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Original Contribution

FETAL HYPOXIA AND MECONIUM IN PRETERM DELIVERIES AND STILLBIRTH

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ABSTRACT

Purpose: This study was undertaken to assess the relationship between the degree of meconium staining of the extraplacental membranes at birth, meconium aspiration, and pulmonary changes in neonates and stillbirth. **Methods:** The lungs, extraplacental membranes and placenta from 20 stillborn with meconium-stained membranes and 13 lungs of perinatal deaths were collected and microscopically examined for meconium, intra-alveolar presence of aspiration and inflammation. **Results**: Microscopically, 32% and 40% of the lungs had evidence of meconium for the stained and nonstained groups, respectively. The microscopic grade of meconium aspiration and inflammatory cells was not different between nonstained and meconium-stained membranes. Aspiration of meconium induced a granulomatous response in the lungs. **Conclusion:** It was concluded that the grade of meconium staining is a good indicator of fetal hypoxia, but not a good predictor for meconium aspiration and MAS in newborn.

Key Words: meconial aspiration • neonatal hypoxia • meconiophages

INTRODUCTION

Meconium staining of the membranes is a common event associated with fetal hypoxia, stillbirths, SGA infants and neonatal mortality. Aspiration of meconium leads to meconium aspiration syndrome (MAS).This study was undertaken to assess the relationship between the degree of meconium staining of the membranes at birth, meconium aspiration, and pulmonary changes in neonates. A total of 33 cases were reviewed. Meconium staining in the membranes was graded as nonstained, mildly, moderately and severely stained. The lungs from 20 stillborn with meconium-stained membranes and 13 lungs of perinatal deaths were collected and microscopically examined for meconium aspiration and inflammation. Rupture of the membranes was significantly higher ($P < 0.01$) in meconium-stained cases. Microscopically, 32% and 40% of the lungs had evidence of meconium for the stained and nonstained groups, respectively. The microscopic grade of meconium aspiration and inflammatory cells was not different between nonstained and meconium-stained membranes. Aspiration of meconium induced a granulomatous response in the lungs. It was concluded that the grade of meconium staining is a good indicator of fetal hypoxia, but not a good predictor for meconium aspiration and MAS in newborn.

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MATERIALS AND METHODS

The lungs, extraplacental membranes and placenta from 20 stillborn with meconium-stained membranes and 13 lungs of perinatal deaths were collected and microscopically examined for meconium aspiration and inflammation. Tissues were embedded in paraffin, sectioned at 4 microns, and stained with hematoxylin and eosin. Periodic acid–Schiff counterstained with hematoxylin was used to identify meconium in cases where the recognition of meconium using hematoxylin and eosin was difficult. The presence and distribution of amniotic fluid cells, meconium, and inflammatory cells were evaluated and scored. The scoring system was defined as follows: absent, minimal, when there were sporadic pieces of meconium; mild (+) when epithelial cells, meconium, or inflammatory cells were present in low frequency; moderate

(++) when epithelial cells, inflammatory cells, and meconium were partially filling the bronchoalveolar spaces; and severe (+++) when the airways were largely filled with epithelial cells, meconium, or inflammatory cells. Immunohistochemistry with CD 68 for identification of meconiophages in membranes, umbilical cord and basal plate of the placenta use applied (ready to use, DAKO,Goldstrap)

RESULTS

The amount of meconium in the lungs was only minimal, mild, moderate or severe. Meconium was found in both grossly visible discolorated extraplacental membranes and basal plate of the placenta **(Fig. 1)**.and was strongly CD 68 positive **(Fig. 2)**. Meconium was not associated with inflammatory cells in lungs of stillborn or died within the first 3-5 days of birth **(Fig. 3A)**. In contrast, neonates that died 5to 7 days after birth had meconium surrounded by pulmonary alveolar macrophages and polymorphonuclear leukocytes. This inflammatory reaction also involved the bronchiolar and alveolar epithelia. In some instances, meconium appeared attached to the alveolar walls. The presence of meconium in the lungs of liveborn was also surrounded by alveolar macrophages, and few multinucleated cells that formed focal granulomas **(Fig. 3B)**.

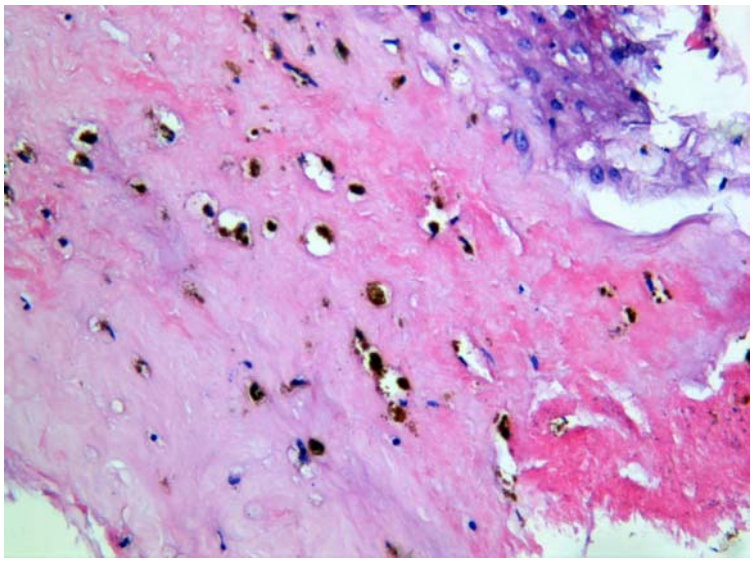

Figure 1. Meconiophages in basal plate of placenta – H&E x20

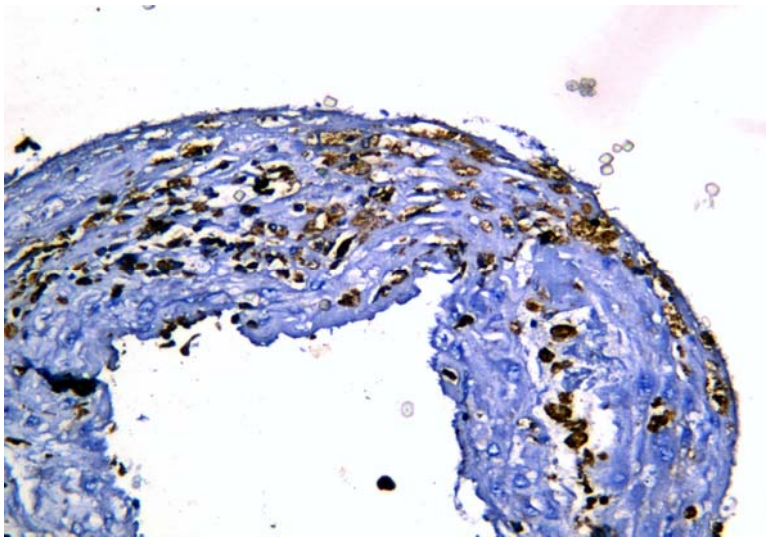

Figure 2. Meconiophages in basal plate of placenta – Immunohistochemistry with CD68 x20

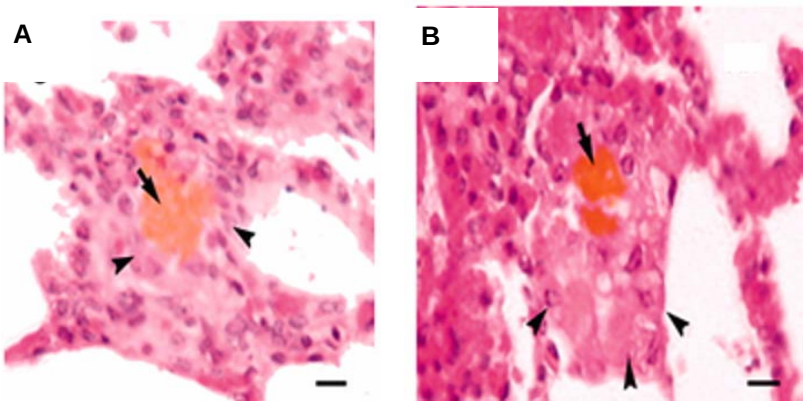

Figure 3. Chronology of the pulmonary response to meconium in neonatal lungs. **A**, meconium (arrow) in alveolar space surrounded by inflammatory cells (arrowheads); **B**, granulomatous response showing meconium (arrow) completely surrounded by macrophages (arrowheads); Hematoxylin and eosin x 40.

Epidermal epithelial cells and keratin consistent with amniotic aspiration were frequently observed in the bronchioles and alveoli of both the stained and nonstained groups. Few polymorphonuclear leukocytes were sporadically seen in the bronchoalveolar spaces, and these cells were not always associated with meconium particles. The intensity of pulmonary edema was slightly higher in meconium-stained membranes. Free red blood cells were commonly observed in bronchoalveolar spaces regardless of whether meconium was present in the lungs. There were no significant differences (P>0.05) in the microscopic findings between meconium-stained and nonstained cases.

Neonatal mortality in this study was higher than the rates of 10% to 30% reported by others.(5) In addition, the percentage of intrapartum stillborns stained with meconium was notably lower (58.2% vs. 86.5%) than the percentage reported in another study.(6) This discrepancy possibly reflects different health status between pregnant women. However, meconium staining was higher in liveborn than in stillborn. The mild to moderate meconium staining is consistent with other studies, and suggests that expulsion of meconium into the amniotic fluid is presumably a common event in perinatology (7, 10). Whether this meconium expulsion results from true anoxia or from an uncomplicated delivery remains to be elucidated. The increased rate of membrane rupture in meconium-stained cases supports the view that premature rupture of the membranes during parturition leads to anoxia and meconium expulsion(10). It also supports the view that violent uterine contractions can lead to membrane rupture and intrauterine hypoxia (9).

DISCUSSION

This study showed that the grade of meconium staining of the membranes did not correlate with the microscopic grade of meconium aspiration into the lungs. This lack of association has also been reported in perinatology (1). Therefore, meconium discolortion of the membranes should be considered a sign of preceding intrauterine distress and fetal hypoxia rather than an indicator of the severity of aspiration. As reported in literature, during the first few days of life, meconium remains free in bronchioles and alveoli, and it is not associated with a intense pulmonary inflammation. In time, meconium becomes surrounded by pulmonary alveolar macrophages and polymorphonuclear leukocytes and eventually forms microscopic granulomas (10). Although, the bronchoalveolar inflammation in response to meconium aspiration is consistent with autopsy findings in babies with clinical MAS, the lungs of newborns from our cases did not show the typical epithelial necrosis and interstitial edema reported experimentally. This lack of a cause-effect relationship suggests that meconium staining at birth is not a good predictor for neonatal viability. It was interesting that gross evidence of meconium was not found in the trachea or bronchi despite the fact that many had microscopic evidence of meconium in the lung. It is likely that during

intrauterine aspiration meconium is passed rapidly into the distal airways or that the amount of meconium in airways is insufficient to be grossly visible. This lack of relationship between gross and microscopic findings also occurs in fetal abortion, where meconium is rarely seen grossly in airways but appears microscopically during routine histopathological examination of lungs (8). We concluded that meconium staining of the skin occurs frequently in stillborn and liveborn. In our observations, meconium staining at birth is a good indicator of premature rupture of the membranes. Meconium staining of the membranes likely relates to the duration of fetal hypoxia but it does not relate to neonatal mortality. Meconium aspiration in liveborn induces a mild multifocal granulomatous inflammation involving all pulmonary lobes. Microscopically, lung lesions are similar to those described in experimental MAS but the long-term sequele need to be further investigated.

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