CLINICOPATHOLOGICAL CASE

Infant with otitis media, meningitis and septic shock

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CLINICAL HISTORY SUMMARY (A-07-31)

We present the case of a 3-month-old male patient who was admitted with irritability, crying, loss of appetite and vomiting. Tonic-clonic seizures took place on four occasions. The patient presented metabolic acidosis and required assisted ventilation.

Family History

The patient's mother is a 23-year-old housewife; the father is a 23-year-old laborer. Both parents completed elementary school. They are Catholic and are healthy. They also have a 2-year-old daughter with cleft lip and palate. Maternal and paternal grandmothers are reported as having systemic arterial hypertension.

Nonpathological History

The patient is native and a resident of the state of Hidalgo in Mexico. The family home has running water, and electricity, but no drainage. The family cooks with firewood and lives with 7 dogs, chickens and goats. The patient had daily baths.

Perinatal and Pathological Antecedents

The patient was exclusively breastfed. He presented with head control and social smile from the age of 2 months. He received BCG, Sabin and DPT/hepatitis B/Hib vaccinations. He was the result of a second pregnancy with appropriate prenatal care. Eutocic delivery took place in the hospital. Birthweight was 4000 g weight, no length or Apgar score was available, and the newborn cried and breathed at birth.

Current Illness

On May 12, 2007, the patient attended a primary care facility due to airway infection without improvement. He was managed with penicillin because of gastroenteritis and was admitted to a second-level care facility between May 13 and May 14 due to fever and abnormal movements. Patient was irritable, with tachycardia, tachypnea and 38.5°C temperature, bulging anterior fontanel, rigid neck, isochoric pupils with poor response to light and right otorrhea. He was diagnosed with neural infection and managed with fasting, IV solutions, phase I ventilation, ampicillin (100 mg/kg/day) + amikacin (7.5 mg/kg/day) as well as bicarbonate correction due to -13 base deficit. No cerebrospinal fluid (CSF) sample was obtained. Patient was intubated because of neural deterioration and 12 respiratory pauses after admission. The following gasometry report showed pH 6.9, PaO_2 85, $PaCO_2$ 114.8, HCO_3 24.4, SaO_2 87% and base excess (BE) -10.8. Ceftriaxone was administered at a nonspecified dose with previous administration of steroid and two doses of furosemide. The patient received diphenylhydantoin and sodium correction of 113-123 mEq/L. Because there was no mechanical ventilator, the patient was transferred to the Intensive Care Unit of

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Hospital Infantil de Mexico Federico Gomez (HIMFG). Lumbar puncture was not carried out due to limited economic resources.

CLINICAL CASE

This is the case of a 3-month-old male patient who was admitted with a 48-h evolution of an illness characterized by irritability and continuous crying associated with oral rejection. There were two episodes of projectile vomiting of gastric contents. Fever reached 38.5°C in two surges and the patient presented four generalized tonic-clonic seizures within the first 24 h with ocular retroversion and postseizure status with somnolence between 15 and 30 min (Table 1).

During physical examination, the patient presented skin pallor, normocephalic, normotense 2 × 2 cm anterior fontanel, myotic pupils with poor response to light, conjugated ocular movements, and normal set ears with purulent discharge from right ear. Oral cavity was well hydrated. He was intubated with a #4 endotracheal tube at 12 cm. Precordium was without alterations and the patient had well-ventilated bilateral pulmonary fields. Abdomen was soft and depressible, and hepatic border was 2 cm below the right costal edge with peristaltic sounds. Genitalia were in accordance with age and gender and normal limbs with pulse and edema in both hands. Patient was sedated secondary to benzodiazepine. Cranial nerve pairs could not be assessed, trophism was preserved, force was not assessed, and there were nonevoked tendinomuscular reflexes. Laboratory test results are shown in Table 2.

Patient was managed with fasting, base solutions (150 ml/kg/day), glucose (5 g/kg/day), sodium and potassium (3 mEq/kg/day), calcium (50 mg/kg/day), three loads of 0.9% physiological solution at 20 ml/kg/dose, calcium gluconate (100 mg/kg/dose), vitamin K (0.3 mg/kg/dose), ranitidine (1 mg/kg/dose), metamizole (10 mg/kg/dose PRN), midazolam (0.2 mg/kg/dose (spell out PVM), phenobarbital (5 mg/kg/day), vancomycin (60 mg/kg/day), cefotaxime (300 mg/kg/day), midazolam (4 µg/kg/min), norepinephrine (0.1 µg/kg/min), hydrocortisone (50 µg/kg/dose), hydrocortisone infusion (180 µg/kg/h), milri-

Table 1. Somatometry and vital signs at admission

Weight	*Length*	*Cardiac frequency*	*Respiratory frequency*	*Arterial pressure*	*Temp.*	*Capillary refill time*
6 kg	59 cm	180 beats/min	30 respirations/min	99/32 (54) mmHg	38.0°C	4 sec

Table 2. Laboratory tests results upon admission to ICU

Hb	*Hct*	*Leuk*	*Seg*	*Lym*	*Mon*	*Bands*	*Plat*	*PT*	*PTT*	*INR*
7.0 g/dL	20.7%	7.4/mm^3	64%	26%	2%	7%	569,000	17.5”	55.5”	1.38

Glu	*BUN*	*Creat*	*Na*	*K*	*Cl*	*Ca*	*P*	*Mg*
78 mg/dL	7 mg/dL	0.4 mg/dL	130 mEq/L	5.1 mEq/L	101 mEq/L	10.0 mg/dL	3.7 mg/dL	1.3 mg/dL

IB	*DB*	*TB*	*TGO*	*TGP*	*LDH*	*ALB*	*GLOB*	*Na U*	*K U*	*Cl U*
0.14 mg/dL	0.11 mg/dL	0.25 mg/dL	38 U	46 U	281 U/L	2.1 g/dL	1.5 g/dL	89 mEq/L	30.1 mEq/L	124 mEq/L

pH	*DU*	*Alb*	*Glu*	*Nit*	*Ketones*	*Bile*	*Urobilin*	*Leuk*	*Bact*	*Eryth*	*Leukocyte cylinders*
5	1020	30 mg/dL	500 mg/dL	-	-	-	-	1-2/mm^3	-	0-1/mm^3	0-1/mm^3

pH	**PaO_2**	**$PaCO_2$**	**HCO_3**	**BE**	**Lactate**	**SaO_2**	**Ca^{++}**
7.34	243	24.4	12.9	–11.3	8.7 mmol/L	100%	1.12 mmol/L

none (0.5 µg/kg/min) and epinephrine (0.1 µg/kg/min). Lumbar puncture could not be carried out or placement of intracranial pressure monitor because of hemodynamic instability. Electroencephalogram reported low-voltage irregular delta wave with asymmetry due to minimal activity in the right hemisphere and severe generalized dysfunction predominantly on right side. Patient continued with torpid evolution, and refractory amine septic shock. Norepinephrine and epinephrine were increased to 0.9 µg/kg/min and milrinone to 0.5 µg/kg/min. Cryoprecipitates were indicated, fresh frozen plasma and red cell concentrate, and an infusion of fentanyl, bicarbonate and levosimendan was added at 0.1 µg/kg/min. Ventilatory phase III PIM was 24, FIO_2 80, PEEP 6, respiratory frequency 28/min, and Kirby 115. The patient presented multiple fever spikes, anisocoria, poor pupillary response, hypokalemia-associated arrhythmias, hyponatremia and persistent high anion gap metabolic acidosis and up to 15 hyperlactatemia. Patient presented cardiopulmonary arrest when being prepared for lumbar puncture and responded to resuscitation maneuvers. Hypertonic sodium solution was administered. Echocardiogram reported healthy cor, good contractility, 84% expulsion fraction and 45% shortening fraction. A Swan-Ganz catheter was placed in the left subclavian artery for hemodynamic monitoring (Table 3).

The patient presented with persistent poor response with high vasopressors, borderline urinary output, low central venous pressure, continuous hypotension, hemodynamic instability, mechanical ventilation parameter changes, persistent metabolic acidosis and hyperlactatemia. Vasopressin was administered (0.02 U/kg/h) and 5% albumin (10 ml/kg/dose). Patient presented cardiopulmonary arrest without responding to advance resuscitation maneuvers.

Imaging Findings (Dr. Eduardo Miguel Flores Armas)

Computed tomography (CT) scan carried out on May 14, 2007 revealed a hypodense image involving both lentiform nuclei. This asymmetrically affects the head of the left caudate nucleus and a hypodense image at the cingulum affecting gray and white matter bilaterally and symmetrically as well as the ventral portion of both thalami. Coronal reconstruction revealed a frank involvement of globus pallidus and putamen as well as frontal lesions at cingulum level with a discreetly asymmetrical involvement of gray matter on the right side. Subarachnoid spaces were wide. Other parts of the brain presented a normal gray-white matter ratio for a 3-month-old patient (Figure 1).

The following differential diagnoses are presented according to imaging:

- Ischemic damage secondary to viral disease (probably Epstein-Barr)
- Associated extrapontine myelinolysis
- Acute disseminated encephalomyelitis (ADEM) considering patient's immunization scheme
- Glutaric aciduria type 1
- Hallervorden-Spatz syndrome (pantothenate kinase-associated neurodegeneration-PKAN-)
- Wilson's disease
- Mitochondriopathy:
  - MELAS—mitochondrial encephalopathy, lactic acidosis and stroke-like episodes

Table 3. Hemodynamic parameters obtained through Swan-Ganz catheter

	May 15, 2007, 14:30 h	*May 16, 2007, 00:10 h*	*May 16, 2007, 09:00 h*
CVP	8 mmHg	10 mmHg	7 mmHg
MPAP	33 mmHg	25 mmHg	22 mmHg
PCP	12 mmHg	6 mmHg	10 mmHg
CI	3.59 L/min/m^2	5.12 L/min/m^2	4.29 L/min/m^2
SVRI	963 dynes sec/cm^2/m^2	578 dynes sec/cm^2/m^2	726 dynes sec/cm^2/m^2
PVRI	624 dynes sec/cm^2/m^2	297 dynes sec/cm^2/m^2	670 dynes seg/cm^2/m^2
PAP	37/30 mmHg	30/19 mmHg	31/14 mmHg
SVI	23 ml/m^2	29.7 ml/m^2	27.8 ml/m^2

CVP, central venous pressure; MPAP, mean pulmonary arterial pressure; PCP, pulmonary capillary pressure; CI, cardiac index; SVRI: systemic vascular resistance index; PVRI, pulmonary vascular resistance index; PAP, pulmonary arterial pressure; SVI, systolic volume index.

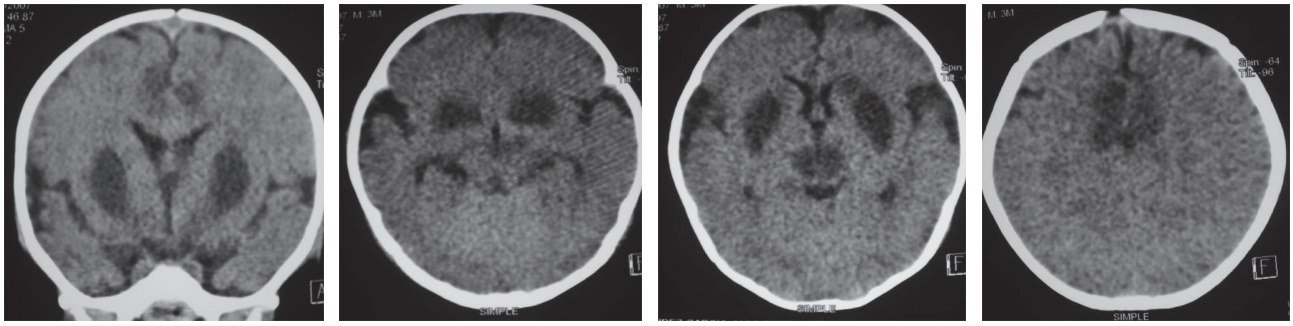

Figure 1. Simple phase computed axial tomography of the skull.

- MERRF—myoclonic epilepsy and ragged red muscle fibers
- Leigh's Syndrome

Discussion (Dr. Armando Partida Gaytan)

This is the case of a 3-month-old male patient who was admitted to our institution on May 14, 2007 and who died on May 16, 2007. According to the patient's clinical history, low socioeconomic and cultural levels were identified as risk factors because they often condition a poor understanding of medical instructions, poor treatment adherence, difficult to identify medical warning signs as well as delayed medical treatment. Living without basic urbanization services, defecating outdoors and living with animals increase the risk of infections, zoonosis and parasitosis. The parents appeared as protective and took appropriate care of their child with daily bathing and exclusive breastfeeding, as well as seeking timely medical care. It seems apparent that the parents recognized medical warning signs that prompted them to search for medical care.

The following clinical syndromes were found:

1) Infectious syndrome with fever (two spikes up to 38.5°C), irritability (continuous crying), oral rejection and right otorrhea

2) Encephalic syndrome with meningeal irritation and intracranial hypertension defined by irritability, alterations of awareness state with drowsiness, projectile vomiting, generalized tonic-clonic seizures, altered breathing control with apnea, alteration of cranial nerve pairs with poor photomotor response, neck rigidity and bulging fontanel

3) Anemic syndrome due to generalized pallor, tachycardia and hemoglobin 7 g/dl.

4) Possible development of a syndrome of inappropriate antidiuretic hormone secretion although there were insufficient biochemical data for a valid diagnosis. However, hyponatremia associated with neurological diagnosis and clinical data suggesting fluid retention (edema in both hands) as well as dilutional syndrome expressed by hypoproteinemia with 2.1 g/L albumin and 1.5 g/L globulin raise this suspicion.

5) Sepsis based on tachycardia, tachypnea and fever involving cardiovascular function manifested by 4 sec capillary refill, wide differential tension and high anion gap metabolic acidosis with hyperlactatemia, which can be considered as a severe sepsis syndrome. Then, because hypotension persisted despite appropriate rehydration, it was considered as a catecholamine-refractory septic shock based on clinical evidence. As a consequence of septic shock, three organ syndromes were identified associated with cardiovascular dysfunction: a) acute respiratory distress syndrome manifested by hypoxemia and increased ventilation parameters (Kirby <200 and pulmonary pressure <18 mmHg); b) pulmonary arterial hypertension syndrome documented through Swan-Ganz catheter with mean pulmonary artery pressure (MPAP) >25 mmHg; c) acute nephritic syndrome documented by increased creatinine levels (double baseline values) and oliguria.

All of the above were in accordance with Acute Dialysis Quality Initiative (ADQI) classification criteria; d) disseminated intravascular coagulation syndrome documented by biochemical values with elongated coagulation time and hypofibrinogenemia. Having these four integrated systems comprises multiple organ dysfunction syndrome.

According to the above, we can diagnose meningoencephalitis suggested by clinical data even though lumbar puncture was not carried out to confirm diagnosis. Evidently, acute otitis media (AOM) can be regarded as the initial infection and leads us to think of a bacterial etiology. Because of the patient's age and immunization

scheme, there are two possibilities: first, *Streptococcus pneumoniae* and second, *Haemophilus influenzae*. The decisive factors from ear infection towards meningoencephalitis were delayed diagnosis and appropriate treatment. Once central nervous system infection was suspected, the opportunity is lost to confirm this diagnosis through lumbar puncture to identify the infectious agent and the most appropriate therapy. Although there are contraindications about this procedure, lack of economic resources should not be among them. Afterwards, clinical status with hemodynamic instability, coagulopathy and hypertense cranium was contraindicated for lumbar puncture; when it was attempted, patient presented cardiorespiratory arrest. Nevertheless, it is considered that initial antimicrobial management was not appropriate even though there was no CSF sample and diagnosis. Optimal schema for this patient should have been a third-generation cephalosporin (cefotaxime or ceftriaxone) and a glycopeptide (vancomycin) in order to consider resistant pneumococci as well as beta-lactamase-producing *H. influenzae*.

When the patient's critical condition was acknowledged with neurological involvement, airways should have been protected through a rapid sequence to avoid emergency intubation (as it was carried out after the apnea episode). This approach, according to the Pediatric Advanced Life Support Provider Manual by the American Academy of Pediatrics (AAP) and American Hospital Association (AHA),[1] was to reduce the risk of gastric aspiration, reduce adverse effects of laryngoscopy and reduce intracranial pressure. After the apnea event, the patient developed hypercapnia, which increased brain damage associated with intracranial hypertension.[1] Another factor associated with brain damage was water-electrolyte imbalance characterized by severe hyponatremia. Blood plasma status was not documented in the clinical file at the time and there was not an appropriate paraclinical approach. As already mentioned, the presence of inappropriate antidiuretic hormone syndrome was suspected. It was important to determine electrolytes as well as serum and urinary osmolarity, verify urinary output and rule out other possibilities such as cerebral salt-wasting syndrome or erroneous management of intravenous solutions. Afterwards, sharp changes in sodium concentration and osmolarity were documented (43 mEq in 48 h), which may have increased the patient's risk for pontine myelinolysis.

On the other hand, management using dexamethasone was appropriate.[2] The use of corticosteroids to aid in the management of bacterial meningitis significantly reduces the mortality rate in children with meningitis associated with *S. pneumoniae* as well as severe hearing loss in children with meningitis associated with *H. influenza* type b.

Another fundamental aspect in regard to this patient's evolution was the decision to transfer the patient. In accordance with the guidelines of the Society of Critical Care Medicine (SCCM) and AAP, a patient in critical condition should be transferred considering the obtained benefit vs. risks.[3] In the case of this patient, a decision was made because technology was insufficient to maintain an appropriate ventilation and monitoring. Transferring a critically ill patient involves certain risks; however, the most important recommendation is to establish an organized and efficient process supported by appropriate equipment and qualified personnel. Parameters that should have been carefully considered during transfer are continuous electrocardiography, continuous pulse oxymetry, orotracheal cannula fixation, capillary glycemia every hour, capnography and continuous measurement of intracranial pressure (ideal conditions). If aminergic support was required, this should have been initiated prior to transfer to ensure hemodynamic stability. According to Orr et al., transferring a patient under these conditions reduces the mortality rate from 23% to 9%.[4]

The patient arrived in poor general condition when he was admitted to our hospital. According to the management guidelines by Rivers et al. in Detroit,[5] Carcillo et al. in Pitsburgh[6] and Zimmerman et al. in Seattle,[7] a goal-oriented management of septic shock has reduced mortality rate from 97% (during the 1960s) to 9% (end of 1999) and even to 6.5% in recent years. However, despite these guidelines, Mikkelsen et al.[8] reported that these recommendations are not initiated in 42% of cases and not complied with in 43% of cases and describes the following risk factors: use of lactate >4.0 as diagnostic criterion without hemodynamic assessment ($p = 0.018$) as well as evaluation and management by a service not specialized in severe sepsis ($p < 0.001$). According to the Pediatric Index of Mortality 2 (PIM2), this patient presented a mortality risk of 42.5% because 1) admission was neither scheduled nor elective, 2) he was not admitted for postoperative recoupment, 3) he presented a high-risk diagnosis (meningitis), 4) he required mechanical ventilation, and 5) he had systolic pressure = 99 and base excess of -11.3 with 0.329 FiO_2/PaO_2 rate.[9]

Cranial CT scan reported nonspecific findings: images suggestive of thalamic infarctions secondary to inflammatory and thrombotic processes associated with meningoencephalitis. Although seizures, hyperlactatemia and brain infarction suggest a metabolic or mitochondrial syndrome, clinical profile and evolution are decisive factors. Without neurological history and appropriate psychomotor and weight-size development, the possibility of these disorders is ruled out. Another infrequent complication in AOM is lateral venous sinus thrombosis with secondary otogenic hydrocephalus. This entity is characterized by signs and symptoms of intracranial hypertension with neurological signs associated with AOM and CSF without pathological changes. This diagnosis requires magnetic resonance imaging studies (with and without contrast media) searching for defects on the lateral venous sinus known as delta sign.

According to the patient's evolution, there was no appropriate response to management because the patient remained hypotense despite vasopressor support; therefore, it was classified as a catecholamine-refractory septic shock. Hydrocortisone was administered later because of suspected adrenal insufficiency. Pizarro et al.[10] documented in 2005 that patients with catecholamine-refractory septic shock presented 18% complete adrenal insufficiency and 26% relative adrenal insufficiency. Since then, we know that patients with adrenal insufficiency have an increased risk to present catecholamine-refractory septic shock with 1.88 relative risk (RR) (95% CI 1.26-2.79). Cortisol determination was relevant for this case although the patient's condition did not improve. It was called to my attention that this patient received blood derivatives including red-cell concentrate but the reported hemoglobin levels were <7.5 g/dl, which could contribute to insufficient oxygen, triggering anaerobic metabolism and lactic acidosis. Recommendations during septic shock include maintaining Hb >10 g/dl.[7-9] Placement of a Swan-Ganz catheter was appropriate although echocardiogram plays an important role in the evaluation of hemodynamics in patients with septic shock. Poor treatment response calls for a more precise and constant monitoring. According to integral hemodynamic assessment that considers central venous pressures, ejection fraction and ventricular shortening reported by echocardiogram and hemodynamic workshop through thermodilution using Swan-Ganz, the patient's cardiac performance was adequate. However, despite the use of high doses of vasopressors, the patient continued with hypotension, which leads us to consider that he developed a vasodilatory septic shock (mortality rate 50%-60%).[11] It is also important that neurological damage could contribute to vasodilatory shock. Again, I consider vasopressin was correctly administered because it improves cardiovascular function, increases median arterial tension, and reduces cardiac rate and norepinephrine requirements.[12] However, the patient did not present a favorable response.

Final diagnoses are as follows:

- Eutrophic male infant
- Right acute otitis media with suppurative discharge
- Right tympanic perforation
- Right acute otomastoiditis
- Possible bacterial meningitis
- Possible syndrome of inappropriate antidiuretic hormone secretion
- Brain infarction
- Catecholamine-refractory septic shock
- Vasodilatory shock
- Possible partial adrenal insufficiency
- Water-electrolyte imbalance: hyponatremia and hypokalemia, then hypernatremia, hyperchloremia and hypophosphatemia
- Possible pontine myelinolysis
- High anion gap metabolic acidosis with type 1 hyperlactatemia
- Multiple organ dysfunction syndrome (disseminated intravascular coagulation, acute nephropathy, acute respiratory distress syndrome)

Cause of death

- Vasodilatory shock (septic and neurogenic components)

ANATOMOPATHOLOGICAL FINDINGS (DR. MARIO PEREZPENA DIAZCONTI)

Postmortem study included analysis of cavities and petrous portion of temporal bone with right and left ear canals. Right ear canal presented destruction of bone structures with green-yellow purulent material (Figure 2). Infectious agents most frequently involved are *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus*, although sometimes the causative agent is not identified.[13]

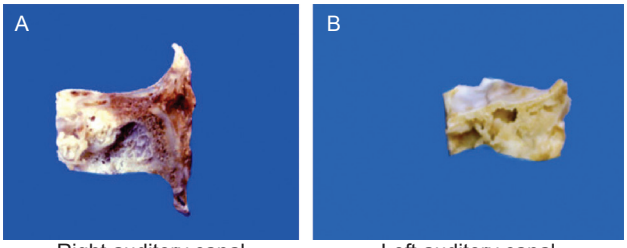

Figure 2. Comparison of right and left ear canals. First (A) shows yellow-green purulent material destroying bone and occupying air spaces. Left ear canal preserves its macroscopic aspect (B).

Complications described for these patients include subperiosteal abscess, Bezold abscess, facial palsy, suppurative labyrinthitis, meningitis, epidural and subdural abscess, brain abscess and lateral sinus thrombophlebitis.[14] Microscopic study revealed intense inflammatory infiltrate of polymorphonuclear leukocytes that occupied the spaces between bone spicules, destroying them focally (Figure 3). Brain weighed 700 g (650 g expected), external surface is opaque and unpolished with gray-yellow purulent material, which is more evident in frontal and parietal lobes. Vessels are dilated, tortuous and congested (Figure 4). Meningitis from infections outside the CNS occurs because of dissemination or are carried by blood. There is an intense polymorphonuclear inflammatory infiltrate in the subarachnoid space that affects even choroid plexuses (Figure 5). Central nuclei reveal neurons with cytoplasm having fusinophilic changes and nuclear retraction secondary to hypoxia.

There was fluid in the right and left pleural cavities as well as fluid in the pericardial cavity. We found a hematoma that dissects soft tissues of the neck. Lungs presented no alterations. Stomach mucosa preserved gastric folds and show brown material deposits, suggesting hemorrhagic gastritis. Kidneys present fetal lobes and bilateral hydrocele. Postmortem cultures did not reveal bacteria except for the colon where we found *Enterococcus faecalis* and yeast.

Final anatomic diagnoses are as follows:

Primary disease

- Right purulent otitis media with ear canal destruction

Concomitant alterations

- Acute meningitis

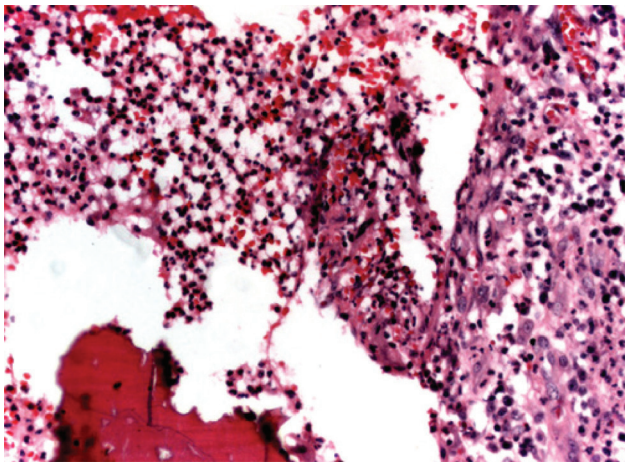

Figure 3. Intense inflammatory infiltrate by polymorphonuclear leukocytes affecting bone fragments. No microorganisms observed.

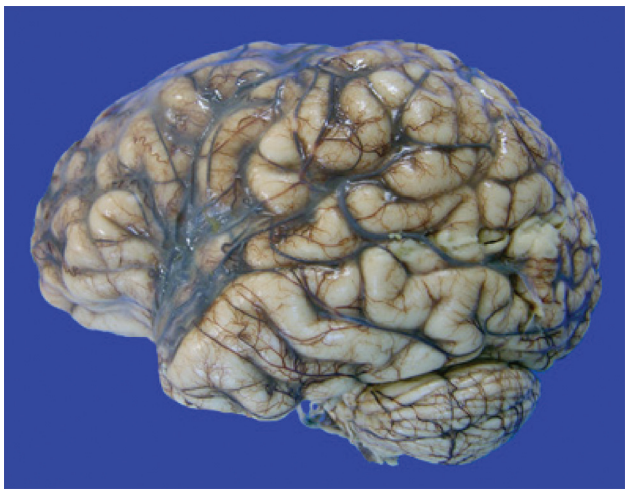

Figure 4. Brain shows a creamy, gray-yellow, opaque aspect, more evident in frontal lobes, and congestion of meningeal vessels, which are also tortuous.

- Brain edema
- Bilateral pleural effusion (right 95 ml, hematic; left 70 ml, pale)
- Fluid in pericardial cavity (10 ml)
- Acute erosive gastritis
- Brown deposits in stomach
- Neck hematoma dissecting soft tissues
- Persistent fetal lobes in kidneys
- Bilateral hydrocele

Shock anatomic data

- Acute involution of thymus

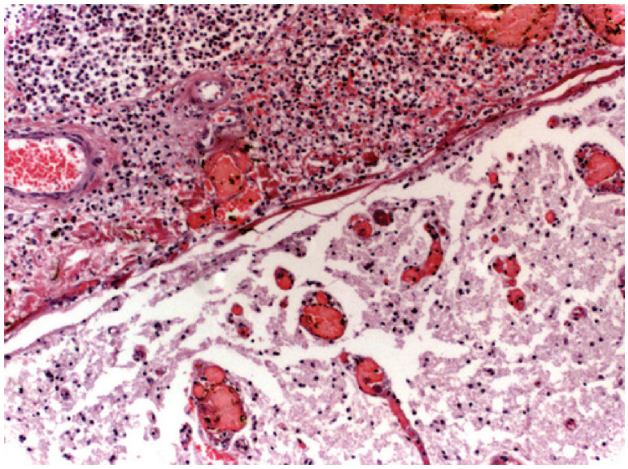

Figure 5. Photomicrograph reveals cellular exudate comprised of polymorphonuclear leukocytes affecting subarachnoid space. Focal migration of inflammatory cells towards parenchyma.

- Contraction bands in smooth muscle of small intestine and colon

Because of the present case, I reviewed 8 years of autopsies and found three studies with primary anatomic diagnosis of meningitis [three male patients (2 and 6 months old and 15 years old)]. Of these three patients, two had a history of upper airway infection. Identified microorganisms were *Streptococcus pneumoniae* in two cases and fermenting gram-negative bacillus in the third case.

Also, there were 11 cases where meningitis diagnosis was included within concomitant diagnoses.

Data are presented here:

- 11 patients: 9 males, 2 females
- Age range: 16 days to 14 years of age
- Three patients with congenital cardiopathy
- Two patients with central nervous system tumors
- Acute otitis media
- Encephalomalacia
- Gastroschisis, intestinal malrotation, microcolon
- Glycogenesis type V
- Agranulocytosis
- Epidermal necrolysis

Causative organisms found in 11 patients with meningitis were as follows:

Gram-positive bacteria: *Streptococcus pneumoniae* (3) and *Enterococcus* sp (1)

Gram-negative bacteria: *Escherichia coli* (2), *Pseudomonas aeruginosa* (2) and *Serratia* sp (1)

Nonidentified agent: 2 cases

Emergency Service Comments (Dr. Victor Olivar López)

There are clinical factors that help to establish the severity of a patient's condition. First, the heart rate receives my attention. Heart rate is frequently associated with fever or anemia; however, this case with 180/min heart rate cannot be explained with a 38ºC temperature. Therefore, we should consider that there must be another problem. Another very important fact is to use goal-oriented management. A very useful factor is an index associated with median arterial pressure minus central venous pressure, which is known as the perfusion index and, in patients of this age, should be >55. This patient presented a perfusion rate of 47; therefore, he should have been managed with the goal to improve arterial pressure and perfusion, which aids us as a prognostic factor. On the other hand, treatment should be carried out early and where the patient is located. There is a report from St. Mary's Hospital (London, 1997) where the mortality rate was reduced from 22.5% to 2.5% in patients with septic shock when the patient was managed early with fluids and peripheral dobutamine before transfer to a specialized hospital. This series applies to our case and, therefore, this patient would have benefitted from this recommendation.

Airways and ventilation were properly managed but circulation was not considered, which would have saved the patient's life. There is evidence that supports an increased survival of 90% in patients whose initial resuscitation maneuvers adhered to current septic shock guidelines; however, when maneuvers do not adhere to guidelines, survival decreases to 60%.[15] Following management guidelines will reduce mortality in patients with septic shock. There is also evidence that each hour without starting resuscitation maneuvers increases death risk two times, and mortality rate for these patients increases up to 50% per hour when treatment does not follow guidelines.[16] Treatment for seriously ill patients may be complex, but when it is carried out promptly and appropriately, results can be greatly improved.

Infectology Service Comments (Dr. Rene Farfan Quiroz)

Initial and empirical treatment was delayed because when a patient presents fever with infection at ear level and neurological symptoms, a neuroinfection should be suspected and appropriate and timely treatment should be initiated, considering the most frequent microorganisms for this age group and patient immunization history. This patient had received only one DPT/hepatitis B/Hib dose, which does not ensure 100% titers for *H. influenzae* type b because it provides up to 80% of protection (in the best scenario) and protection rate increases to >95% after two or three dosages with clinical efficiency between 95% and 100%.[17] *S. pneumoniae* should have also been considered for this age group. Empirical therapy using ampicillin and amikacin is not suitable for this patient's age group or for possible presentation of microorganisms.[18] Therapy should have included a third-generation cephalosporin and a glycopeptide. It has been documented that cefotaxime is indicated for sensitive and mildly resistant pneumococci (300 mg/kg/day, four doses/6 h). However, highly resistant pneumococci are well treated using a glycopeptide.[19,20]

Treatment should have been started independently from CSF analysis or culture because the patient's condition was critical and he required early treatment. When antibiotics were not started within the first hour, mortality rate can become as high as 40% and increase exponentially. In my opinion, this patient presented an infectology emergency.[2]

Intensive Care Comments (Dr. Adrian Chávez López)

Something must be done in Mexico because we are moving slowly. Current trend calls for medical care systematization and we are lagging behind. We should practice evidence-based medicine. Otherwise, we will continue obtaining poor outcomes. There is evidence where being cared for by a nonspecialized physician considerably increases the mortality risk of critically ill patients. For instance, in "first world" countries such as Denmark and The Netherlands there are case-control studies for patients with septic shock associated with meningococci that have demonstrated that patients cared for in a hospital without intensive care units present a 12 times higher risk of death.[21] In a hospital where there is an intensive care unit but the child is cared for only by an intensive care resident physician, the risk of death is nine times higher than if care is supervised by a senior intensivist physician. A relatively recent study in France evaluated quality of care for children at Emergency Services with data suggesting sepsis/septic shock and found a similar scenario: when the patient is cared for by inexperienced physicians, the risk of death is 18 times higher. The same situation occurs when antimicrobial treatment is not initiated appropriately (risk of death is 12 times higher).[22]

It is worth mentioning that 18 months ago in Sao Paulo, Brazil, the first well-validated and structured clinical trial was carried out comparing the usefulness of Carcillo guidelines with the addition of specific goals for hemodynamic management obtained through continuous monitoring using a fiberoptic catheter placed in the pulmonary artery of children with septic shock diagnosed according to SCCM/ACCM guidelines (Society of Critical Care Medicine). In this study, Olivera et al. were able to reduce mortality rates three times when they followed guidelines and specific goals, finding that mortality rate for the treated group was 10% and for the nontreated group was 42%.[23] Specific goals are central venous oxygen saturation >70%, cardiac output between 3.3 L/min and 6.6 L/min and urinary output >1 ml/kg/h, in addition to maintaining hemoglobin ≥10%.

Nephrology Comments (Dra. Rebeca Gomezchico Velasco)

It is very important to appropriately evaluate patients with hyponatremia. We know that hyponatremia can be associated with two mechanisms: renal insufficiency due to excess body water diluting sodium or an excessive water supply. Therefore, we should evaluate the patient to determine which mechanism is producing this insufficiency. Then, whether this is an actual or false hyponatremia should be verified, which can be caused by hyperlipidemia and hyperglycemia. If we determine that the patient has actual hyponatremia, we should assess if it is accompanied by edema to infer which loss is higher, water or sodium, and to evaluate if losses are renal or extra-renal. I consider that this patient presented an actual hyponatremia secondary to brain alteration that produced actual sodium losses. It is important to highlight that sodium correction was carried out from 113 to 123 mEq, which is acceptable because it is recommended to maintain corrections <10 mEq/24 h. However, the patient presented 130 mEq upon admission to our hospital and the next recorded value was 156 mEq after administration of hypertonic sodium. We know that when the onset of hyponatremia is rapid, it may produce damage

and acute neurological symptoms; likewise, hypernatremia may produce new neurological damage with devastating consequences. In this patient, the level increased 26 mEq in 24 h, which may have added to neurological damage.

Final Comments (Dr. Jeronimo Sánchez Medina)

This case prompts our attention to strengthen training and treatment protocols to improve quality and timely medical care. In this case, an infant with AOM who did not receive opportune treatment presented severe complications. According to management guidelines of the AAP and the American Association of Family Physicians (AAFP), treatment for patients of this age group (<6 months old) is antimicrobial therapy at time of diagnosis independent of diagnostic certainty, considering these patients with a severe illness if they present otalgia or fever >39°C during the previous 24 h. An observation period is not recommended for these patients, waiting for a spontaneous resolution.[24] A meta-analysis identified that signs and symptoms of AOM in patients with bilateral disease <2 years old and in patients with otorrhea may be prolonged without appropriate antimicrobial treatment.[25] Antimicrobial drug is chosen according to its clinical and microbiological efficiency, oral acceptance, toxicity and secondary effects, convenience of dosing schedule and cost. Amoxicillin is recommended because of its effectiveness, safety, affordability and because it has an appropriate antimicrobial spectrum.[26]

By duplicating the dosage from 40 to 80 mg/kg/day, we increase concentration in the middle ear, improving its activity against most mildly resistant and some highly resistant strains of *S. pneumoniae*.[27] As a result of the above, we expect that amoxicillin provides a response at high dosages in up to 80% of AOM patients.

Macrolide antibiotics are recommended when the patient presents anaphylaxis or urticaria to penicillin. Treatment should last 10 days in patients <2 years of age. In this age group, we recommend an 8- to 12-week follow-up to document clinical profile resolution, especially in AOM with discharge.[28] Timely diagnosis and appropriate treatment for otitis media ensure that patients receive opportune and appropriate management and prevent misapplication of antimicrobial drugs, which may generate bacterial resistance. Establishing diagnosis in patients <2 years old can be difficult because of the lack cooperation and poor visibility of tympanic membrane associated with ear wax. Also, symptoms of upper airway infection can be confused with AOM.[29] Diagnosis is facilitated when tympanic membrane is explored systematically, carrying out pneumatic otoscopy and using specific diagnostic criteria. Therefore, it is important to improve these aptitudes using appropriate training programs.

REFERENCES

1. American Academy of Pediatrics, American Heart Association. Pediatric Advanced Life Support Provider Manual. U.S.: AHA; 2006. pp. 1-43.
2. van de Beek D, de Gans J, McIntyre P, Prasad K. Corticosteroides para la meningitis bacteriana aguda (Revisión Cochrane traducida). In: La Colaboración Cochrane. Revisiones Cochrane 2008;4. Oxford: Update Software Ltd. Available at: http://www.update-software.com.
3. Warren J, Fromm RE Jr, Orr RA, Rotello LC, Horst HM; American College of Critical Care Medicine. Guidelines for the inter- and intrahospital transport of critically ill patients. Crit Care Med 2004;32:256-262.
4. Orr RA, Felmet KA, Han Y, McCloskey KA, Dragotta MA, Bills DM, et al. Pediatric specialized transport teams are associated with improved outcomes. Pediatrics 2009;124:40-48.
5. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knolich B, et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-1377.
6. Carcillo JA, Fields A; American College of Critical Care Medicine Task Force Committee Members. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. Crit Care Med 2002;30:1365-1378.
7. Dellinger J, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008;36:296-327.
8. Mikkelsen ME, Gaieski DF, Goyal M, Miltiades A, Munson JC, Pines JM, et al. Factors associated with nonadherence to early goal-directed therapy in the emergency department. Chest 2010;138:551-558.
9. Slater A, Shann F, Pearson G, Paediatric Index of Mortality (PIM) Study Group. PIM2: a revised version of the Pediatric Index of Mortality. Intensive Care Med 2003;29:278-285.
10. Pizarro CF, Troster EJ, Damiani D, Carcillo JA. Absolute and relative adrenal insufficiency in children with septic shock. Crit Care Med 2005;33:855-859.
11. Landry DW, Oliver JA. The pathogenesis of vasodilatory shock. N Engl J Med 2001;345:588-595.
12. Hollenberg SM. Vasopressor support in septic shock. Chest 2007;132:1678-1687.
13. Abdel-Aziz M, El-Hoshy H. Acute mastoiditis: a one year study in the pediatric hospital of Cairo University. BMC Ear Nose Throat Disord 2010;10:1-6.
14. Gliklich RE, Eavey RD, Iannuzzi RA, Camacho AR. A contemporary analysis of acute mastoiditis. Arch Otolaryngol Head Neck Surg 1996;122:135-139.
15. Nguyen HB, Corbett SW, Steele R, Banta J, Clark RT, Hayes SR, et al. Implementation of a bundle of quality indicators for

early management of severe sepsis and septic shock is associated with decreased mortality. Crit Care Med 2007;35:1105-1112.
16. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006;34:1589-1596.
17. American Academy of Pediatrics. *Haemophilus influenzae* infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book: 2006 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics; 2006. pp. 310-318.
18. Feigin RD, McCracken GH Jr, Klein JO. Diagnosis and management of meningitis. Pediatr Infect Dis J 1992;11:785-814.
19. Paris MM, Ramilo O, McCracken GH Jr. Management of meningitis caused by penicillin-resistant *Streptococcus pneumoniae*. Antimicrob Agents Chemother 1995;39:2171-2175.
20. Friedland IR, Klugman KP. Cerebrospinal fluid bactericidal activity against cephalosporin-resistant *Streptococcus pneumoniae* in children with meningitis treated with high-dosage cefotaxime. Antimicrob Agents Chemother 1997;41:1888-1891.
21. Ninis N, Philips C, Bailey L, Pollok J, Nadel S, Britto J, et al. The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases. BMJ 2005;330:1475-1478.
22. Launay E, Gras-Le Guen C, Martinot A, Assathiany R, Blanchais T, Mourdi N, et al. Suboptimal care in the initial management of children who died from severe bacterial infection: a population-based confidential inquiry. Ped Crit Care Med 2010;11:469-474.
23. De Oliveira CF, De Oliveira DS, Gottschald AF, Moura JD, Costa GA, Ventura AC, et al. ACCM/PALS haemodynamic support guidelines for paediatric septic shock: an outcomes comparison with and without monitoring central venous oxygen saturation. Intensive Care Med 2008;34:1065-1075.
24. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. Pediatrics 2004;113:1451-1465.
25. Rovers MM, Glasziou P, Appelman CL, Burke P, McCormick DP, Damoiseaux RA, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. Lancet 2006;368:1429-1435.
26. Dowell SF, Butler JC, Giebink GS, Jacobs MK, Jernigan D, Musher DM, et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance: a report from the drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. Pediatr Infect Dis J 1999;18:1-9.
27. Seikel K, Shelton S, McCracken GH Jr. Middle ear fluid concentrations of amoxicillin after large dosages in children with acute otitis media. Pediatr Infect Dis J 1997;16:710-711.
28. Rothman R, Owens T, Simel DL. Does this child have acute otitis media? JAMA 2003;290:1633-1640.
29. Pelton SI. Otoscopy for the diagnosis of otitis media. Pediatr Infect Dis J 1998;17:540-543.