

A Fullterm Neonate with Respiratory Distress and Meconium Staining* — Case SNUCH CPC-34 —

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PRESENTATION OF A CASE

This male newborn baby was transferred from a private OB/GY clinic because he had not cried at birth on August 28, 1987. He was the second baby to a 32-year-old mother and was born by vacuum extraction at the gestational age of 38 3/7 weeks. At birth his skin was stained with meconium and he did not cry. In spite of resuscitation, he had no regular self respiration. He was transferred to SOWHA Children's Hospital one hour after birth.

On physical examination, the body weight was 3,250 gm, height 51 cm, head circumference 36 cm and chest circumference 33 cm. Respiration was irregular. The skin was cyanotic and stained with meconium. The anterior fontanel was open and flat. A large caput succedaneum was noticed. The neck was supple. Chest wall retraction was prominent. Respiration was irregular but breathing sounds were unremarkable. The heart murmur was not heard. The abdomen was soft without distension. The liver and the spleen were not palpable. Extremities and external genitalia were unremarkable without cyanosis or deformity. General activity, Moro and sucking reflexes were poor.

Laboratory data on admission; CBC revealed Hb 19.3 gm%, Hct 58% and WBC count 34,500

/cmm (seg; 40%, lym; 59%, mono; 1%). Platelet count was 250,000/cmm. C-reactive protein was negative. The blood glucose was 56 mg/dl. Serum calcium and phosphorus were 10.5 mg/dl and 6.3 mg/dl, respectively. The serum VDRL was non-reactive. Cultures of blood and urine failed to grow microorganisms. The peripheral blood gas analysis revealed pH 6.516, pCO₂ 115.0 mmHg, pO₂ 142.4 mmHg, HCO₃⁻ 9.0 mEq/L, BE -35.4 mmol/L and O₂ sat. 83.7%.

The chest X-ray showed an ill defined haziness on the right mid and lower lung fields with air bronchograms. After admission, IPPV with FiO₂-0.9, RR-60/min, I/E-0.7, PIP-20cmH₂O and PEEP-2cmH₂O was applied after endotracheal intubation. Dexamethasone and luminal were injected. Bivon mixed with dextrose/water was dripped. Two hours later, the BGA revealed pH 6.411, pCO₂ 140.9 mmHg, pO₂ 31.2 mmHg, HCO₃⁻ 8.6 mEq/L, BE -36.4 mmol/L and O₂ sat. 8.7%. Respiration rate was increased to 100 per min and I/E decreased to 1/2. Tolazoline was injected.

Five hours after admission, gastric bleeding was noticed. Hemoglobin and hematocrit were 14.3 gm/dl and 43%, respectively. Prothrombin time was over 1 minute and PTT was over 2 minutes. Platelet count was 220,000/cmm.

Six hours after admission, bradycardia was noticed. He had no response after external cardiac massage and intermittent ambubagging. CSF was bloody. Eight hours after admission, he expired.

DISCUSSION

Dr. Choi: First, I will summarize the problems of

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this case. This male newborn baby was born by vacuum extraction as a term baby with birth weight of 3,250 gm AGA (appropriate for gestational age) at a local clinic. His skin was stained with meconium and he didn't cry at birth. In spite of resuscitation he had no respiration. After being transferred to SOWHA Children's Hospital, he had respiratory distress with cyanosis, chest retractions and meconium-stained skin. All reflexes were very poor. Laboratory abnormalities were leukocytosis, severe metabolic and respiratory acidosis, hypercarbia and hypoxia. In spite of being treated with mechanical ventilation and tolazoline, he died of respiratory failure, gastric bleeding, and intracranial hemorrhage.

It would be helpful to review the radiographic findings at this time, because it may help me to pursue a differential diagnosis. Could we see the chest X-ray of this case?

Dr. Yeon (Pediatric radiology): Chest X-ray film (Fig. 1) of this patient shows bilateral densities, more in the right lung. The nature of the density appears to be massive aspiration of amniotic fluid and meconium. Presence of superimposed pneumonia cannot be determined by this film.

Dr. Choi: As Dr. Yeon has pointed out to us, this patient's chest X-ray showed the presence of

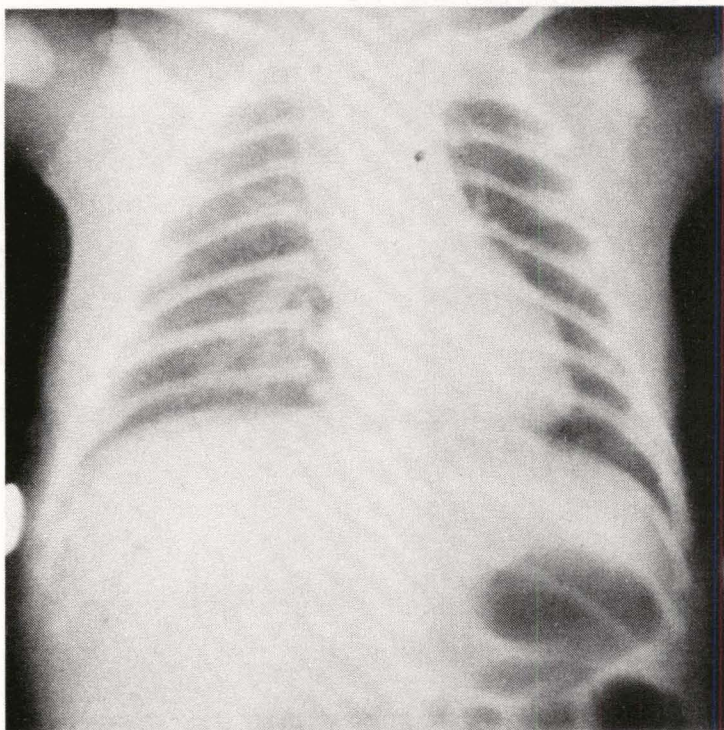


Fig. 1. Chest X-ray of the patient, showing bilateral densities in the lungs.

pneumonic infiltrations on the RML (right middle lung) and RLL (right lower lung) fields, indicative of meconium aspiration pneumonia.

In this patient, it is possible that a single process, 'perinatal asphyxia', may explain the full evolution of his clinical course. It is well known that perinatal asphyxia in newborn infants leads to high mortality and a high rate of sequelae. Asphyxia is a word that means 'without pulsation' in Greek and is an ultimate form of severe oxygen lack. Asphyxia neonatorum is defined as a failure to establish spontaneous respiration at birth. Clinically (practically), it is defined as less than 6 at 5 minutes of Apgar score. Although the Apgar score was not recorded in the protocol of this patient, perinatal asphyxia could be suspected from the fact that he had not cried, had no self-respiration and meconium-stained skin at birth. But, there was no mention about the causes of perinatal asphyxia, i.e. hypoxic insults like preeclampsia, diabetes, abruptio placenta, etc. After he was admitted to SOWHA Children's Hospital, his clinical course deteriorated very rapidly. This could be explained by the sequential pathophysiologic events following perinatal asphyxia (Perlman *et al.* 1989; Volpe 1987). When there is a hypoxic insult to the fetus or to the newborn infant, cardiac output would be redistributed as an adaptive circulatory response. Initially, a large proportion of the cardiac output would flow to the brain, heart, and adrenal gland. Contrast to this, blood flow to kidney, liver, GI tract, lung, and muscles would be greatly decreased. Therefore, each organ may experience different injuries.

I will explain the possible hypoxic injury of each specific organ from now on. **1) Kidney:** Increased PaCO₂ leads to increased renal vascular resistance and decreased renal blood flow. Eventually, ATN (acute tubular necrosis) may occur, especially in the proximal tubule. Renal tissue necrosis, myoglobinuria, and ARF (acute renal failure) occurred by hypoxia. Perlman and Tack (1988) reported that β_2 -microglobulin and oliguria were associated with late neurological sequelae. **2) G-I tract:** Decreased blood flow to the G-I tract leads to ischemia of the bowel, which may cause NEC (necrotizing enterocolitis). **3) Liver:** Hepatic tissue necrosis may occur due to decreased hepatic blood flow

caused by hypoxia. **4) Lung:** Acidosis and gasping may occur due to decreased pulmonary blood flow and meconium aspiration pneumonia caused by hypoxia. **5) Hematologic:** DIC (disseminated intravascular coagulopathy) may occur due to vascular endothelial injury caused by hypoxia and acidosis. **6) Metabolic:** Hypoglycemia may occur due to increased anaerobic glycolysis, decreased ATP, and increased hypoxanthin by hypoxia. Hyponatremia may occur due to SIADH. **7) Cardiovascular system:** Initially, aerobic glycolysis and systemic blood pressure may be maintained by increased coronary arterial blood flow to the heart. But, if hypoxia persists, systemic blood pressure and combined ventricular output may be decreased and eventually, congestive heart failure and cardiogenic shock may occur. ST-T change on EKG due to ischemic necrosis of cardiac papillary muscle may appear. **8) Brain:** Initially, aerobic glycolysis may be maintained by increased cerebral blood flow. But, if hypoxia persists, hypoxic-ischemic encephalopathy may occur due to decreased vascular autoregulation, cerebral perfusion pressure, and cerebral blood flow (Hill and Volpe 1989). In this patient, ATN, acidosis, DIC, NEC, myocardial damage and

severe hypoxic-ischemic encephalopathy are suspected as subsequent pathophysiologic events of perinatal hypoxia.

Next, let's consider the meconium aspiration syndrome of this patient. The important points in meconium aspiration syndrome are the constituents of meconium, the relation between asphyxia and meconium, the time and cause of the passage of meconium into the amniotic fluid, the time and cause of meconium aspiration, and the mechanism of respiratory distress with the presence of meconium in the lung. Meconium is first evident in the fetal intestine at 70-85 days of gestation. Its constituents are undigested portions of swallowed debris, various products of secretion, excretion, and desquamation by the G-I tract like bile pigments, bile salts, lanugo, squamous cells, mucopolysaccharides, and cholesterol. Normally, it is retained within the fetal colon due to high viscosity, anal sphincter tone, and lack of peristalsis. Passage of meconium may occur due to vasoconstriction of the fetal gut, hyperperistalsis, and relaxation of the fetal anal sphincter by fetal hypoxia. Without hypoxia, it may occur due to parasympathetic (vagal) stimulation by umbilical cord compression and due to spon-

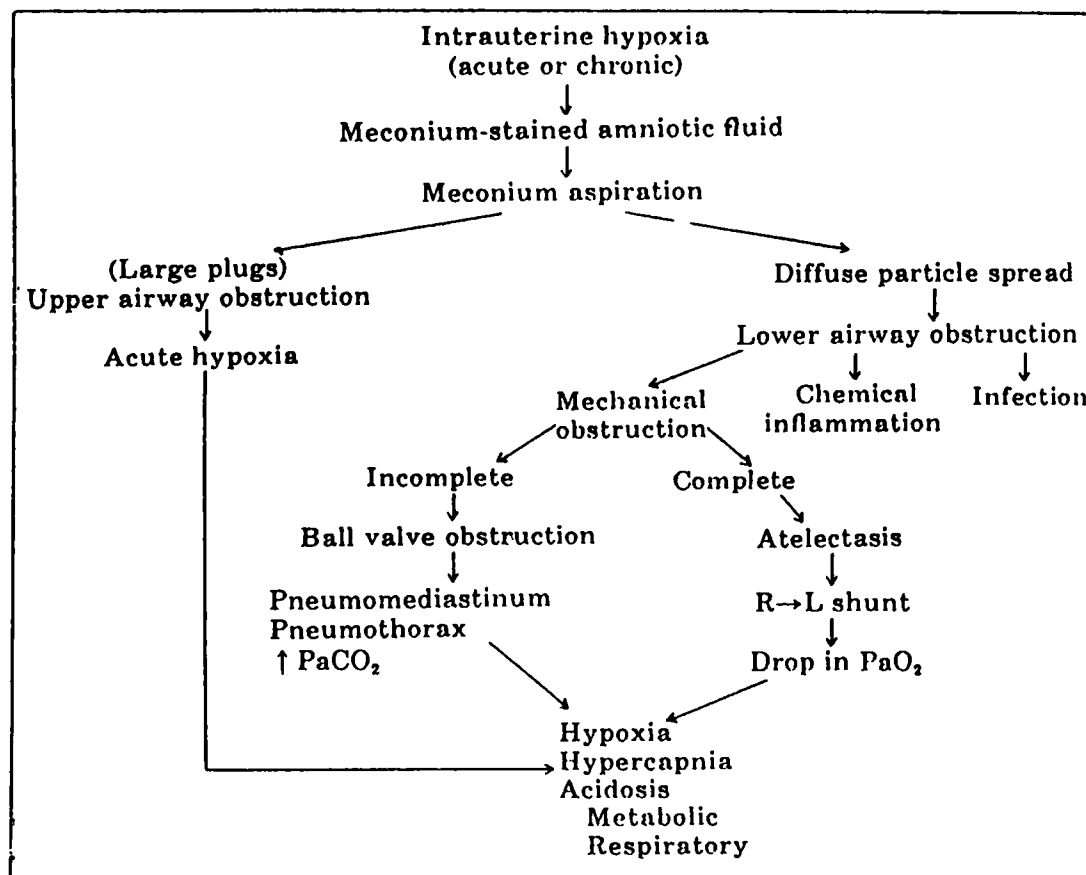


Fig. 2. Schema of the pathophysiology of meconium aspiration.

taneous G-I motility in post-term infants by normal physiologic maturation of the fetal gut. The incidence of meconium-stained amniotic fluid is 8-10% of all deliveries (Gregory *et al.* 1974). It was reported as 46% in cases of less than 6 at 1 minute and 19% in cases of less than 6 at 5 minutes of Apgar scores. The color of the meconium is very important to assess the time of passage of the meconium in utero. Green-colored meconium indicates a recent passage and yellow-colored meconium indicates an older passage, an ominous sign due to prolonged fetal hypoxia. The quantity (thick or thin) of the meconium is indicative of the severity of meconium-staining amniotic fluid. It is controversial as to whether aspiration of meconium may occur in utero or after birth. But, it is generally accepted that aspiration of meconium may occur at first breathing or at air breathing during resuscitation after birth (Thibeault and Gregory 1986). The mechanisms of respiratory distress in the presence of meconium in the lung are explained as atelectasis due to complete obstruction of the small and large airways by large particles, or emphysema due to partial obstruction of the small and large airways by small particles, or chemical pneumonitis due to bile salts and proteolytic enzymes in the meconium, or bronchoconstriction due to airway irritation (Vidyasagar *et al.* 1975) (Fig. 2). The natural courses of the clinical manifestations are as follows; In mild cases, tachypnea, low PaO₂, and normal pH may be resolved within 48-72 hours of birth. In moderate cases, an insidious, gradual increase of respiratory distress may reach maximum severity at 24 hours after birth and may be resolved within 4-7 days after birth. In severe cases, respiratory failure with CO₂ retention, respiratory and metabolic acidosis, and profound hypoxemia may occur after birth or within the first few hours of life. Mechanical ventilation may be necessary due to respiratory failure and clinical symptoms and signs, with hyperinflation of the chest (barrel shape), rales or rhonchi on auscultation of the lungs, marked cyanosis or pallor, and increased inspiratory efforts. Discrepancy of clinical features may occur due to failure to assess the accurate time and quantity of meconium passed. If there is a sudden deterioration of the infant's condition, tension pneumothorax or

PPHN (persistent pulmonary hypertension of newborn) may be considered (Thibeault and Gregory 1986).

Finally, primary asphyxia and severe hypoxemia secondary to pulmonary insufficiency resulting from meconium aspiration may induce non-pulmonary problems (renal failure, NEC, DIC, myocardial dysfunction, PPHN, and hypoxic-ischemic encephalopathy, etc). In this patient, there were most of the above-mentioned pulmonary and non-pulmonary problems, which did not respond to any treatment (mechanical ventilation, tolazoline, and cardiac massage). The reasons for the rapid deterioration of this patient were suspected to be due to severe perinatal asphyxia, PPHN, and inadequate initial intensive care. Eventually, he died of respiratory failure, gastric bleeding, and intracranial hemorrhage.

Clinical Diagnosis:

1. Full-term newborn infant with AGA and vacuum extraction
2. Perinatal asphyxia and subsequent events
 - Pulmonary; Meconium aspiration pneumonia
r/o Secondary bacterial overgrowth
 - Non-pulmonary: Hypoxic-ischemic encephalopathy
ATN and ARF
r/o NEC
r/o Myocardial dysfunction
DIC
3. r/o Sepsis
4. Respiratory failure
5. PPHN
 - PDA &/or PFO
6. Gastric bleeding
 - due to r/o NEC or r/o stress ulcer
7. ICH (intracranial hemorrhage)
 - r/o SAH or intracerebral hemorrhage
8. Large caput succedaneum or cephalhematoma
9. Acid-base derangement
 - metabolic and respiratory acidosis

Pathologic Findings

Dr. Chi: At postmortem examination this baby weighed 3440 gm. The crown heel length was 52 cm. There was a large cephalhematoma in the vertex. A small melanocytic nevus was seen in the



Fig. 3. A lung section shows a bronchiole filled with squames and meconium. H&E X100.

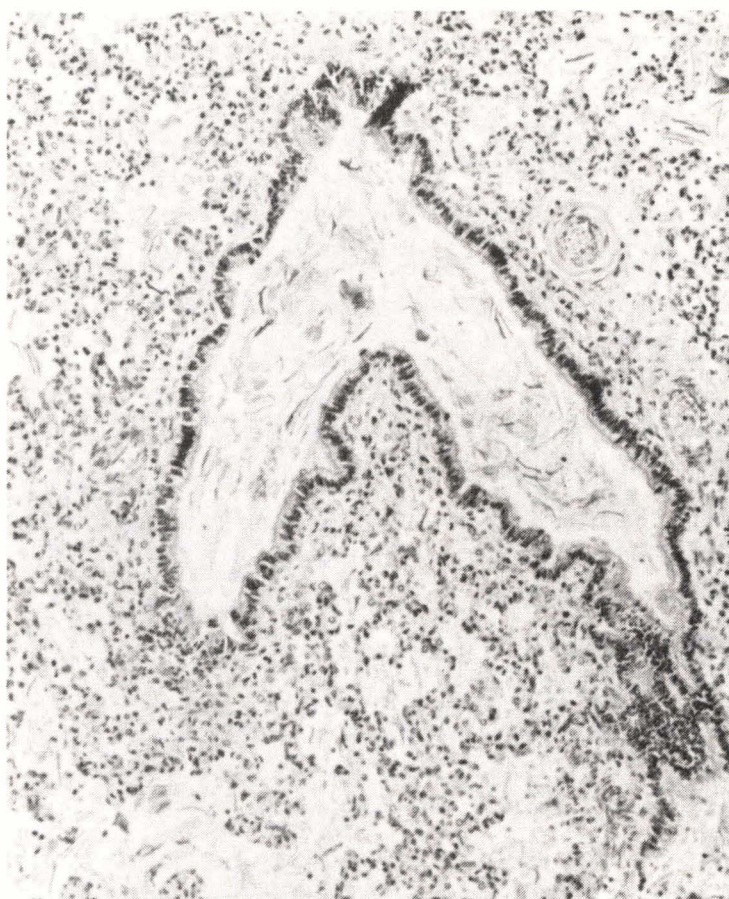


Fig. 4. The alveoli of the lung are distended with aspirated amniotic material and meconium. H&E X250

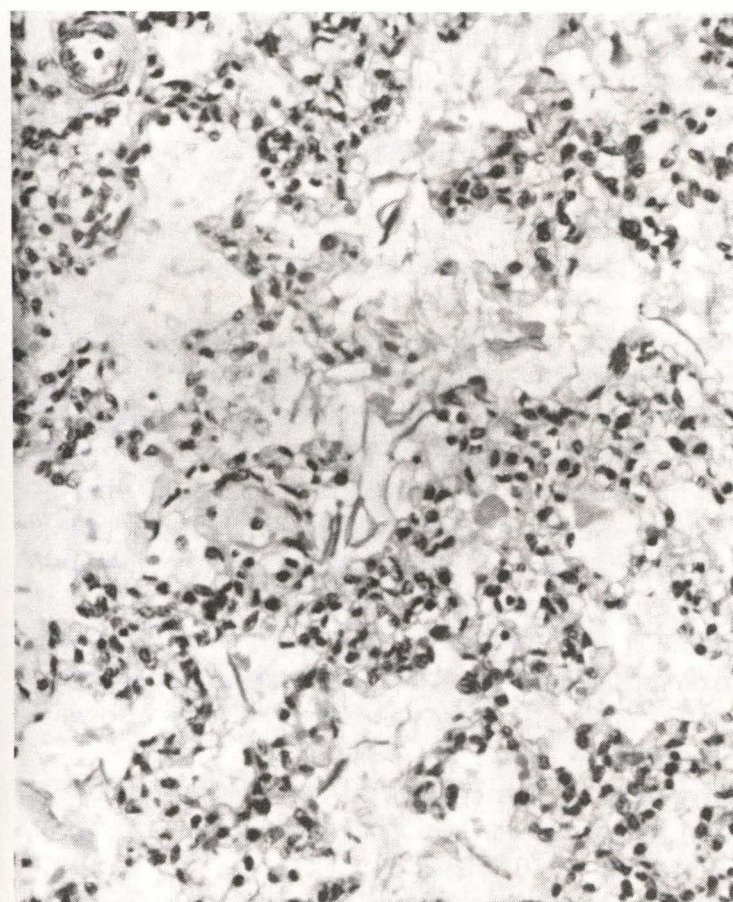


Fig. 5. Microscopic view of the lung, showing massive aspiration of squames and meconium in the alveoli. H&E X100.

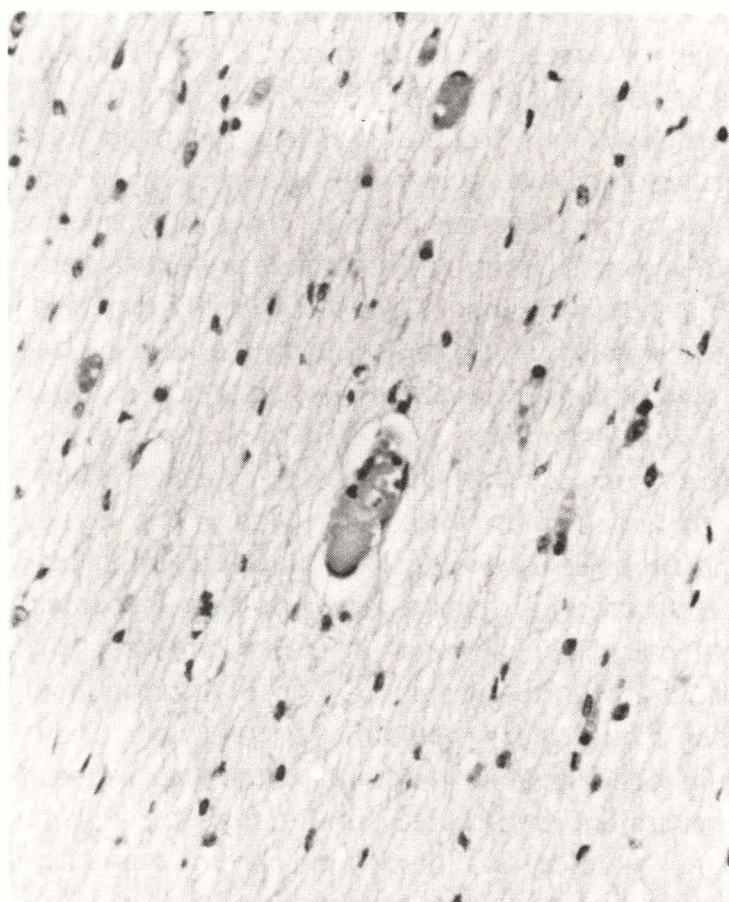


Fig. 6. A brain section shows fibrin thrombus in a small vessel. H&E X100

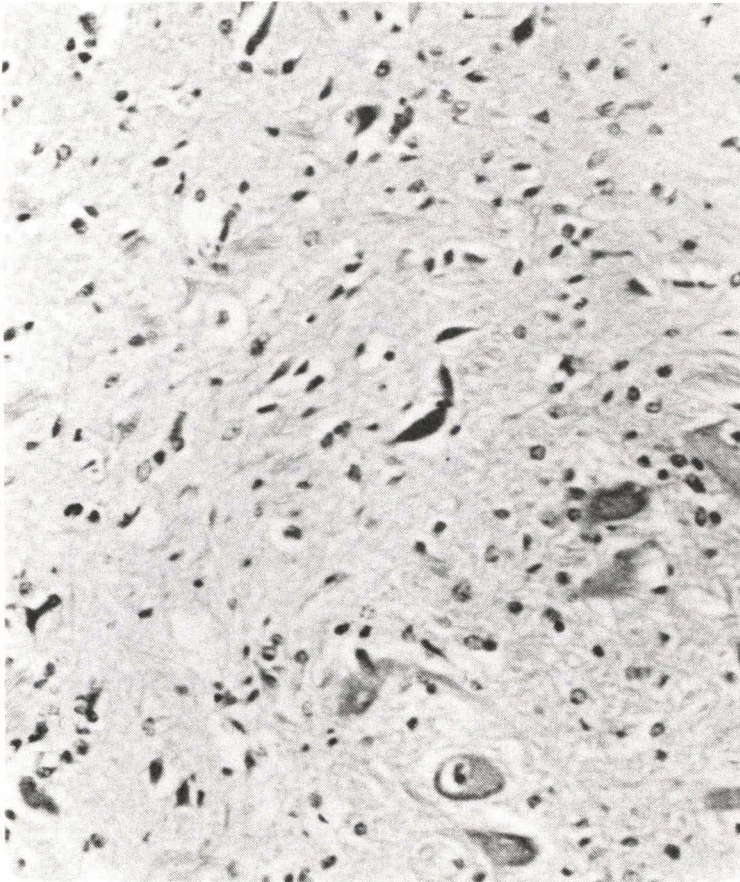


Fig. 7. A spinal cord section shows pyknotic neurons in the anterior horn. H&E X250

face below the right ear. Externally no petechiae or jaundice was noted. The heart (20.7 gm) showed patent ductus arteriosus, 1.5×0.5 cm but the foramen ovale was closed. The lungs weighed 54.4 gm together and showed diffuse consolidation with focal emphysematous change in the right middle lobe. Multiple hemorrhagic patches were also seen on the pleural surface. The trachea and bronchial trees were largely patent but partly filled with green-brown material. Cut sections of the lungs showed no focal lesion other than focal fresh hemorrhage. Microscopically the lung showed massive meconium and amniotic material stuffed in the alveoli and bronchioles (Fig. 3, 4, 5). However, no inflammatory cells were associated with these aspirated materials. The aspiration of meconium was fairly diffuse throughout the entire lung. In addition focal fresh intra-alveolar hemorrhage was seen. There were occasional fibrin thrombi in the lung vessels. Postmortem lung culture grew *Klebsiella pneumoniae*. The abdominal organs did not show any significant gross findings except for scattered petechiae in the gastrointestinal tract mucosa, kidneys, testes and adrenals. Microscopically, these hemor-

rhages were fresh and interstitial, with frequent fibrin platelet thrombi in the small vessels in the kidneys and bowels. The fibrin thrombi were also seen in the thymus and brain (Fig. 6). The adrenal showed fresh hemorrhage in the cortex. The brain (427 gm) showed features of hypoxic-ischemic encephalopathy. The cerebral cortical neurons, Purkinje cells and anterior horn cells of the spinal cord showed nuclear pyknosis (Fig. 7) and diffuse white matter damage. However, germinal matrix hemorrhage was not noted. There was subarachnoid hemorrhage in both temporal tips. The ventricular system was unremarkable.

Pathological Diagnosis:

1. Massive meconium and amniotic material aspiration.
2. Persistent fetal circulation
 - patent ductus arteriosus
3. Disseminated intravascular coagulation due probably to *Klebsiella* sepsis
 - scattered fibrin thrombi.
 - diffuse gastrointestinal hemorrhage.
 - multiple petechiae, viscera.
 - adrenal cortical hemorrhage.
4. Hypoxic ischemic encephalopathy.

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