Fat Embolism Syndrome*

Changing Prognosis

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Patients with the fat embolism syndrome are reported to have a severe course, with mortality as high as 15 percent. Recent studies have attributed improved prognosis to one or another treatment modality. We reviewed the 54 patients with clinical evidence of the posttraumatic fat embolism syndrome documented at the Foothills Hospital from 1968 to 1977. The criteria for diagnosis were fever (54/54), hypoxemia (52/52), diffuse pulmonary infiltrates (49/54), changes in sensorium (41/54), and petechiae (39/54). Therapy included supplemental oxygen (54), assisted ventilation with positive end-expiratory pressure (5), and corticosteroids (7). There were no deaths. Patients who have the fat embolism syndrome without associated life-threatening disease have a relatively good prognosis with modern therapy, in contrast to reports in most of the published literature.

The fat embolism syndrome has been recognized clinically for more than 100 years,1,2 but its incidence and clinical course remain uncertain. According to retrospective studies3-5 and small-scale prospective studies,6-8 the incidence after long-bone fractures may range from less than 1 to 17 percent. A recent estimate suggests a considered figure of 1 to 5 percent.7 Postmortem studies of trauma victims have identified fat embolism much more frequently (39 to 100 percent), but the relationship of histologic emboli to the cause of death frequently was unclear.1

Early reports emphasized a high mortality; clinical series in the 1960s and early '70s reported mortality of 12 to 35 percent.5,8-10 The mortality reported frequently was spuriously high because these posttraumatic patients usually died of associated injuries. Furthermore, patients reported to have nontraumatic fat embolism generally have severe systemic disease, such as diabetes, sickle cell anemia, and severe sepsis. Therefore, it is not surprising that two small series with no mortality attributed their success to definitive treatment programs.11,12

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Critical comparison of various reports is not possible. There are no uniformly accepted and precise diagnostic criteria. Furthermore, recognition of the syndrome, time of diagnosis, and details of management are highly variable. Since the condition is uncommon, it seems well suited to a multicenter study. However, the low incidence after trauma and the wide range of physician groups first involved with these patients would make such a prospective clinical study very costly.

It was our impression that the commonly reported mortality rates did not apply currently. Therefore, while waiting for appropriate, large-scale prospective studies, we assessed the prognosis of patients with the fat embolism syndrome whose survival was not determined by other organ injuries or disease and who received modern care and management.

Patients

All patients with recorded clinical evidence of the posttraumatic fat embolism syndrome at the Foothills Provincial General Hospital were reviewed for the years 1968 to 1977. Of the 59 reported patients, five had insufficient evidence to support the diagnosis, one of whom died as a result of acute renal failure, severe gastrointestinal bleeding, and septic shock with no evidence of fat embolism at autopsy. Since fat embolism might have been overlooked in some patients who died after trauma, all autopsies were reviewed during the same period. All early posttraumatic, unexplained, or postsurgical deaths are subjected to autopsy by provincial law. Only one additional (clinically unsuspected) case with fat embolism was identified, but the cause of death was injury to the head and great vessels. This study therefore includes the 54 patients who had at least two of the major features—fever (temperature greater than 38°C), changes in sensorium, hypoxemia, petechiae, and diffuse pulmonary infiltrates, and in whom there was little evidence for aspiration, infection, lung contusion, or other cause for the abnormalities. These criteria, while not precise, remain the best clinical criteria in the current literature.6,8,9,12

Results

The 54 patients ranged in age from 15 to 74 years (mean, 27.3 years). Forty-three were male and 11 were female. The mechanism of injury and fracture sites are listed in Tables 1 and 2. The recorded manifestations are summarized in Table 3. Twenty-three patients had all 5 manifestations, 25 had 4, 3 had only 3, and 3 had only 2 manifestations. These

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last three patients had hypoxemia and fever, with no other clinical explanation and a typical course for the fat embolism syndrome.

Fifty-two of the 54 patients had arterial blood gas analysis done. The remaining two, seen before 1970, were described as cyanotic and given oxygen. In 36 patients, arterial blood drawn while the patients were breathing room air showed severe arterial hypoxemia, with a mean Pao2 of 43 mm Hg (range, 23 to 72); pH, 7.48 (range, 7.36 to 7.55), and Paco2, 28 mm Hg (range, 19 to 38). The calculated alveolar-arterial oxygen gradient was 51 mm Hg (range, 27 to 75).* The first arterial blood was drawn in 18 patients while they were breathing supplemental oxygen that had been instituted because of the clinical suspicion of severe hypoxemia. Each of these patients showed marked elevations of alveolar-arterial oxygen gradients as estimated from the supplemental oxygen. Carbon dioxide retention only occurred in patients whose lung disease was sufficiently severe to require ventilator support.

**MAJOR THERAPEUTIC INTERVENTIONS**

All 54 patients were given supplemental inhaled oxygen. Five required assisted ventilation and were given PEEP to reduce the level of inspired oxygen and maintain an adequate arterial Pao2. Since a variety of physicians were responsible for initiating treatment in these patients, antibiotics were frequently given early in the course, intravenous (IV) alcohol was administered for a short period in two patients, and anticoagulants were administered in four until thromboembolism was reasonably excluded by lung scans. Corticosteroids were administered IV to seven patients (ranging from a single dose of 100 mg of hydrocortisone to methylprednisolone sodium succinate, 35 mg kg/day). Three of the five patients who required ventilator treatment received IV corticosteroids. The series is too small and the course too variable to permit critical analysis of the duration of respiratory failure or general outcome in the group given steroid treatment compared with the group that received no steroids.

**DISCUSSION**

The fat embolism syndrome represents an elusive scientific challenge. The lack of definitive diagnostic criteria, the unpredictable course, and frequent associated disease have made it difficult to standardize patient populations. Clinical criteria permit identification of a distinctive group of patients, but the commonly abnormal laboratory test results lack specificity. The diagnostic value of determining hypercalcemia, hypoalbuminemia, anemia, thrombocytopenia, fat globules in the blood, urine, or sputum, and elevated blood lipase levels all have been questioned.* In prospective studies, patients with long-bone fractures have had platelet counts, determinations of fibrinogen, blood or urine lipids, or serum lipase demonstrated abnormalities, but none of the patients had the syndrome.* Similarly a prospective study of 17 high-risk patients by serial measurement of diffusing capacity was unhelpful, since none had the syndrome. Unfortunately, all of these parameters may be abnormal in patients without the clinical syndrome, and, conversely, patients with the clinical syndrome may lack many of these manifestations. Consequently, every

**Table 1—Method of Injury**

<table>
<thead>
<tr>
<th>Method of Injury</th>
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<tbody>
<tr>
<td>Motor vehicle accident</td>
<td>26</td>
</tr>
<tr>
<td>Motorcycle accident</td>
<td>10</td>
</tr>
<tr>
<td>Skiing accident</td>
<td>4</td>
</tr>
<tr>
<td>Snowmobile accident</td>
<td>3</td>
</tr>
<tr>
<td>Miscellaneous (includes falling and postoperative bone surgery)</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total No. of patients</strong></td>
<td><strong>54</strong></td>
</tr>
</tbody>
</table>

**Table 2—Fracture Sites**

<table>
<thead>
<tr>
<th>Fracture Site</th>
<th>No.</th>
</tr>
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<tbody>
<tr>
<td>Femur</td>
<td>40</td>
</tr>
<tr>
<td>Tibia</td>
<td>23</td>
</tr>
<tr>
<td>Fibula</td>
<td>17</td>
</tr>
<tr>
<td>Ribs</td>
<td>24</td>
</tr>
<tr>
<td>Pelvis</td>
<td>13</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>32</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>149</strong></td>
</tr>
</tbody>
</table>

**Mean fractures per patient** 2.7

**Table 3—Major Manifestations of Fat Embolism**

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>54 (100)</td>
</tr>
<tr>
<td>Increased alveolar-arterial oxygen gradient</td>
<td>52 (100*)</td>
</tr>
<tr>
<td>Diffuse infiltrates on chest film</td>
<td>44 (81)</td>
</tr>
<tr>
<td>Changes in sensorium</td>
<td>41 (76)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>39 (72)</td>
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</tbody>
</table>

*Two patients did not have arterial blood gases measured.
patient group must be defined on the grounds of the parameters used, and can be compared only with other patient groups similarly defined.

The inability to develop well-controlled clinical trials led to enthusiasm for work in experimental models. The extensive use of oleic acid injections to produce alveolar injury in animals has permitted detailed assessment of that model of lung edema in controlled trials. However, there is evidence that the lung injury is dose-related and that the amount of pulmonary edema that develops is highly sensitive to hydrostatic pressures and osmotic pressure. The injury may be modified somewhat by use of corticosteroids. However, the lesion being studied is not clinical fat embolism, but an experimental model whose relevance remains to be established.

Early immobilization of the bone fragments, early and adequate fluid and blood replacement, use of antibiotics, and careful observations are principles commonly accepted in current therapy. In patients with the established syndrome, oxygen therapy, monitoring of fluid replacement, judicious use of diuretics, and ventilator support may be critical determinants of survival. Use of alcohol and anticoagulants was once accepted on limited rationale, but generally has been discontinued. The use of glucocorticoids has been popular, but none of the studies report the large clinical trials that would be necessary to establish their efficacy. Only seven patients in this study received steroids and only three of them were in the severely ill group. Studies of the preventive effects of salicylates, steroids, and hypertonic glucose have been inconclusive.

The incidence of the syndrome is too low to permit conclusions from the small studies reported and the reports deal largely with modulation of laboratory abnormalities by various treatment programs.

The major difficulty in designing specific treatment lies in the uncertainty regarding the cause of tissue injury. Whether neutral fat, fatty acids, or other factors initiate the injury has not been established. Furthermore, the resulting sequence of capillary permeability changes, resulting in microvascular leaking with life-threatening consequences in the brain and lungs, is unexplained. Until these mechanisms are better defined, no therapeutic approaches can have specificity.

In this study we have reviewed the patients and autopsies for ten years in our institution to assess the role of fat embolism in determining survival after trauma. Not a single death was attributable to fat embolism in 54 patients with the syndrome (48 of whom had at least four of the major criteria). These observations suggest that the outcome in this decade is far superior to that of the 1960s. No single factor can be credited for this outcome, although oxygen administration with PEEP was judged to be essential in five patients. Survival in most patients is not dependent on the use of corticosteroids; however, whether the severity of the alveolar injury is reduced or repaired more rapidly with steroid treatment remains to be assessed.

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REFERENCES