

FDA - Adverse Event Reporting System (AERS)

ISR Information Report for ISR #4174386-X

ISR Information:

ISR #: 4174386-X
Case #: 3949654
ISR Type: Expedited (15-Day)
FDA Revd. Date: 08/27/2003
Outcome(s): DE,HO

Best Rep. ISR: Yes
eSub ISR: Yes

Initial or Follow-up ISR: Follow-up
Verbatim Follow-up #:

Manufacturer Information:

Sender Mfr.: NOVARTIS PHARMACEUTICALS CORP.
Mfr. Control #: PHEH2003US03656
Mfr. Rcvd. Date: 05/01/2003
Primary Suspect (A)NDA/PLA #:

Patient Information:

Patient ID:
Age:
DoB:
Gender: Female
Weight: 2 Kilogram
Event Start Date: 05/01/2003

Reporter Information:

Reporter Name:
Reporter Org.:
Reporter Street:
Reporter Zip:
Reporter Phone:
Reporter City:
Health Prof.: YES **Occupation:** PHYSICIAN
Reporter State:
Reporter Country: UNITED STATES

Reporter Name:
Reporter Org.:
Reporter Street:
Reporter Zip:
Reporter Phone:
Reporter City:
Health Prof.: YES **Occupation:** PHARMACIST
Reporter State:
Reporter Country: UNITED STATES

Product(s)	Role	Dosage Text	Route	Lot #	Indication(s)	Therapy Start Date	Therapy End Date	Interval 1st Dose to Event:	DeC	ReC
SANDOSTATIN	P	8 ug/kg, QH	INTRAVENOUS		CHYLOTHORAX		05/02/2003			
SANDOSTATIN	S	4 ug/kg, UNK				04/25/2003				
HYDROCORTISONE	C	1 mg/kg, TID	INTRAVENOUS			04/21/2003	05/02/2003			
LASIX	C	1 mg/kg, BID	INTRAVENOUS			04/29/2003	05/02/2003			
VERSED	C	UNK, UNK				04/20/2003	05/02/2003			
MORPHINE	C	UNK, PRN								
MULTI-VITAMINS	C									

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Reaction(s)

ReC

- ABDOMINAL DISTENSION
- ADRENAL INSUFFICIENCY
- ATRIAL THROMBOSIS
- CALCINOSIS
- CEREBRAL THROMBOSIS
- CLOSTRIDIUM COLITIS
- GASTRIC MUCOSAL LESION
- GASTROINTESTINAL MUCOSAL NECROSIS
- HEPATIC NECROSIS
- HISTIOCYTOSIS HAEMATOPHAGIC
- HYPERKALAEMIA
- HYPOALBUMINAEMIA
- HYPONATRAEMIA
- HYPOTENSION
- LETHARGY
- LIVER DISORDER
- LUNG DISORDER
- PNEUMATOSIS INTESTINALIS
- RENAL FAILURE
- RENAL TUBULAR NECROSIS
- RESPIRATORY FAILURE
- STAPHYLOCOCCAL SEPSIS
- STRESS

Relevant Laboratory Data: [redacted] echocardiogram showed thrombus in right atrium. [redacted] Chest x-ray and Kidney/ureter/bladder (KUB): portal air [redacted]
 Echocardiogram: Atrial thrombus [redacted] ultrasound examination: history of heterogenous appearance of liver and decreased artery flow Autopsy report: Final pathologic diagnosis:
 1. Transposition of the great arteries: Status post arterial switch procedure on day [redacted] of life, all anastomoses intact, no evidence of thrombi in cardiac chambers, inferior vena cava, pulmonary
 arteries or aorta, bilateral chylothorax 2. Extensive necrosis and calcification of liver, anterior subcapsular region of right and left lobes, history of heterogeneous appearance of liver on
 ultrasound examination on [redacted] 3. Clinical diagnosis of necrotizing enterocolitis: mucosal necrosis, small and large bowel with pneumatosis coli and luminal distention, no evidence of
 perforation 4. Acute renal tubular necrosis 5. Diffuse alveolar d

Test Date	Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail Y/N
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Relevant Medical History

Disease/Surgical Procedure	Start Date	End Date	Continuing	Comment
CHYLOTHORAX	04/01/2003		YES	Developed subsequent to cardiac repair on [redacted]

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Disease/Surgical Procedure	Start Date	End Date	Continuing	Comment
MULTIPLE SCLEROSIS			YES	
NUTRITIONAL SUPPORT			UNKNOWN	Nutrition - Tolorex
CYANOSIS NOS			UNKNOWN	at birth
EXTRASYSTOLES NOS			UNKNOWN	junctional ectopic tachycardia - after cardiac surgery
BRADYCARDIA NOS			UNKNOWN	one episode - after cardiac surgery
CATHETER PLACEMENT			UNKNOWN	right intrajugular
NEONATAL RESPIRATORY DISTRESS SYNDROME			UNKNOWN	Day <input type="text"/> of life
CHEST TUBE INSERTION			UNKNOWN	Day <input type="text"/> of life
WHITE BLOOD CELL COUNT INCREASED			UNKNOWN	postoperative Day <input type="text"/> not treated with antibiotics since there was no other symptoms of infection
INTUBATION NOS			UNKNOWN	
EXTUBATION			UNKNOWN	<input type="text"/> day of life, one day prior to starting Sandostatin
CHOROIDAL HAEMORRHAGE			UNKNOWN	possible choroid plexus hemorrhage noted in head ultrasound on <input type="text"/>
THALAMUS HAEMORRHAGE			UNKNOWN	<input type="text"/> right thalamic hemorrhage noted in head ultrasound <input type="text"/>
CARDIAC OPERATION NOS			UNKNOWN	Transposition of great arteries, status post arterial switch procedure on day <input type="text"/> of life.

Medical History Product(s)	Start Date	End Date	Indication(s)	Reaction(s)
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Event/Problem Narrative

This report combines initial information received from the pharmacist on and with follow-up information received on and . On a one month old infant started treatment with Sandostatin 4 mcg/kg/hr (continuous infusion) for chylothorax, which she developed subsequent to cardiac repair surgery on . Concomitant medications included intravenous hydrocortisone, intravenous Lasix, Versed, Morphine and multivitamins orally. On Sandostatin was discontinued. On echocardiogram revealed thrombus in the right atrium. Vancomycin, Cefepime and Clindamycin were initiated. On Sandostatin was discontinued. On the infant expired. Cause of death was reported as unknown. Follow up received 18 August 2003 from the physician combined with receipt of discharge summary and autopsy report on 22 Aug 2003: The physician reported that the immediate causes of death were respiratory and renal failure. The preliminary autopsy was significant for the following: bilateral chylothorax, extensive necrosis and calcification of the liver, cardiac repair intact and no evidence of thrombosis. The leading events with fatal outcome were atrial thrombus and necrotizing enterocolitis with onset date of . Relevant medical history included multiple sclerosis and Tolorex feeds. The infant's weight was 2.48 kg. Result of a chest x-ray and kidney/ureter/bladder performed on revealed portal air. Sandostatin was administered intravenously from . The initiation dose was 4 mcg/kg which was increased to 8 mcg/kg every hour. The dates and dose for Lasix and hydrocortisone were added as well as the dates for Vancomycin and Versed. The physician considered the necrotizing enterocolitis to be suspected and the atrial thrombus to be not suspected. The discharge summary noted a term, AGA female infant who was admitted on and discharged on . The diagnoses at death included those discussed in the clinical-pathological correlation below with the addition of respiratory failure, relative adrenal insufficiency, hypoalbuminemia secondary to chylothorax, hyponatremia and terminal hyperkalemia, and renal failure. Autopsy report: Final pathologic diagnosis: 1. Transposition of the great arteries: Status post arterial switch procedure on day five of life, all anastomoses intact, no evidence of thrombi in cardiac chambers, inferior vena cava, pulmonary arteries or aorta, bilateral chylothorax 2. Extensive necrosis and calcification of liver, anterior subcapsular region of right and left lobes, history of heterogeneous appearance of liver on ultrasound examination on 3. Clinical diagnosis of necrotizing enterocolitis: mucosal necrosis, small and large bowel with pneumatosis coli and luminal distention, no evidence of perforation 4. Acute renal tubular necrosis 5. Diffuse alveolar damage, healing 6. Gastric mucosal ulceration 7. Hemophagocytosis, bone marrow, recent transfusion Autopsy cultures were essentially negative. Clinicopathologic correlation: This patient was cyanotic at birth and found to have transposition of the great arteries with intact ventricular septum and patent ductus arteriosus. She underwent an arterial switch procedure at days of life. She was difficult to extubate and developed persistent chylous pleural effusions. On day of life coagulase-negative Staphylococcus aureus was cultured from her blood and was treated with antibiotics. On day of life, a head ultrasound demonstrated dilated ventricles, a right lateral ventricular thrombus and a possible right thalamic lesion. She became lethargic on day of life. At days a large right atrial mass interpreted as a thrombus was found on echocardiographic examination. She then deteriorated acutely and developed abdominal distension with dilated, thickened bowel loops and portal vein

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Event/Problem Narrative

gas, diagnosed as necrotizing enterocolitis. Hypotension developed thought to be due to sepsis. Heterogeneity of the liver was found on ultrasound examination, and decreased renal artery flow was detected. Support was withdrawn on day of life. The major findings at autopsy, including necrotizing enterocolitis, acute renal tubular necrosis, diffuse alveolar damage, and hepatic necrosis, were most likely due to the patient's poor cardiac output and recent hypotension. The gastric ulcers are probably related to stress, and the hemophagocytosis is most likely a sequela of recent blood transfusion (the patient received red blood cells one day prior to death). It is not clear why no mass or thrombus was found in the right atrium or lungs. If a thrombus accounted for the mass, then it may have resolved spontaneously or responded to low molecular weight heparin therapy.

Study Report?: No

Study Name:

Study Type:

Sponsor Study #:

Protocol #:

IND #:

Literature Text:

DISCHARGE SUMMARY

DIAGNOSES AT DEATH:

1. Term, AGA female infant 1 month of age.
2. Transposition of the great vessels status post arterial switch procedure.
3. Bilateral chylothoraces.
4. Respiratory failure.
5. Staph sepsis, treated.
6. Relative adrenal insufficiency, treated.
7. Hypotension.
8. Right atrial mass.
9. Hypoalbuminemia secondary to chylothorax.
10. Hyponatremia and terminal hyperkalemia.
11. Probable necrotizing enterocolitis with portal air, resolving.
12. Renal failure.
13. Thalamic and choroid plexus hemorrhages.

ADMITTING HISTORY AND PHYSICAL: Baby Girl [redacted] was a 2635 gm product of an approximately 38-week gestation who was born at 1639 on [redacted] Hospital. Her mother is a [redacted]-year-old Gravida 1, para 0, now 1 woman. Her blood type was A negative. She was VDRL negative, hepatitis B negative, and group B strep negative. She was rubella immune. Pregnancy reportedly was uncomplicated. Labor was induced, and there was artificial rupture of membranes approximately three hours prior to delivery. Fluid reportedly was clear. The mother did receive an epidural anesthesia. Fetal heart rate monitoring was performed and was within normal limits. A spontaneous vaginal delivery ensued, and this infant received blow-by oxygen in the delivery room. She was then allowed to transition with her mother when at approximately 3-1/2 hours of age, she was noted to be dusky. She was brought to the nursery, and an oximeter was placed. Her oxygen saturations were in the 70s in room air. She was then placed in hood oxygen, and an arterial blood gas was done, which showed a pH of 7.30, pCO₂ of 22, pO₂ of 39 and base deficit of -15. At that point, a normal saline bolus was administered and prostaglandin was initiated at 0.05 mcg/kg/min when the transport team arrived. The infant was transferred on the prostaglandin as well as 100% FiO₂. She did have one episode of apnea during transport; therefore, she was intubated with a 3.0 ET tube, the third attempt. There was some decrease in heart rate with this procedure, but the infant responded well with bag mask ventilation. Also, the infant had umbilical artery, umbilical venous catheters placed upon her arrival in the [redacted]

DISCHARGE SUMMARY - Page 2 of 6

ADMITTING PHYSICAL EXAMINATION: An AGA, term female infant. **VITAL SIGNS:** Weight of 2700 gm. Head circumference 32.5, length 46 cm, temperature 36.4, pulse 148, respiratory rate 68, blood pressure 55/30 with a mean arterial pressure of 39. Physical examination was remarkable for the infant being intubated and on mechanical ventilatory support. **CARDIOVASCULAR:** Regular rate and rhythm without murmur. **ABDOMEN:** Soft without organomegaly. Femoral pulses were good. **NEUROLOGIC:** Normal tone and reflexes. **EXTREMITIES:** Within normal limits as was the H&T examination.

HOSPITAL COURSE BY SYSTEMS:

1. **Cardiorespiratory:** This infant was continuing on her prostaglandin in the intensive care nursery, and close monitoring of blood gases were obtained to assure the absence of acidosis. The infant was taken to surgery on the []th day of life, and an arterial switch procedure was performed by Dr. Lupinetti. The infant was on bypass for 126 minutes and was cross clamped for 49 minutes. The infant was recovered in the pediatric intensive care unit. There, she had junctional ectopic tachycardia as well as one episode of bradycardia. She was treated with epinephrine drip for 48 hours as well as a dopamine drip for 96 hours. She also required 24 hours of milrinone and approximately 48 hours of amiodarone infusions. She also was given calcium gluconate and Lasix drips for the first several days postoperatively. She received fentanyl anesthesia and also perioperative antibiotics. She had placement of a right intrajugular catheter. The infant did have closure of her chest wound on the third day postop. Attempted extubation was made. This was unsuccessful, and also on day # [] an attempt was unsuccessful. However, the following day, the infant was successfully extubated after brief course of dexamethasone. The infant did relatively well extubated but had increasing respiratory distress and significant chylothorax was noted; and, therefore, a right-sided chest tube was placed, which did have significant amount of drainage. The infant was switched from breast milk to Portagen and continued on Portagen feedings to attempt to diminish chest tube output. However, this was not successful, and the infant had attempt at increasing her feeds to make up for chest tube losses as all of her central lines and IV's had been discontinued making intravenous fluid administration less than desirable. Of note, the infant did have an increase in her white blood cell count on postoperative day # [] but apparently had no other symptoms of infection and, therefore, was not begun on antibiotic therapy. It was at that point that the infant was transferred back from the PICU to the intensive care nursery for further care. While the infant initially was transferred in

DISCHARGE SUMMARY - Page 3 of 6

room air, she did develop increased respiratory distress requiring oxygen supplementation and eventual reintubation. Repeat blood cultures at that time did reveal staph sepsis, and the infant was begun on Vancomycin with a good response. The infant was extubated successfully on the []th day of life, [] and had two subsequent days of nasal prong oxygen. She was then in room air until [] when, again, she developed increasing respiratory distress requiring intubation and ventilatory support despite the fact her chylothoraces were diminished. The chylothoraces had been treated with vigorous fluid replacement therapy with albumin and FFP as well as normal saline. Also, the infant was fed Tolcrex for its low fat content, and on April 25, she was begun on octreotide for treatment of the chylothoraces. This continuous drip was increased to a maximum dose of 8 mcg/kg/hr on two days prior to her death. This was achieved. On the day prior to her death, with evidence of necrotizing enterocolitis, the octreotide was discontinued as were her feedings. The infant's significant deterioration on [] was not clearly explained by worsening pulmonary function or definite infection; therefore, a cardiac echo was obtained to evaluate cardiac functioning. Quite surprisingly, there appeared to be a 9 mm by 4 mm mass in the right atrium that was mobile but attached. The infant had fairly good cardiac function at this point but did need dopamine for her blood pressure maintenance. Of note, the infant had continued on the hydrocortisone that had been initiated during her initial staph sepsis at replacement doses for hypotension, and she did respond well to this, and it has been weaned but had been close to discontinuation. The day prior to [] death, she had increasing abdominal distension secondary to probable necrotizing enterocolitis and pneumatosis as well as portal error was visualized on abdominal x-rays. Therefore, she was not a candidate for surgical intervention, but her increasing abdominal distension did continue to compromise her respiratory, renal and cardiac functioning. She was begun on high frequency jet ventilation as well as pressor support with dopamine and epinephrine. She also developed arrhythmias associated with hyperkalemia and, therefore, was begun on a sodium bicarbonate and insulin drip. She received multiple volume boluses as well. Despite this aggressive resuscitation, she continued to be hypotensive, acidotic, and a discussion was held with her parents, and she was made a DNR status with continuation of other aggressive support. Through that night, the infant continued to deteriorate, and the parents gradually requested discontinuation of the infant's intravenous drip medications. We complied with this, and when the infant's heart rate was in the 30s-40s, at approximately 7:00 a.m., I extubated the infant, and the family continued to

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hold the infant for the remainder of her life. I auscultated her chest at 0818 and heard no heart rate pronouncing her dead at that time. The parents did request an autopsy.

2. **Infectious disease:** This infant was initially begun on ampicillin and gentamicin pending culture results. Cultures were negative, and these antibiotics were discontinued at 72 hours. Perioperatively, the infant also received cefuroxime for four days. On [REDACTED], the infant showed evidence of sepsis with elevated white blood cell count, temperature and increased respiratory distress. A blood culture at that time revealed coag negative staph, and the infant was begun on Vancomycin and cefotaxime. The infant completed a full seven-day course of Vancomycin treatment. She also, during that episode of sepsis, required hydrocortisone for blood pressure stability in addition to multiple volume boluses. The day prior to death, [REDACTED] was again begun on antibiotics therapy secondary to necrotizing enterocolitis. Vancomycin, cefepime, and clindamycin were all initiated early on [REDACTED]. These medications were continued until her death. Cultured drawn from this point, however, remained negative.
3. **Hematology, hyperbilirubinemia:** This infant's blood type was A negative. Her Coombs was negative as well. She did receive multiple transfusions and her most recent hematocrit was 53.4 post transfusions. The infant also did develop the clotting disorder noted above with her thrombosis in her right atrium, and on her last day of life, she also had evidence of clots and low blood flow in her renal and liver vessels. She was initiated on Lovenox when her atrial clot was discovered, and [REDACTED] did assist in the management of this. This anticoagulant was discontinued when the infant developed necrotizing enterocolitis and upper intestinal bleeding.
4. This infant did have a head ultrasound obtained shortly after her return to the intensive care nursery secondary to a full, somewhat firm fontanelle. This head ultrasound done on [REDACTED] did reveal dilated right, left, and third ventricles with a mildly prominent fourth ventricle. There was also thrombus noted in the right and left ventricles as well as the third ventricle. Possible choroid plexus hemorrhage was seen as well as a right thalamic hemorrhage. There were also abnormal areas of increased linear echogenicity within the left thalamus suggesting pathology there as well. A repeat ultrasound was obtained and showed similar findings. Secondary to these findings, and consultation was obtained with [REDACTED] who recommended an EEG. This was nonspecific and the results that the infant did not require anti-convulsant medication. While there was some concern with these intracranial

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hemorrhages and the initiation of Lovenox, the risk factors were weighed carefully by the parents, me, [REDACTED], and it was agreed that we should progress with the therapy as the hemorrhages were somewhat old and, hopefully, established. No ultrasound was obtained after the Lovenox was discontinued, however. This infant was kept comfortable during her hospital course with fentanyl, morphine, Ativan, and versed.

5. As noted above, the infant did have umbilical venous and arterial catheters placed, and both were discontinued in the pediatric intensive care unit as was a right jugular line. The infant also had a percutaneous central venous catheter placed, which was in place at the time of death. The infant was treated with total parental nutrition when she was unable to tolerate feedings, and this had maximum concentrations of 14% dextrose, 2% amino acids, and 2% intralipids because it was primarily peripherally administered. The infant also received multiple albumin boluses for her hypoalbuminemia as well as normal saline boluses for her hyponatremia. On her last day of life, she did require therapy as well for hyperkalemia secondary to her anuria. With her renal failure, a nephrology consultation was obtained with the nephrologist, [REDACTED]. He felt that this infant was not a candidate for peritoneal or hemodialysis and that our current therapies were all appropriate. This infant did receive feeds primary by OG tube but occasionally she nipped small amounts of breast milk. She received Portagen initially in the PICU but then was switched to Tolerex. She did appear to tolerate this nutrition until there was an acute deterioration on the day prior to admission with an acute abdominal distension and tenderness, and x-rays showed florid portal air as well as pneumatosis, and the infant had bloody stools. The diagnosis of necrotizing enterocolitis was made, and feedings were discontinued and antibiotics initiated. Despite this, the infant continued to have gastrointestinal bleeding and pulmonary renal and cardiac deterioration with her eventual death on the morning on [REDACTED].

Autopsy results are pending at this time.





DISCHARGE SUMMARY - Page 6 of 6



AUTOPSY REPORT

Patient Name:
Med. Rec. #:
DOB:
Gender: F
Soc. Sec. #:
Physician(s):

Client:
Location: NICT
Service:
Billing #:
Copy To:

Accession #:
Expiration Date:
Autopsy Date: 5/5/03
Reported: 7/30/03

Post Mortem Hours: 48

Authorized By:

Relationship to

Reason for Autopsy: Requested by Family

Autopsy Restrictions: Exclude brain

Final Pathologic Diagnosis

- I. TRANSPOSITION OF THE GREAT ARTERIES
 - A. STATUS POST ARTERIAL SWITCH PROCEDURE ON DAY OF LIFE
 - B. ALL ANASTOMOSES INTACT
 - C. NO EVIDENCE OF THROMBI IN CARDIAC CHAMBERS, INFERIOR VENA CAVA, PULMONARY ARTERIES OR AORTA
 - D. BILATERAL CHYLOTHORAX
- II. EXTENSIVE NECROSIS AND CALCIFICATION OF LIVER, ANTERIOR SUBCAPSULAR REGION OF RIGHT AND LEFT LOBES
 - A. HISTORY OF HETEROGENEOUS APPEARANCE OF LIVER ON ULTRASOUND EXAMINATION,
- III. CLINICAL DIAGNOSIS OF NECROTIZING ENTEROCOLITIS
 - A. MUCOSAL NECROSIS, SMALL AND LARGE BOWEL, WITH PNEUMATOSIS COLI AND LUMINAL DISTENTION
 - B. NO EVIDENCE OF PERFORATION
- IV. ACUTE RENAL TUBULAR NECROSIS
- V. DIFFUSE ALVEOLAR DAMAGE, HEALING
- VI. GASTRIC MUCOSAL ULCERATION
- VII. HEMOPHAGOCYTOSIS, BONE MARROW
 - A. RECENT TRANSFUSION,

Clinicopathologic Correlation

This patient was cyanotic at birth and found to have transposition of the great arteries with intact ventricular septum and patent ductus arteriosus. She underwent an arterial switch procedure at days of life. She was difficult to extubate and developed persistent chylous pleural effusions. On day of life coagulase-negative Staphylococcus aureus was cultured from her blood and was treated with antibiotics. On day of life a head ultrasound demonstrated dilated ventricles, a right lateral ventricular thrombus, and a possible right thalamic lesion. She became lethargic on day of life. At days a large right atrial mass interpreted as a thrombus was found on echocardiographic examination. She then deteriorated acutely and developed abdominal distension with dilated, thickened bowel loops and portal vein gas, diagnosed as necrotizing enterocolitis. Hypotension developed, thought to be due to sepsis, heterogeneity of the liver was found on ultrasound examination, and decreased renal artery flow was detected. Support was withdrawn on day of life.

Autopsy Report

At autopsy, the anastomoses associated with the arterial switch procedure were intact. Bilateral chylothorax was found. However, no thrombi were found in any of the cardiac chambers, inferior vena cava, pulmonary arteries, lungs or aorta. The small and large intestines were distended, and mucosal necrosis and pneumatocele coli were found, without evidence of perforation. The liver was extensively necrotic in a subcapsular pattern. Acute renal tubular necrosis and healing diffuse alveolar damage were found. There were several superficial gastric ulcers, and hemophagocytosis was noted in the bone marrow. Autopsy cultures were essentially negative.

The major findings at autopsy, including necrotizing enterocolitis, acute renal tubular necrosis, diffuse alveolar damage, and hepatic necrosis, were most likely due to the patient's poor cardiac output and recent hypotension. The gastric ulcers are probably related to stress, and the hemophagocytosis is most likely a sequela of recent blood transfusion (the patient received red blood cells one day prior to death). It is not clear why no mass or thrombus was found in the right atrium or lungs. If a thrombus accounted for the mass, then it may have resolved spontaneously or responded to low molecular weight heparin therapy.

Clinical Summary

The patient was a [redacted] old girl who was born on [redacted] Hospital at 38 weeks gestation by induced vaginal delivery to a [redacted] year-old G1P0 mother (A negative, antibody negative, RPR non-reactive, rubella immune, hepatitis negative). Apgar scores were 7 at 1 minute and 8 at 5 minutes; weight was 2,835 kg. The baby was cyanotic, and was transferred to [redacted] PICU.

On physical examination at admission, the patient was cyanotic but comfortable and in no distress. Echocardiographic examination revealed transposition of the great arteries with intact ventricular septum and a large patent ductus arteriosus, with left to right shunting. The aortic arch was intact. The foramen ovale was patent and good atrial shunting was present. Two coronary arteries were seen. The patient was started on prostaglandin E1. Metabolic acidosis was present. The patient was intubated and placed on a ventilator. She had good pulses. Antibiotics were given. On [redacted] the patient was extubated, and cardiac surgery was planned for [redacted] she was reintubated because of apnea thought to be due to prostaglandin therapy. She was otherwise doing well, and antibiotics were discontinued as cultures were negative. On [redacted] mild jaundice was noted. On [redacted] an arterial switch procedure was performed, with closure of the ASD, relocation of the coronary arteries to the neo-aortic root, and division of the ductus. The patient was stable following surgery, with the chest left open. Right ventricular diastolic dysfunction with junctional ectopic tachycardia were noted. She was given amiodarone, and was easily ventilated. On [redacted] the chest incision was closed. On [redacted] the patient was extubated and developed respiratory acidosis; she was reintubated. The creatinine was persistently elevated. She was subsequently extubated and reintubated again. On [redacted] a right chest tube was placed for pleural effusion. On [redacted] she was again extubated, and chylous fluid drained from the chest tube. On [redacted] she had emesis, and wound erythema, fever, and leukocytosis developed. Cultures of blood and pleural fluid proved to be negative.

On [redacted] she was transferred to the NICU.

On [redacted] she was felt to be malnourished. The sternal wound was increasing in size and redness. The chest tube was replaced, and Portagen and TPN were started. The WBC was elevated to 32,400, and her chest wound was thought to be infected. She was given vancomycin and ceftazidime. On [redacted] gram positive cocci were cultured, and antibiotics were continued. On [redacted] an ultrasound examination of the head demonstrated dilated ventricles, a thrombus in the right lateral ventricle, and a possible right thalamic lesion. She was extubated on [redacted] and was alert and active. On [redacted] she still had chronic pleural drainage and had become lethargic with decreased tone. On [redacted] she had decreased right chest tube drainage, but the right lung was hazy on chest x-ray. Echocardiographic examination demonstrated a large right atrial mass interpreted as a thrombus, adherent to the lower atrial septum and free-floating. No tricuspid valve obstruction or shunting were detected. A pediatric hematology/oncology consultation recommended low molecular-weight heparin therapy. She then underwent acute deterioration, with increased work of breathing and retractions. She was reintubated. Abdominal distension developed, and an x-ray demonstrated dilated, thickened bowel loops and possible portal vein gas. On [redacted] the patient was hypotensive, and diffuse bowel disease due to sepsis and necrotizing enterocolitis were suspected. She was treated for sepsis; 1+ Klebsiella was grown from her endotracheal aspirate, but blood cultures were negative and an x-ray revealed no free abdominal air. "Do not resuscitate" status was instated. A nephrology consultation was requested for hyperkalemia; it was recommended that she not be given hemodialysis or peritoneal dialysis but that she be treated medically. An abdominal ultrasound examination demonstrated heterogeneity of the liver, interpreted as hepatitis or venous obstruction. She also had decreased flow in her renal arteries. It was felt that medical therapy had been maximized. ON [redacted] medical support was gradually withdrawn at the parents' request. Her heart rate decreased and she was pronounced dead. Permission was given for an autopsy excluding the brain.

Gross Description

The body is that of a well-developed, well-nourished, female infant weighing 3668.5 g and measuring 50.0 cm crown-heel and 31.0 cm crown-rump. The head is normocephalic, has no evidence of trauma, and is covered by brown hair in a normal pattern. The head, chest and abdominal circumferences are 36.0, 37.0, and 38.0 cm respectively. The right and left toe-heel lengths are each 7.5 cm. The face is somewhat edematous. The palpebral fissures are 4.5 cm each and the inner-canthal and outer-canthal distances are 4.5 and 6.5 cm respectively. The sclerae are white. The irides are grey and surround equal pupils. The conjunctivae are pale. The choanae are patent. The lips and palate are intact. The tongue is normal. The ears are normally formed and positioned and the external auditory canals are patent and contain no exudate. The neck is symmetrical and has no palpable masses. The trunk is well formed. Breast buds are absent. The abdomen is markedly protuberant. The umbilicus is not covered by granulation tissue. The external genitalia are normal. The labia majora completely cover the labia minora. The urethral opening and the anus are patent. Examination of the back reveals a normal dorsal midline. Livor mortis is evident over the back and posterior thighs. Examination of the upper and lower extremities reveals no abnormalities. The fingernails reach the

Autopsy Report

tips of the fingers and the toenails reach the tips of the toes. The fingernail beds are cyanotic. The skin is pink. No lymphadenopathy is palpated. Rigor mortis is absent.

External evidence of therapeutic intervention:

A healed surgical incision measuring 8.5 cm in length is present over the sternal midline. Lines enter the right and left sides of the chest. A bruise measuring 1.3 X 0.6 cm is present in the anterior chest. Venipuncture sites are seen on the left arm at the wrist, antecubital fossa, and axilla, and on the right arm at the wrist and antecubital fossa. A Star-Strip is present on the right side of the head. Venipuncture sites are seen on the left and right sides of the head.

Initial incision:

The body is opened with a Y-shaped incision revealing a well-hydrated panniculus measuring 0.5 cm in thickness and well-developed musculature. Bloody pleural effusions are present, and shaggy yellow exudate lies over the left lower lung lobe. Chest tubes are coiled in the left and right pleural spaces. Posterior fibrous pleural adhesions are present. The abdomen does not contain free fluid or display anatomic abnormalities. The diaphragm is intact. Shaggy exudate is present over the proximal jejunal serosa, but the serosal surfaces are otherwise smooth, transparent and glistening. The internal inguinal rings are closed. The liver edge lies 1.0 cm below the right costal margin; the spleen tip does not extend below the left costal margin. Cultures are obtained from the right pleural fluid, peritoneal fluid, and left upper lung lobe.

Cardiovascular system:

The heart-lung block weighs 124.5 g (normal: 85±32 g). The epicardium is rough and erythematous. The coronary arteries follow their normal course. The right atrium is unremarkable. The foramen ovale is closed. The tricuspid valve leaflets and their insertions are unremarkable. The right ventricle is unremarkable. The right ventricular wall measures 0.3 cm thick at its base. The cusps of the pulmonic valve are unremarkable. The left atrium is unremarkable. The mitral valve leaflets and their insertions are unremarkable. The left ventricle is unremarkable. The left ventricular wall measures 0.6 cm thick at its base. The cusps of the aortic valve are unremarkable. The myocardium is homogeneous red-brown. The circumference of the valves measure as follows: tricuspid 3.0 cm, pulmonary 1.7 cm, mitral 2.2 cm, and aortic 1.2 cm. Superior to the pulmonic valve lies a suture line connecting the neopulmonic root to the main pulmonary artery; a similar suture line connects the neo-aortic root to the ascending aorta. The coronary arteries are sutured to the neo-aortic root in an end-to-side fashion. The aorta distal to the suture line and the great arteries are of normal size and relationship, and their major branches are normal.

Respiratory system:

The epiglottis, larynx, trachea, and bronchi are lined by a tan, glistening mucosa. No lesions are noted. The pleural surfaces are partially covered by shaggy, yellow exudate. The lungs are inflated with formalin through the trachea. On sectioning following fixation, the parenchyma is firm and brown.

Gastrointestinal tract:

The esophagus is lined by a longitudinally-plicated, grey-white mucosa, and no lesions are noted. The stomach contains a moderate amount of mucus, and the mucosa is tan and glistening with the normal rugal folds. The small and large intestines are distended. The contents of the small and large bowel are within normal limits. The mucosa of the jejunum is somewhat roughened but the bowel mucosa is otherwise tan with normal plical folds. The wall of the large intestine displays a number of small, bubble-like nodules. The appendix is present.

Pancreas:

The pancreas is of normal size and shape, and on sectioning is tan-pink and lobulated.

Hepatobiliary system:

The liver weighs 141.1 g (normal: 139±31 g). The capsule displays tan discoloration posteriorly but is otherwise smooth, glistening, and transparent. The parenchyma is rubbery-soft. Reddish-tan and white apparent necrosis are present in a subcapsular pattern involving much of the posterior portions of the right and left lobes; the remaining parenchyma is homogeneous red-brown in color. The portal vein is patent. The gallbladder contains approximately ml of dark green, viscous bile and the mucosa is green and velvety. The extrahepatic biliary tree is patent.

Genitourinary system:

The right and left kidneys weigh 18.1 and 17.5 g respectively (normal combined weight: 31±6 g). The capsules strip easily revealing fetal lobulations. The cortices of both kidneys appear of normal thickness and are well-demarcated from the medullae, which are markedly congested. The pyramids are normal in size, shape, and number. The papillae are congested. The calyces and pelvis are not dilated. The ureters are of normal caliber and are patent to the trigone of the bladder. The bladder is lined by wrinkled, tan-white mucosa which displays focal hemorrhages. The uterus and tubes reveal no gross abnormalities. The ovaries are hemorrhagic.

Reticuloendothelial System:

The thymus is surgically absent. The spleen weighs 5.5 g (normal: 11±4 g). The capsule is smooth, glistening, and grey-purple. On sectioning the parenchyma is soft and homogeneous red-purple with prominent Malpighian corpuscles. There is no lymphadenopathy. The bone marrow is dark red-brown.

Endocrine system:

The thyroid is the usual, midline, bilobed organ, which on sectioning is tan-red and glistening. The combined weight of the adrenal glands is 4.1 g (normal: 4.8±1.9 g). Sectioning reveals well-developed yellow cortices and grey medullae of the usual thickness.

Musculoskeletal system:

The musculature is well developed and no skeletal abnormalities are noted.

Cultures: Pleural fluid, peritoneal fluid, left upper lung lobe.

Summary of blocks:

1A Liver
1B Right ventricle

Autopsy Report

1C	Left ventricle
1D	Right upper lung lobe
1E	Right middle lobe
1F	Right lower lobe
1G	Left upper lobe
1H	Left lower lobe
1I	Neck organs
1J	Trachea, mainstem bronchi
1K	Esophagogastric junction, gastric body ulcers
1L	Gastroduodenal junction
1M	Small intestine
1N	Large intestine
1O	Liver
1P	Liver
1Q	Liver
1R	Pancreas
1S	Left kidney
1T	Right kidney
1U	Urinary bladder
1V	Uterus, fallopian tubes, ovaries
1W	Spleen
1X	Mesenteric lymph nodes
1Y	Adrenal glands
1Z	Diaphragmatic skeletal muscle
1AA	Skeletal muscle
1BB	Skin
1CC	Soft tissue
1DD	Spinal cord
1EE	Vertebral bone and marrow
1FF	Vertebral bone and marrow

Microscopic Description

Heart (1B, 1C): The myocardium is unremarkable. Epicardial fibrosis and minimal lymphohistiocytic infiltrates are present, consistent with cardiac surgery.

Lungs (1D, 1E, 1F, 1G, 1H): There is diffuse vascular congestion, predominantly in alveolar capillaries. Numerous type II pneumocytes are present in the alveolar spaces, often in chains, consistent with healing diffuse alveolar damage. There is no evidence of pneumonia or fibrosis.

Trachea and bronchi (1I, 1J): Mild hyperplasia of respiratory mucosa is noted. No inflammation or fibrosis is seen.

Thyroid gland (1I): No pathologic diagnosis.

Esophagus (1K): No pathologic diagnosis.

Stomach (1K, 1L): Focal mucosal ulcers are present in the body, displaying a fibrinous base but no inflammation.

Duodenum (1L): No pathologic diagnosis.

Small intestine (1M): Extensive mucosal damage is present, representing autolysis and possible necrosis.

Large intestine (1N): The mucosa is autolyzed and possibly necrotic. Pneumatosis coli is prominent, with gas bubbles present in the submucosa and muscularis propria. No necrosis is seen, and no inflammatory or foreign body reaction to the pneumatosis is observed.

Liver (1A, 1O, 1P, 1Q): Extensive subcapsular coagulative necrosis corresponding to the areas seen grossly is observed. The necrosis is accompanied by hemorrhage, congestion, and calcification. Viable liver is congested but no zonal pattern of congestion is seen.

Pancreas (1R): No pathologic diagnosis.

Lymph nodes, peripancreatic and mesenteric (1R, 1X): There is marked lymphocyte depletion, with congestion and hemorrhage in the mesenteric nodes.

Kidneys (1S, 1T): Acute tubular necrosis is prominent with extensive cortical tubular necrosis; some of this necrosis may reflect autolysis. Mitoses and apoptotic bodies are seen in preserved cortical tubules. Focal congestion and hemorrhage is also present.

Urinary bladder (1U): No pathologic diagnosis.

Uterus, vagina, fallopian tubes, and ovaries (1U): Marked tubal and ovarian hemorrhage is seen.

Spleen (1W): Mild congestion and hemorrhage of cords and sinuses is seen. The lymphocytes are markedly depleted.

Adrenal glands (1Y): No pathologic diagnosis.

Diaphragmatic skeletal muscle (1Z): Fibrosis, hemorrhage and foreign body reaction is noted on the pleural surface, consistent with post-surgical changes.

Skeletal muscle (1AA): No pathologic diagnosis.

Abdominal skin (1BB): No pathologic diagnosis.

Soft tissue (1CC): No pathologic diagnosis.

Spinal cord (1DD): No pathologic diagnosis.

Autopsy Report

Vertebral bodies (1EE, 1FF): The bone is unremarkable. The marrow displays trilineage hematopoiesis but is markedly immature. Numerous histiocytes demonstrate hemophagocytosis, consistent with recent blood transfusion.

Culture results:

Pleural fluid: Negative.

Peritoneal fluid: Negative.

Left upper lung lobe: 1+ mixed normal respiratory flora.

SNOMED Code(s)

(Not Entered)