. Finally, the chest roentgenograms of 387 patients treated in a clinic for intravenous drug abuse were examined, and the six (2 percent) who showed evidence of bullous pulmonary damage were assigned to group 1. Patients with bullous pulmonary damage and histories of intravenous drug abuse who had antecedent tuberculosis or pneumonia were excluded from the study.

Clinical parameters were tabulated for each group. All chest roentgenograms were interpreted by a radiologist who was unaware of these patients' histories and the nature of this study. Tests of pulmonary function, when available, included spirometry, pulmonary volumes, single-breath diffusing capacity for carbon monoxide, and arterial blood gas levels. The data were compared using Student's unpaired t-test.

Results

Twenty-six patients with bullous pulmonary damage were studied. Eleven were users of intravenous illicit drugs and were assigned to group 1; the remaining 15 patients, who did not use intravenous drugs, comprised group 2. All 26 patients were men and were cigarette smokers, but the duration and extent of cigarette use are not known.

Clinical characteristics of patients in group 1 and group 2 are presented in Table 1. All but one of the patients in group 1 were black (our population of drug users is predominantly young and a mixture of whites, Hispanics, and blacks). All had large bullae confined to the upper lobes. These bullae occupied at least one half of the upper lobe and often more. A representative chest roentgenogram is shown in Figure 1. Review of the chest roentgenograms of the 387 intravenous drug abusers produced six patients who also had bilateral upper lobe bullae, an incidence of 2 percent. The mean age was 37 ± 7 years (± SD). Patients in group 2 included whites and blacks. They were significantly older than patients in group 1 (48 ± 11 years; p<0.01). Only four had bullous changes confined to the upper lobes. The remaining 11 patients in group 2 had bullous...
changes in multiple sites of both lungs with little or no upper lobe involvement. For both groups, tests of pulmonary function revealed normal total lung capacity (TLC), reduced vital capacity (VC), moderately severe to severe obstruction of airways, reduced single-breath diffusing capacity for carbon monoxide (Dsbt), mild hyperventilation, and mild hypoxia with an increased alveolar-arterial oxygen difference. Patients in group 1 had a significantly lower TLC than patients in group 2 (p<0.05), but none of the other parameters differed significantly (Table 2).

Table 2—Comparison of Intravenous Drug Abusers and Nonusers*

<table>
<thead>
<tr>
<th>Data</th>
<th>Intravenous Drug Abusers</th>
<th>Nonusers</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC†</td>
<td>67.0</td>
<td>72.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>FEV1/FVC%†</td>
<td>52.4</td>
<td>44.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>TLC†</td>
<td>82.3</td>
<td>98.20</td>
<td>&lt;0.05‡</td>
</tr>
<tr>
<td>Dsbt†</td>
<td>42.7</td>
<td>45.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Pco2, mm Hg</td>
<td>35.4</td>
<td>35.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Po2, mm Hg</td>
<td>72.5</td>
<td>78.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Age, yr</td>
<td>36.7</td>
<td>48.1</td>
<td>&lt;0.01‡</td>
</tr>
</tbody>
</table>

*Data are means for group.
†Percent of predicted normal.
‡Significant difference.

Figure 1. Representative chest roentgenogram from one intravenous drug user.
DISCUSSION

We have compared two groups of patients with bullous pulmonary damage (both groups were cigarette smokers with chronic obstruction of the airways; one group was intravenous drug abusers and the other not). Clinical features distinguished these two groups, supporting our belief that bullous pulmonary damage and intravenous drug abuse are pathogenetically related. The group of drug abusers was younger than the nonusers. The drug users had large bullae confined exclusively to the upper lobes, while the nonusers had bullae that varied in size, were generally diffuse, and were rarely limited to the upper lobes. Ideally, we would have measured levels of α1-antitrypsin in both groups to determine if deficiency of this enzyme might have contributed to the bullous damage described. This was not possible in our retrospective analysis; however, one can virtually exclude α1-antitrypsin deficiency as a pathogenetic factor in the drug users, since this group consisted predominantly of black subjects. The incidence of α1-antitrypsin deficiency among blacks is less than 1 percent,14,15 and typically, this abnormality produces panacinar emphysema in the lower lobes.16 We stress that our drug users were predominantly blacks only as evidence to exclude α1-antitrypsin deficiency as a pathogenetic factor. We do not imply any racial predilection for bullous damage or for drug abuse. We expect that white drug users may develop similar bullae as well; and, indeed, our report contains such an individual. In some of these patients' youth, the upper lobe predilection, and the high likelihood that α1-antitrypsin deficiency was not a factor suggest a pathogenetic association between intravenous drug abuse and bullous pulmonary damage.

Since pulmonary tissue from these patients was not available for pathologic examination, we can only speculate on the nature of such a pathogenetic process. Bullae may develop from known complications of intravenous drug abuse; for example, foreign-body granulomas10-12 could produce pulmonary fibrosis and microbullae. Subsequent coalescence of these with the formation of large bullae would mimic the process of stage 4 sarcoidosis.11 Alternatively, septic or foreign-body emboli may damage the pulmonary capillary bed to form thin-walled cavities. Repeated intravenous drug abuse would increase the numbers of these cavities, and their coalescence would result in large bullae.

Thomashow et al.10 provided support for the latter hypothesis. In 12 intravenous drug abusers with normal chest roentgenograms, these investigators noted abnormal 99mTc technetium perfusion lung scans with two or more nonsegmental defects in perfusion in each scan, while ventilation scans were normal. They interpreted their findings as compatible with occlusive disease at the arteriolar-capillary level. Furthermore, in ten of their 12 patients, perfusion defects were found in the upper lobes. The ventilation scans were normal in these areas. Conceivably, microemboli which lodge in apical pulmonary capillaries produce microbullae and, subsequently, the giant bullae seen in our patients. Since we do not know what substances our drug users injected, it may be unnecessary to assign primarily "occlusive" vs "destructive" events as the offenders leading to bullous pulmonary damage.17-19 Indeed, both may occur.

Functionally, all of our patients had reduced VC with expiratory airflow obstruction. Total lung capacity was at the lower limits of normal (82 percent of predicted) in the drug abusers, and this was smaller than in the nonusers with bullous emphysema. While this suggests that large bullae compressed adjacent areas of lung, these patients also had reduced Ds (43 percent of predicted), implying that there was considerable parenchymal pulmonary damage. In such patients, the potential benefit of bullectomy is doubtful.20

In conclusion, we believe that our finding of large (bilateral) upper lobe bullous pulmonary damage in young intravenous drug users, among whom α1-antitrypsin deficiency was highly unlikely, strongly implicated drug abuse in the pathogenesis of those bullae.

ACKNOWLEDGMENTS: We thank Ms. Fran Goldberg for her secretarial assistance.

REFERENCES

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ACCP Course: Lung Pathology


Course Description: This four-day course will provide a comprehensive review and thorough update on lung pathology. The course will be taught by internationally known experts in the area of the lung. The content of the course is structured for pathologists, practicing chest physicians, chest radiologists and fellows in chest medicine. It will be particularly helpful for fellows preparing for Board Examinations. Emphasis will be placed on clinico-pathologic relationships and on recent advances in lung disease. The course will feature the following: Normal anatomy and histology, chronic airflow obstruction, interstitial lung disease, infiltrative lung disease, altered gene expression in lung cancer, pulmonary vascular disease, disorders of cilia, neoplasia, alveolar filling diseases, viral infections, occupational lung disease, non-infectious angiitis and granulomatosis, selected non-viral pulmonary infections, cytology, adult respiratory distress syndrome, and lung disease in the immunocompromised host.

The course will again include four case discussions in which a clinician and a pathologist will relate clinical findings, radiology, pulmonary function abnormalities and pathology. The final presentation will be a correlation of radiologic, abnormalities of pulmonary function and morphology.