MENINGITIS IN A NEONATE & MEDICAL ETHICS

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Grand Rounds
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OBJECTIVES

- Case presentation
- Common pathogens involved in Meningitis
- Management & Treatment of Meningitis
- Futile care
- Ethical cases
- Conclusion
CHIEF COMPLAINT

- Vomiting and acting fussy x 1 day
Pt is a 3 day old female ex-40 WGA born via normal spontaneous vaginal delivery with no complications.

Presented with 24 hours of acting fussy and decreased po intake. Emesis x 1 of chalky appearing substance.

Parents think pt may have became apneic while in playpen with older sibling earlier in the day, but are unclear about this.

In ED, was noted to have seizure activity x 1-clonus and increased tone throughout.
Maternal history: HIV negative, RPR NR, GC/Chlamydia negative, GBS UNKNOWN

PMHX: none
Medications: none
PSHx: none
FHX: non-contributory
Immunizations: Hep B
Allergies: NKDA
ROS- PERTINENT NEGATIVES

- General: denied recent illness/fevers
- Resp: denied cough/sneezing
- Neuro: denied recent head trauma
- Skin: denied rashes/breaks in the skin
PHYSICAL EXAM

- T 98.8  P 115  R 40  B/P 85/53  Wt: 3Kg
- General: Awake, drowsy
- HEENT: PERRL, full anterior fontanelle, no obvious trauma
- Resp: CTA B
- CV: RRR, no MRG
- Abd: soft, n/t, n/d, bs+
- GU: no rashes or lesions
- Skin: no rashes/lesions/ petechiae
- Neuro: awake, moving spontaneously, DTR present, normal tone
ADMISSION LABS

- WBC: 1.15
- Hb: 13
- HCT: 37.5
- Platelets: 153
- Segs: 3
- Bands: 20
- Lymph: 15
- Mono: 10
Labs Continued

- Na: 135
- K: 5
- Cl: 100
- CO2: 21
- BUN: 15
- Cr: 0.6
- Glucose: 92
- Ca: 9.5
- TP6.4/Alb 2.6/T.bili 8/AST 29/AP 148/ALT 13
CSF RESULTS

- Green, cloudy
- WBC  27, 288
- RBC  15,840
- Neutrophils  88
- Mono  12
- Gram stain: Bacteria + RBC’s present
- Glucose <1
- Protein 2,415
MICROBIOLOGY

- VP negative
- Latex CSF: + S. pneumoniae
- CSF Cx: S. pneumoniae
- BCx: S. pneumoniae
- Ucx: S. pneumoniae & GBS
- HSV CSF PCR Negative
IMAGING STUDIES

- Admission CT HEAD: extensive hypodensity throughout the temporal occipital and parietal lobes predominantly of the white matter but also involving the cortex. Consistent with acute meningitis. Minimal hemorrhage that may be birth related.

- CXR: normal
EEG

- Diffuse slowing with encephalopathy and irritable cortex.
Hospital Course

- Initially started on acyclovir, ampicillin & cefotaxime.

- Loaded with phenobarbital due to initial seizure activity.

- On Day 2 en route to repeat CT (increased lethargy and decreased mental status), became apneic and was intubated.
Hospital Course

- Repeat CT HEAD: evolution and progression of patchy edema with new areas of involvement seen in the cerebellum.

- MRI HEAD: multifocal areas of brain parenchymal involvement to include right posterior inferior cerebellum, pons, midbrain, basal ganglia, thalami and scattered cerebral gray and white matter due to known purulent meningitis.
Once cultures speciated, de-escalated to cefotaxime only.

Had been clinically stable, but repeat EEG done on day 7 showed subclinical status epilepticus and she was re-loaded with phenobarbital & keppra. No further seizures clinically evident and repeat EEG showed resolution of status.
**HOSPITAL COURSE**

- Day 16- after several conversations with the family regarding outcome and prognosis, the decision was made to extubate.

- Initially had apneic episodes, but resolved and she was transferred to the floor.

- As per ID, total of 8 weeks of IV antibiotics.

- A/I workup:
  - IGG, IGA, IGM, IGE WNL
  - Lymphocyte subpopulation WNL
  - CH50 WNL; IRAK4 gene sequence normal
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Pneumococcal and meningococcal meningitis occur with an annual incidence in the range of 4 to 5 and 2.5 cases per 100,000 children younger than 5 years of age, respectively.

Group B *Streptococcus* (GBS) remains the predominant bacterial pathogen in the neonatal population.
COMMON CAUSES OF BACTERIAL MENINGITIS VARY BY AGE GROUP:

- NEWBORNS: GROUP B *STREPTOCOCCUS*, *ESCHERICHIA COLI*, *LISTERIA MONOCYTOGENES*

- INFANTS AND CHILDREN: *STREPTOCOCCUS PNEUMONIAE*, *NEISSERIA MENINGITIDIS*, *HAEMOPHILUS INFLUENZAE* TYPE B

- ADOLESCENTS AND YOUNG ADULTS: *NEISSERIA MENINGITIDIS*, *STREPTOCOCCUS PNEUMONIAE*
**S. PNEUMONIAE**

- Studies in the United States estimate an incidence of 1%-10% of all neonatal sepsis or meningitis.

- *S. pneumoniae* is not part of the usual vaginal flora, and the incidence of its colonization in pregnant women is exceptional (0.03%-0.75% of cases).
Data from the Centers for Disease Control and Prevention from the year 2000 confirmed 17,000 cases per year of invasive pneumococcal disease among children younger than 5 years of age, including 700 cases of meningitis and 200 deaths in the United States.

Children younger than 1 year of age have the highest risk for meningitis, with an estimated incidence of approximately 10 per 100,000 population.
The pathogenesis of pneumococcal meningitis occurs primarily through nasopharyngeal colonization, with subsequent bacteremia and seeding of the choroid plexus.

Although 90 pneumococcal serotypes are known, 7 serotypes (14, 6B, 19F, 18C, 23F, 4, and 9V) have been noted to account for 78% of invasive strains.
VIRAL PATHOGENS

- HSV
- Enteroviruses
CLINICAL MANIFESTATIONS OF MENINGITIS

- Infants younger than 1 month of age who have viral or bacterial meningitis can present with a constellation of constitutional, nonspecific signs, including fever, hypothermia, lethargy, irritability, and poor feeding.

- Signs and symptoms of increased intracranial pressure and meningeal inflammation such as vomiting, apnea, and seizures also can occur.
HISTORY

- For infants, a birth history, maternal GBS colonization status and treatment, and maternal history of sexually transmitted infection should be elicited.

- Infants and children who have bacterial meningitis usually have been healthy previously. It is important for clinicians to ask about and record child care exposure to facilitate chemoprophylaxis in appropriate situations.
Concerning Physical Exam Findings

- Altered levels of consciousness can present as irritability, somnolence, lethargy, or coma.
- Concerning signs and symptoms of increased intracranial pressure include papilledema; diplopia; unilateral or bilateral dilated, poorly reactive pupils; or a bulging fontanelle in infants.
- Although meningismus is suggestive of meningeal irritation, this sign generally is not present in the young infant. Instead, paradoxic irritability is the usual sign of meningeal irritation.
- The infant who has meningitis does not wish to be handled but prefers to remain motionless. Often, the parent has noted this behavior and refrains from holding or rocking the infant.
- Marked irritability with a high-pitched cry may be noted by the clinician while moving the infant during the physical examination.
Suggested algorithm for suspected bacterial meningitis

Mann K, and Jackson M A Pediatrics in Review
2008;29:417-430
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Bacterial meningitis is characterized by CSF pleocytosis (WBC often greater than $1.0 \times 10^3/\text{mcL} \ [1.0 \times 10^9/\text{L}])$, with a predominance of polymorphonuclear leukocytes.

The glucose concentration usually is less than one half of the measured serum value, and the protein value often is greater than 1.0 g/dL (10 g/L).

CSF culture remains the gold standard for diagnosing bacterial meningitis.
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**MANAGEMENT**

- Prompt initiation of therapy, use of the appropriate antimicrobial with correct dosing and duration.
- Admission to PICU is appropriate for children whose GCS scores are less than 8 or who are in shock or have respiratory compromise, focal neurologic findings, or clinical signs of elevated intracranial pressure.
- Therapy **should not be delayed** if CNS infection is suspected.
- If you cannot perform a lumbar puncture or there are contraindications to CSF examination, a blood culture should be obtained and antibiotics administered promptly.
- Among common bacterial pathogens, pneumococcus usually can be identified in the CSF up to several hours after the administration of appropriate drugs, whereas sterilization of meningococcus may occur in less than an hour.
- Therefore, if antimicrobial pretreatment occurs in the setting of meningitis and microbiologic confirmation is not possible, the practitioner needs to continue therapy based on the most likely pathogens.
For infants whose CSF is suspicious for bacterial meningitis, ampicillin (300 mg/kg per day divided every 6 hours) and cefotaxime (200 to 300 mg/kg per day divided every 6 hours) is appropriate.

If the child is younger than 4 to 6 weeks of age, acyclovir (60 mg/kg per day divided every 8 hours) should be added if HSV infection is a concern.

In the young infant, if the Gram stain suggests pneumococcus, vancomycin (60 mg/kg per day given every 6 hours) should be added.
Experimental studies have revealed a correlation between outcome and the severity of the inflammatory process in the subarachnoid space. In animal models of bacterial meningitis, the use of dexamethasone has been associated with decreased inflammation, reduced cerebral edema and ICP, and lesser degrees of brain damage.

Subsequent controlled, double-blind clinical trials demonstrated the beneficial effects of adjunctive dexamethasone in infants and children with Hib meningitis. The incidence of neurologic and audiologic sequelae was significantly decreased on follow-up examination. As a result, the IDSA guidelines recommend adjunctive dexamethasone for these patients.
A meta-analysis by Mongelluzzo et al did not find corticosteroids to be beneficial in children with bacterial meningitis. Survival and time to hospital discharge did not differ significantly between the corticosteroid treatment group and the untreated group.

A prospective, double-blind, placebo-controlled, multicenter trial in adults with bacterial meningitis documented benefit in patients with pneumococcal meningitis but not in others.
Given the lack of a clear benefit favoring the use of dexamethasone in older infants and children and the concerns that such use may lead to decreased antibiotic penetration in the CSF, the decision to give dexamethasone must be made on a case-by-case basis after the potential risks and benefits have been carefully weighed.

The data are likewise insufficient to allow recommendation of adjunctive steroid therapy in neonates with bacterial meningitis.
Intellectual deficits, hydrocephalus, spasticity, blindness, and severe hearing loss are the most common sequelae. Hearing loss occurs in approximately 30% of patients, can be unilateral or bilateral, and is more common in pneumococcal than meningococcal meningitis.

Accordingly, all children who have bacterial meningitis should have their hearing evaluated before hospital discharge. Developmental follow-up is necessary for all children.
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Futile care

The Society of Critical Care Medicine’s Ethics Committee published a consensus statement in which the following definitions of medically futile treatments are offered: Since these conflicts are typically about differences in values rather than disagreements about facts, clinicians should be very cautious about labeling these therapeutic options as futile. Seen in this context, (“futile”) treatments may be classified into four categories:
1) treatments that have no beneficial physiologic effect;

2) treatments that are extremely unlikely to be beneficial;

3) treatments that have beneficial effect but are extremely costly;

4) treatments that are of uncertain or controversial benefit.
Treatments that fall into the first category, i.e., those treatments that offer no physiologic benefit to the patient, should be labeled as futile. Treatments that fall into the other three categories may be considered inappropriate and hence inadvisable, but should not be labeled futile (Lee, 2005).
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On October 13, 1992 Baby K was born at Fairfax Hospital in Virginia. She was born with anencephaly, which means she did not have a cerebral cortex but she did have a brainstem. She had reflexes including sucking, coughing and swallowing, but she was permanently unconscious. She was unable to see, hear or feel pain.

Shortly after birth, Baby K started to experience difficulty breathing and requiring respiratory support with mechanical ventilation. When she was discharged from the hospital, she was placed in a nursing home, but suffered additional episodes of respiratory distress that required multiple hospital visits.
Fairfax hospital tried to convince the mother to sign a do not resuscitate order (DNR), so that they would not have to continually provide what was thought to be futile care.

The mother declined to do so, which then promoted the hospital to file suit with a federal district court stating that they no longer felt there was medically necessity to provide emergency ventilator support to Baby K when she entered the hospital in distress.

Court ruled deemed that withholding care for the baby would violate The Emergency Medical Treatment and Active Labor Act (EMTALA), the Rehabilitation Act of 1973 (the "Rehab Act") and the Americans with Disabilities Act (ADA) (Healthcare ethics, 2013).

Withholding care of this type would also violate the fourteenth amendment of the mother which allows a parent to raise his or her children as they see necessary.
This outcome created quite a stir and it was appealed to the Supreme Court. The Supreme Court refused to entertain the case and the prior ruling was upheld.

Dr. Michael Grodin, a pediatrician who heads the Program on Medical Ethics at the Boston University School of Medicine and Public Health, said that for him, the point was that parents should have enormous discretion to decide the medical care for their children except at the extremes. One extreme is not to treat a treatable condition, while at the other end, there is nothing more extreme than anencephaly.

He said that sustaining the life of an anencephalic baby was the ultimate inappropriate use of health care resources. Although respiratory care was not futile in the sense that it did keep the baby alive, you have to define treatment in terms of the goal of therapy. For a baby that has no brain and is born dying, life for just another minute or another day is not an appropriate goal. It’s saying that it’s the technology that has life, not the patient (Greenhouse, 1993).
In support of the above remarks by Dr. Grodin, is the fact that parents to anencephalic babies are able to make the decision to donate their organs while they are still breathing.

The American Medical Association's Council on Ethical and Judicial Affairs says it is "ethically permissible" to use anencephalic infants as organ donors even while they are still alive (Brown, 1994).
This is of course atypical, since generally a patient must be declared deceased in order to donate organs. But, anencephalic babies will never gain consciousness.

For some parents organ donation is a way to ensure that their baby lives on by giving others the gift of life.

The cost of keeping an anencephalic baby in the hospital is nearly fifteen hundred dollars a day, a strain to both the hospital and the insurance company. This is in part due to the fact that they often require admission to the intensive care unit in order to receive ventilator support.
Opposing views to the above case were expressed by Dr. Dr. Robert M. Veatch, director of the Kennedy Institute of Ethics at Georgetown University, who was actually involved in the trial and testified on behalf of the mother.

He did deem that the baby was brain dead and should not be treated, but reflected on the mother’s right to treat her child however she saw fit and that requesting continued support for her child was well within her parental rights (Greenhouse, 1993).

This case raised many ethical questions. Who has the right to make a decision of whether or not a baby should continue care? Is it the parent who is hoping for a miracle to save the baby? Or is it the physician who is viewing the baby as a biological creature that cannot sustain life without support?
On October 16, 1993 at Southern Regional Medical Center in Georgia, a baby boy who was born premature was gravely ill in the neonatal intensive care unit. He was found to have kidney failure and multiple organ dysfunctions.

The night of his death, his physician, Dr. Eva Carrizales was on call at the hospital. With the baby’s declining state, Dr. Carrizales notified the family that the baby was dying.

Throughout the night his heart rate was steadily dropping and requiring multiple life saving medications in order to help his heart beat. Once his heart rate returned, Dr. Carrizales was overhead by nurses stating that she did not want to get the parents hopes up that the baby would live, when she knew that he was dying.
She was heard by multiple witnesses that she was going to cut off the blood supply to his brain since his dying process could have went on for hours. She compressed his carotid artery and placed her hand over the infant’s mouth, which hastened his death and the baby was soon declared dead (Siegel, 1994).
Dr. Carrizales insisted that she was feeling for a pulse and closed the baby’s mouth only so the family would not see the thick secretions that were coming out.

The case was brought before a grand jury and Dr. Carrizales was found guilty of homicide.

The official autopsy did not show any signs of suffocation or bruising to signify that the physician did indeed smother the baby. But, several witnesses all reporting the same story was what truly led to the guilty verdict.
This case depicts the conflict of emotions that physicians feel and how these actions are perceived by the general public.

Dr. Carrizales did not intend to murder this baby, but wanted to end his suffering. Unfortunately, in the eyes of the law a clear difference is evident between withdrawing care and withdrawing support for life versus hastening death.

Watching a patient die is one of the hardest things a physician has to endure, yet is an unavoidable part of the job description. Ending a patient’s life, regardless of the reasoning behind the decision, is unlawful.
Carrizales was previously revered as a hero by her patients and she believed that a baby should die in someone’s arms rather than hooked up to a machine in an incubator. The controversy surrounding the ruling, prompted additional investigations into Carrizales’ career.

As a result, a discovery was made that there had been another case. In this case, Carrizales quickly pushed potassium chloride into a baby with a low heart rate, whereas the standard practice would have been to slowly infuse the potassium. This solidified the mindset of those who were unsure if this verdict was just.
In the summer of 1988, Sammy Linares was eight months old. He swallowed a balloon and was brought into the emergency department. By the time he reached the hospital he had suffocated. The staff physicians at the Chicago hospital where he was taken, placed him on a ventilator until further studies were completed that investigated his functional ability. These tests showed that there was no brain activity and left the baby in a vegetative state.

The parents wanted the hospital to take Sammy off of the ventilator and allow him to die naturally.

The hospital refused to allow this and explained that taking a baby off of life support was against the hospital policy. After several months of begging to take his child off the ventilator, the father decided to take action.
In December, he disconnected the ventilator, but nurses quickly re-connected it. In April 1989, the father refused to allow his son to persist in a vegetative state any longer and returned to the hospital with a gun.

He disconnected the respirator and allowed his then sixteen month old son to die, which happened shortly after the ventilator was turned off. Once his son died, he gave up his gun and was immediately taken into custody.

The father was charged with first degree murder and assault with a deadly weapon. The decision of the jury found him guilty of assault, but threw out the murder charge.
This case deals with the complex issue of a minor on life support and the difficult decisions both medical staff and families are faced with.

The outcome of the jury supports the notion that parents have the legal right to decide when to cease care of their child if the child is in a state of perpetual un-recovery.

This decision is not an easy decision for any parents to realize, but it may be their given right. There are many limitations to this circumstance, since the patient would have to be deemed clinically brain dead and not just gravely ill.

If a patient still has a chance of a meaningful recovery and the family is pushing to end life support this is another ethical issue that is fraught with its own challenges.
In February of 1994 in Michigan, Dr. Gregory Messenger, a dermatologist, and his wife were expecting their second child. Mrs. Messenger went into early labor and the fetus was confirmed via ultrasound to be twenty-five weeks gestational age at that time. Mrs. Messenger gave birth to a baby boy via cesarean section, Michael Messenger, who weighed one pound and eleven ounces. The family was informed of the outcome of a baby who was facing this degree of prematurity.

“At 6:30 p.m., Dr. Padmani Karna from the NICU staff saw the Messengers in consultation. She told them that the child, at this age, had a 30-50% chance of surviving but a 90% chance of developing intracranial bleeding if it survived, risking some degree of mental and physical handicap. The Messengers at that point instructed Dr. Karna that they did not want the baby resuscitated after birth or placed on intensive life support (Brody, 1995).”
A misunderstanding may have occurred.

When the family went to see their child, they were shocked to learn that the baby was on full ventilator support keeping him alive. At the time of birth, he was cyanotic and required oxygen and resuscitation efforts. By the time the parents saw the baby he had regained a pink color.

During the visit with their child, Dr. Messenger disconnected the ventilator and the baby died soon after. He was brought to trial for manslaughter as a result of this action.

The outcome yielded an acquittal and is clear evidence of how important communication is between families and physicians.
Joelle Rosebush was an eleven year old female that was in a serious motor vehicle accident, which left her with a severed spinal cord at the level of C1. The location of the injury resulted in complete paralysis of the child from the neck down. At the scene of the accident, she went into cardiac arrest and before being resuscitated she suffered severe brain damage- left in vegetative state.

Joelle was under eighteen years old and was a minor in the eyes of the law. She was in a nursing facility where she was unable to breathe on her own and was on a ventilator. After a year of seeing their daughter in this state, Joelle’s parents wanted to move her to a Children’s hospital where she could be taken off of the ventilator and die peacefully.

The facility obtained a temporary restraining order and junction that prevented the transfer of the patient. A Michigan trial court authorized that Joelle’s parents had the right to make decisions for her and this included termination of life support. This decision was appealed by the Oakland County Prosecutor, but the Court of Appeals upheld the decision.
The court also confirmed that an individual does not lose the right to accept or decline medical treatment on account of being incompetent or a minor. In such cases where an individual lacks the capacity to make treatment decisions, another individual acting as that person’s surrogate may exercise this right on the patient’s behalf. Specifically, as to minors such as Joelle, the court held that parents speak for their minor children in matters of medical treatment, including decisions to forego, i.e., withdraw or withhold, life-sustaining measures. The court upheld Joelle’s parents’ right to withdraw support measures that were keeping Joelle alive.”
Medical Ethics in Pediatrics

- Ethical cases can be difficult for both the physician and the families involved.
- Communication is important to avoid additional complications.
- Ethical cases involving the pediatric population can be even harder than in adults.
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CONCLUSION

- *S. pneumoniae* is a rare case of neonatal meningitis.

- Neonatal meningitis is characterized by vague non-specific symptoms.

- Prompt initiation of antibiotics is critical.

- Neurological complications are a common sequelae to meningitis.
Medical ethics is a complicated, controversial issue.

Brain death, futile care, withdrawal of care issues and persistent vegetative states are important ethical dilemmas that require communication and decision making by both parents and physicians.
REFERENCES

- Meningitis. CDC. (2014).
THANK YOU!