

Localized Intestinal Perforation

(Clinico-Pathologic Conference)

- SNUH CPC 94-3 -

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CASE HISTORY

This newborn baby was transferred to Neonatal Intensive Care Unit from Delivery floor at 11:45 am December 30, 1993. She was born as a second baby of identical twins to a 26 years old primigravid mother after 31 weeks of gestation.

The mother was admitted on December 28, 1993 because of preterm labor pain. Her pregnancy course was uneventful except for the fact that she had taken medicine for hyperthyroidism until the third month of pregnancy. After admission she was placed on Dexamethasone and delivery was induced by Yutopar infusion.

The birth weight was 1450 gm. The first baby weighted 1200 gm. The initial crying was delayed. Her Apgar score was 5 at 1 minute. After oxygen mask Apgar score at 5 minute was 8. She had frequent spells of apnea and bradycardia. Physical examination revealed heart rate of 143 per minute, respiratory rate of 55 per minute and body temperature 36.5°C. The head circumference was 25.5 cm. General appearance was fair. There was no acute respiratory distress or cyanosis. The anterior fontanel was isotensive and no facial dysmorphism was noted. The chest showed symmetrical expansion without re-

traction. Breathing sound was clear and heart beat was regular without murmur. The abdomen was soft, and bowel sound was inactive. The liver and spleen were not palpable. Multiple bruise was noted on both sole. Moro reflex was not definite.

On the day of admission (1st day, December 30, 1993), she had a mild abdominal distension without signs of respiratory distress. However, at night she developed apneic spells, for which aminophylline was given. She was on oxygen hood (FiO₂ 0.3) and placed on ampicillin and gentamicin.

On the second day (December 31, 1993) early in the morning spells of apnea and cyanosis increased approximately 5 times per hour. She also developed pitting edema on both feet, for which diuretics and dopamine were administered. She was intubated in the afternoon based of arterial blood gas analysis. Her urine output was 7.6 cc/kg/hr.

On the third day (January 1, 1994) the bilirubin level rose to 6.0 mg/dl. The meconium was passed after glycerin enema. In the afternoon cardiac murmur and increased pulse pressure were noted. And pitting edema extended generally. Pontal was prescribed for suspicious patent ductus arteriosus.

On the fourth day (January 2, 1994) chest X-ray showed stomach dilatation and no visualization of intestinal gas. The heart rate increased to 190 per minute and urine volume decreased to 1.4 cc/kg/hr. The respirator setting was switch-

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ed to CPAP.

On the fifth day (January 3, 1994) early in the morning a rapid decrease of oxygen saturation to 60% and blood gas analysis showed a marked abnormality. The urine volume became consistently smaller. Then generalized tonic clonic seizure developed, together with severe abdominal distention. Echocardiography showed atrial septal defect of bidirectional shunt, patent ductus arteriosus and pulmonary hypertension. Brain sonography showed increased periventricular echogenicity, germinal matrix hemorrhage and intraventricular density. Abnormal ABGA and electrolyte abnormalities (hyperkalemia and hypoglycemia) did not improve. She remained unresponsive despite tolazolin and biven infusion. After a period of bradycardia she expired

at 4:00 pm on the same day.

DISCUSSION

Dr. Kim : This case record describes a premature infant who presented initially with recurrent apnea, which had not been reponded with supportive care. During hospital course, patent ductus arteriosus was suspected and then generalized tonic clonic seizure developed, together with severe abdominal distension. After then acute renal failure, persistent fetal circulation and periventricular-intraventricular hemorrhage were complicated. Ultimately she expired with intractable hypoxia and acidosis. Her last complete blood count revealed that hemoglobin was 4.8 g/dl, hematocrit 14.5%, white cell count 5,

Table 1. Laboratory date according to clinical progression

Hematology											
Date	Hb	Hct	WBC	Plt	myel	meta	band	seg	lymp	mo	normoblast
12/30	14.6	42.3	5,950	247,000				70	26	4	9
1/3	4.8	14.5	5,380	40,000	1	3	9	54	21	12	
Blood chemistry											
Date	Ca /P	Glu	Chol /Prt /Alb	T-Bill	SAP /OT /PT	BUN /Cr	Electrolyte				
12/30	11.21/	49				2/0.5	132/4.3/113/17				
12/31		55(BST)				16/1.2	1136/5.0/115/16				
1/1		109(BST)		6.0		27/1.2	136/4.6/111/17				
1/2		80		4.8		30/1.4	135/5.6/110/15				
1/3	7.8/9.6	8	32/3.8/2.3	5.2	366/29/5	47/1.9	142/7.6/116/ 9				
Blood gas analysis											
Date	pH	PCO ₂	PO ₂	HCO ₃ ⁻	Ventilator care						
12/30	7.27	37	91	17	O ₂ via hood with 3L/min						
12/31	7.34	29	120	15							
	7.39	19	118	11	FiO ₂ 0.4 Frq 5/m PIP/PEEP 15/3cm ₂ O I _T 0.31sec.						
	7.36	33	87	15	CPAP apnea subsided						
1/1	7.28	31	64	14	FiO ₂ 0.25 Frq 5/m PIP/PEEP 15/3cm ₂ O I _T 0.30sec						
	7.40	29	89	18	"						
1/2	7.36	27	131	15	"						
	7.29	31	111	14	CPAP						
1/3	4am	7.09	31	59	9	FiO ₂ 0.3 Frq 10/m PIP/PEEP 15/3cm ₂ O I _T 0.30sec					
	MD	6.84	47	25	8	FiO ₂ 1.0 Frq 110/m PIP/PEEP 20/4cm ₂ O I _T 0.24sec					
	2pm	7.04	18	41	5	FiO ₂ 1.0 Frq 90/m PIP/PEEP 37/4cm ₂ O I _T 0.29sec					

380/mm³ with marked shift to left and platelet count was 40,000/mm³. Blood glucose was 8 mg/dl (Table 1).

May we review the x-ray films at this time ?

The film of chest taken on admission was normal. The abdominal film which taken on the fourth hospital day demonstrated stomach dilatation and no visualization of intestinal gas. In view of the history and this constellation of findings I think that there was a paralytic ileus. It could be caused by sepsis, hypokalemia and peritonitis.

The doctors caring for this patient initially faced with a premature infant in multiple episodes of apnea. Apnea was intractable with supportive care and aggravated progressively. There are a number of causes which induce apnea. Infection, intracranial pathology, drugs, gastroesophageal reflux, thermal instability, impaired oxygenation, metabolic disorders and prematurity itself should be considered (Marchal et al. 1987). Usually the apnea is most often associated with prematurity itself, but the diagnosis should be made by exclusion of other causes. In this case, she was a premature baby with moderate birth asphyxia and initial white cell count was 5,950/mm³ (corrected count was less than 5,000/mm³), so sepsis must be considered. Intracranial pathology such as intraventricular-periventricular hemorrhage might be considered, but at that time there was no definite symptoms and signs of intracranial pathology. Other causes could be ruled out by clinical and laboratory findings.

Cardiac murmur, increased pulse pressure and generalized edema were noted on the third hospital day. Under the impression of patent ductus arteriosus, pontal (mefenamic acid) was prescribed. The most common cause of above findings in the premature baby is patent ductus arteriosus. In order to rule out shunt dependent cardiac lesions, echocardiography should be done. But unfortunately echocardiography couldn't be available at that time. Initially ductal shunt might be mainly left to right and there was no evidence of persistent fetal circulation. But at the end of hospital course, severe hypoxemia was noted in spite of maximum ventilatory support. Echocardiography showed atrial septal de-

fect of bidirectional shunt, patent ductus arteriosus and pulmonary hypertension. Above findings are compatible with persistent fetal circulation. The main pathophysiology of persistent fetal circulation is known as pulmonary hypertension in the presence of patent ductus arteriosus. Hypoxia, acidosis and myocardial dysfunction can increase pulmonary arterial pressure. On the 5th hospital day, CBC profile revealed leukopenia with bandemia and severe thrombocytopenia. Blood sugar showed marked hypoglycemia. Clearly there was definite sepsis, which may result in pulmonary hypertension and decreased systemic blood pressure. I think that persistent fetal circulation was caused by fulminant sepsis.

X-ray showed stomach dilatation and no visualization of intestinal gas on the fourth hospital day. Severe abdominal distention was followed. The most striking finding of this case are no visualization of intestinal gas and severe abdominal distention. The differential diagnosis of abdominal distention in the neonate includes organomegaly, mass, gaseous distention and fluid accumulation. Organomegaly and mass could be ruled out by time onset and physical examination. Gaseous distention could be ruled out by radiographic findings. In this case intraabdominal fluid accumulation must be considered. Diagnostic workup for ascites should be done such as ultrasonograph or paracentesis. Ultrasonography may demonstrate fluid and sometimes intraabdominal abnormalities. Paracentesis may demonstrate sanguinopurulent or dark brown fluid accumulation of the progressive necrotizing enterocolitis because bowel rupture of any size may produce a significant amount of fluid in the absence of a telltale amount of free peritoneal air. Dark brown fluid may also accumulate from gangrenous unperforated bowel also (Korones and Bada-Ellzey 1993). If there were no visualization of intestinal gas and severe abdominal distention, paracentesis should be considered and it would be very helpful for diagnosis and management.

Recently isolated spontaneous rupture at any level of the GI tract has been reported repeatedly in association with oral and intravenous ad-

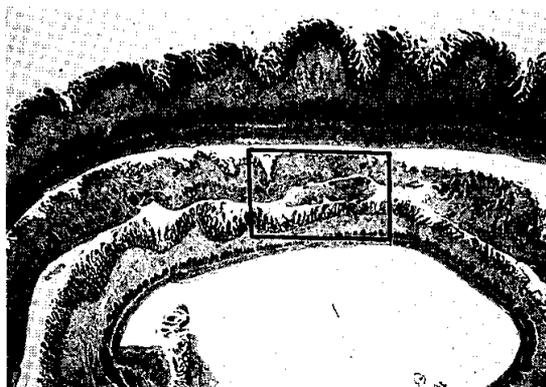


Fig. 1. Photomicrograph of small bowel, showing granular thinning of intestinal wall together with chronic and acute inflammation. H & E



Fig. 2. Higher magnification of inset in Fig. 1, Showing extreme thinning, impending perforation, fibrin exudation and inflammation.

ministration of indomethacin, which was given for closure of a patent ductus arteriosus (Aschner et al. 1988, Buchheit and Stewart 1994, Wolf et al. 1989). Even though mefenamic acid, which had been used in this case is not same as indomethacin, pharmacological property and its side effects would be very similar with indomethacin. The most important pathophysiology of necrotizing enterocolitis is known as a decreased mesenteric blood flow. In this case patent ductus arteriosus, repeated episodes of hypoxia due to apnea and the use of mefenamic acid could reduce the mesenteric blood flow. So no visualization of intestinal gas and severe abdominal distention in this case lead me consider the possibility of an intestinal perforation due to necrotizing enterocolitis or isolated spontaneous rupture. Although necrotizing enterocolitis was reported rarely in infants who have never been enterally fed (Marchildon et al. 1982), enteral feeding is known to be a significant risk factor for necrotizing enterocolitis. So I think that localized or isolated intestinal perforation is the more preferable diagnosis.

On last hospital day, generalized tonic clonic seizure was noted. Brain sonography showed periventricular-intraventricular hemorrhage.

CLINICAL DIAGNOSIS (Dr. Kim)

1. Sepsis
2. Localized intestinal perforation > Necrotizing enterocolitis
3. Patent ductus arteriosus, Atrial septal defect - persistent fetal circulation
4. Intraventricular hemorrhage and periventricular leukomalacia
5. Acute renal failure

PATHOLOGICAL FINDINGS

Dr. Chi : At autopsy icteric baby showed irregular hardening of entire subcutaneous fat in the trunk and extremities. The abdominal cavity was the site of acute fibrinopurulent peritonitis with dusky discoloration and adhesion of bowel loops. There was a well defined perforation in the ileum 13cm from the ileocecal valve. There were fibrinopurulent exudate near the perforation, that extended throughout the abdominal cavity. The bowel loops were adherent but not distended. The mucosa of the small and large bowels showed flattening and scattered shallow ulcers. Microscopically there a mild acute and chronic inflammatory cell infiltration in the

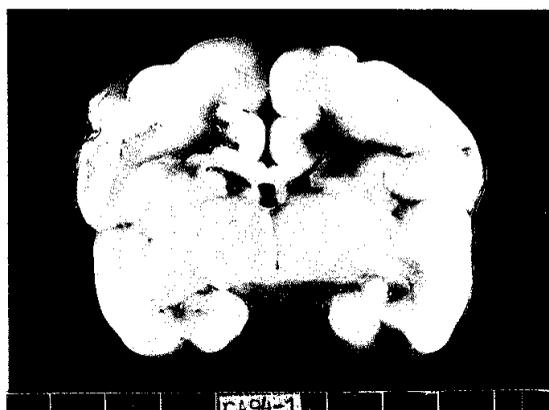


Fig. 3. Coronal section of the brain, showing characteristic yellow discoloration involving nuclear groups.

propria and submucosa. There was an area of extreme thinning and transmural inflammation (Fig. 1 & Fig. 2). The stomach and esophagus showed petechiae in mucosa. The chest organs were unremarkable except for atrial septal defect of ostium secundum type and focal bronchopneumonia. The heart showed ischemic change in the myocardium. The brain showed kernicterus involving dentate nucleus, hippocampus, olivary nucleus and thalamus (Fig. 3). There was a massive neuronal death in cerebral gray matter and spinal cord anterior horn cells. Periventricular leukomalacia was also present, together with bilateral germinal matrix hemorrhage.

PATHOLOGICAL DIAGNOSIS

1. Localized intestinal perforation (perforation

site: 13 cm proximal to ileocecal valve)

2. Acute fibrinopurulent peritonitis
3. Sepsis
4. Kernicterus
5. Periventricular leukomalacia and intraventricular hemorrhage
6. Sclerema neonatorum
7. Focal bronchopneumonia
8. Atrial septal defect, ostium secundum type
9. Patent ductus arteriosus

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