Squamous cells in the maternal pulmonary circulation

Steven L. Clark, M.D., Zdena Pavlova, M.D., Jeffrey Greenspoon, M.D.,
Janet Horenstein, M.D., and Jeffrey P. Phelan, M.D.
Los Angeles, California

Identification of squamous cells in the maternal pulmonary arterial circulation, either at autopsy or in blood aspirated from a pulmonary artery catheter, is currently regarded as pathognomonic for amniotic fluid embolism. Sixteen pregnant women underwent pulmonary arterial catheterization for a variety of medical indications. Examination of the buffy coat fraction of the distal lumen aspirate resulted in the identification of squamous cells in all cases. Squamous cells were similarly identified in control specimens from 17 nonpregnant patients; however, the difference in cell count between the pregnant and nonpregnant patients was significant. Such cells presumably reflect, in part, bloodstream contamination from sites of venous access. Reliable differentiation of adult from fetal squamous cells is not possible; however, the significant increase in cell count documented in pregnant patients suggests a possible fetal origin for some squamous cells detected during pregnancy. The detection of squamous cells in the pulmonary arterial circulation of pregnant women is not pathognomonic for amniotic fluid embolism. In a critically ill obstetric patient, such a finding should not deter the clinician from a thorough search for other causes of hemodynamic instability. (Am J Obstet Gynecol. 1986;154:104-6.)

Key words: Amniotic fluid embolism, fetal squamous cells, pulmonary artery catheter

Amniotic fluid embolism is an uncommon obstetric condition characterized by hypotension, hypoxia, and, in 40% of cases, disseminated intravascular coagulation. Maternal mortality approaches 80%. Detection of squamous cells in the pulmonary arterial circulation, either at autopsy or in blood aspirated from the distal lumen of a pulmonary arterial catheter, is traditionally regarded as being pathognomonic for this condition because of the diversity of the clinical presentation, such documentation is considered essential for diagnosis. This study was undertaken in order to define the frequency with which squamous cells may be isolated from the pulmonary arterial circulation of pregnant women.

Methods

Between November, 1983, and July, 1984, 16 pregnant women underwent pulmonary arterial catheterization for a variety of medical indications. Proper placement was confirmed by waveform and chest x-ray film. In all cases, the route of insertion was the right internal jugular vein. Gestational ages ranged from 28 to 43 weeks. Samples were collected and prepared in an identical manner from 17 nonpregnant patients in medical and surgical intensive care units. Three milliliters of blood was aspirated from the distal catheter lumen and discarded. An additional 7 ml was then withdrawn and injected into a heparinized tube. The specimen was centrifuged and smears were made from the Buffy coat layer. Standard Wright and Sudan Black preparations were then examined by one of us (Z. P.) from the Department of Pathology for detection of squamous cells. The solution for the Wright stain was delivered in a closed system, and automated slide preparation was used. Throughout the study, utmost care was taken to avoid any epidermal contact with the slide surfaces. In the final 18 patients, all slide handling was undertaken by a technician wearing both gloves and a hair net.

From each specimen, two Wright-stained smears from the Buffy coat were examined for semiquantification of squamous cells. A count was made of all squamous cells identified for a distance of two low-power fields from the peripheral feathered-edge and one low-power field from the lateral margins. Only undistorted cells exhibiting the classic morphologic and staining characteristics of squamous cells were counted. Reported cell counts represent the mean for both slides. Following our initial observations, several slides were examined by an independent pathologist who confirmed identification of squamous cells.

Results

Squamous cells were identified in every patient (Fig. 1). Table I details the medical complications of pregnant patients undergoing pulmonary arterial catheterization. Also listed is the mean number of squamous cells identified during the prepartum and postpartum.
Fig. 1. Wright stain preparation of pulmonary arterial blood of patient with term pregnancy and New York Heart Association Class IV mitral stenosis.

Table I. Pulmonary arterial catheterization in pregnant patients

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patients</th>
<th>Mean squamous cell count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe pregnancy-induced hypertension</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Septic shock</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Severe cardiac disease during labor</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Unresponsive hypovolemic shock</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Pulmonary edema, unknown cause</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

*Excluding patient with clinical amniotic fluid embolism.

Comment

In a study in healthy pregnant patients, Sparr and Pritchard injected chromium-labeled erythrocytes into the amniotic cavity. Examination of peripheral blood failed to demonstrate the presence of labeled red blood cells. This experiment has been cited as evidence that embolization of amniotic fluid debris does not occur in normal pregnancy. Based on these data and the detection of squamous cells and other debris of presumed amniotic origin in the pulmonary vasculature of peripartum patients with the syndrome of hypotension, hypoxia, and coagulopathy, it has been presumed that such a finding is both necessary and sufficient for the diagnosis of amniotic fluid embolism. Recently, in response to a case report of amniotic fluid embolism, a letter appeared describing two pregnant patients with other medical conditions in whom squamous cells were detected in pulmonary arterial blood. We have demonstrated that squamous cells are almost universally detected in the pulmonary arterial circulation of pregnant patients.

There are several possible explanations for the seeming discrepancy between our findings and those of Sparr and Pritchard. The latter study involved a series of artificially induced physiologic manipulations and measurements in an effort indirectly to examine the possible release of squamous cells into the maternal circulation. The possibilities of error in such a complex experimental design were discussed at length by the authors of this work. In their study, peripheral blood was examined at frequent intervals for up to 4 days following injection of chromium-labeled erythrocytes into the amniotic cavity. Assuming that asymptomatic embolization of amniotic fluid debris is a gradual pro-
cess, it seems possible that 4 days would be insufficient time to permit detectable embolization with the methods of this study. Certainly, the simple design of the present study, involving direct examination of pulmonary arterial blood, is much less susceptible to experimental error.

Every attempt was made to eliminate the possibility of artifact or contamination from this study. Strict adherence to the previously described criteria for squamous cell identification, as well as independent examination of the preparations by a pathologist from an unrelated institution, eliminates, in our opinion, the possibility of the former. The closed system stain delivery and mechanical slide preparation, in addition to meticulous handling of specimens by all individuals involved in the project, minimizes the latter possibility. A further procedural change late in the study to include gloves and a surgical hairnet during all slide handling did not alter the frequency with which squames were detected.

The release of adult epidermal cells into the circulation from the site of introducer sheath placement in all likelihood accounts for the significant number of squamous cells detected in nonpregnant patients. Squamous cells are commonly found in peripheral blood smears obtained by venipuncture and represent epidermal contamination. The fact that nonpregnant control specimens yielded a significant difference in cell count from that observed in postpartum patients, as well as the trend in pregnant subjects toward increasing numbers of squamous cells in postpartum samples, suggests that fetal cells may have contributed to the total cell count observed in pregnant patients. Unfortunately, reliable histologic differentiation of adult from fetal squamous cells is not possible; thus the fetal origin of such cells can only be inferred. However, regardless of the origin of these cells, the implication of this report remains the same: The detection of squamous cells in meticulously handled pulmonary arterial blood of critically ill pregnant patients is not sufficient for the diagnosis of amniotic fluid embolism.

It is well established that trophoblastic cells are commonly found in the maternal venous circulation. One may postulate that small-scale embolization of fetal squamous cells is, in a similar manner, a common and generally benign phenomenon and that the symptoms commonly associated with amniotic fluid embolism occur only with larger volumes of debris. It was, therefore, surprising that we could not detect a quantitative difference in cell count between one patient with fatal amniotic fluid embolism and other pregnant patients. This finding corroborates data indicating a poor correlation between clinical symptoms and the volume of experimentally injected fetal debris and suggests that in clinical amniotic fluid embolism, such cells may possibly simply be a marker of a condition caused by an abnormal substance within amniotic fluid. Alternate ly, this finding may reflect rapid clearance of squamous cells from the pulmonary arterial circulation. Jaques et al. demonstrated the possibility of such clearance with subsequent detection of squamous cells in distal organs.

The results of this study have important clinical implications suggesting that detection of fetal squamous cells in significant numbers in blood aspirated from the distal port of a pulmonary arterial catheter is not diagnostically of amniotic fluid embolism. This perhaps explains, to some extent, the heterogeneity of clinical situations in which amniotic fluid embolism has been alleged to occur,13 as well as the variety of clinical findings and hemodynamic aberrations commonly attributed to this single pathologic entity. The detection of squamous cells in the maternal pulmonary arterial circulation may be a necessary, but not sufficient, condition for the diagnosis of amniotic fluid embolism. In a critically ill obstetric patient, such a finding should not deter the clinician from a thorough search for other causes of hemodynamic instability (sepsis, cardiac disease, thromboembolism, etc.). Confirmatory studies may further contribute to our understanding of the phenomenon of amniotic fluid embolism.

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REFERENCES