MECHANISMS OF HUMAN DISEASE AND PHARMACOLOGY & THERAPEUTICS

SMALL GROUP DISCUSSION

SESSION I

MHD I

Monday, September 9, 2013

STUDENT COPY

Helpful Resources for Session

Murray's Medical Microbiology, 7th edition

Table 15-1, p 147-153 - Overview of Selected Bacterial Pathogens (includes summary of clinical features, epidemiologic features, virulence factors)
Table 15-2, p 153 -155 – Summary of Bacteria Associated with Human Disease
Chapter 18 p 174-187
Chapter 26, p 253- 256

Pathophysiology of Disease: An Introduction to Clinical Medicine, 6th

(Available on line through LUMC Health Science Library E-Books)
Chapter 4, Infectious Diseases – Meningitis (will provide an introduction to the interpretation of cerebrospinal fluid analyses for case 3)

"Introduction to Laboratory Medicine"

Independent learning modules on LUMEN MHD site
The goal of the MHD "Introduction to the Principles of Laboratory Medicine and Laboratory Data Interpretation" modules is to for students to understand the broad principles needed to appropriately use laboratory testing for achieving safe and effective care to patients.

CASE 1

Chief Complaint: Fever and Rash x 2 days

HPI: The patient is a 16 year old female who was well until 2 days prior to admission when she developed a fever and vomiting. The fever was as high as 39.9^{0}C. The emesis was bilious, no blood. On the morning of admission she had loose brown stools, continued fever, and persistent vomiting. She also noticed a rash.
The patient denied headache, photophobia, abdominal pain, and shortness of breath.
The patient's mother brought her to the pediatrician's office. After prompt evaluation the pediatrician established intravenous (IV) access, began IV fluids, called an ambulance and had the patient transported to the hospital where she is being admitted to the Pediatric Intensive Care Unit.

She has had no hospitalizations and no surgeries. She is up to date on her immunizations. She takes no medications. She has no known drug allergies.

She is a high school student. She denies tobacco, alcohol and illicit drug use. She is not sexually active.

Review of Systems
Pulmonary – Denies cough or dyspnea
Genitourinary – She denies dysuria or frequency. Her menstrual period began 4 days ago
Ear, nose throat – She denies sore throat, difficulty swallowing, runny nose, ear pain.

Physical Exam – Blood pressure 76/46, Pulse 120, Respirations 26, Temperature 38.9^{0}C
She is lethargic
There are no oral lesions or ulcers. Her oral mucosa appears dry.
There is bilateral nonpurulent conjunctivitis.
The neck is supple without lymphadenopathy.
Lungs are clear to auscultation and percussion bilaterally.
On cardiovascular exam patient is tachycardic. There is a normal S1 and S2. No murmurs are heard.

The abdomen is non-distended. The bowel sounds are normoactive. There is mild diffuse tenderness throughout on palpation. There is no evidence of rebound or guarding. There is no hepatosplenomegaly.
During pelvic exam a tampon is removed from the vaginal canal. The vaginal mucosa is erythematous. The visualized cervix is normal appearing. There is no pain or masses on bimanual exam.
On skin examination there is an erythematous maculopapular rash which is most prominent on the trunk. It also involves the palms and soles.
Kernig's and Brudzinski's signs are negative.
There are no focal neurologic signs.
Her radial and dorsalis pedal pulses are decreased in intensity.

Laboratory Data

CBC w/ DIFF

WBC	19.5	H	[4.0-10.0] k/ul
RBC	3.49	L	[3.60-5.50] m/ul
Hgb	10.4	L	[12.0-16.0] gm/dl
Hct	31.2	L	[34.0-51.0] %
MCV	82	L	[85-95] fl
MCH	28.3		[28.0-32.0] pg
MCHC	33.3		[32.0-36.0] gm/dl
RDW	16.6	H	[11.0-15.0] %
Plt Count	98	L	[150-400] k/ul
Diff Type	Manual		
Bands%	18		
Bands #	3.5		
Gran	78	H	[45-70] %
Gran #	15.2	H	[2.0-7.0] k/mm3
Lymph	3	L	[20-45] %
Lymph #	0.59		[1.0-4.0] k/mm3
Mono	1		[0-10] %
Mono #	0.2		[0.0-1.0] k/mm3
Eo	0		[0-7] %
Eo #	0		[0.0-0.7] k/mm3
Baso	0		[0-2] %
Baso #	0.0		[0.0-0.2] k/mm3

COMPLETE METABOLIC PANEL

Sodium	139		[136-146] mm/l
Potassium	3.9		[3.3-5.1] mm/l
Chloride	96		[98-108] mm/l
CO2	18	L	[20-32] mm/l
Bun	56	H	[7-22] mg/dl
Creatinine	2.5	H	[0.6-1.4] mg/dl
Glucose	101		[70-110] mg/dl
Albumin	3.2	L	[3.6-5.0] gm/dl
Protein, Total	6.8		[6.5-8.3] gm/dl
Calcium	8.9		[8.9-10.3] mg/dl
Alkaline Phosphatase	112	H	[30-110] iu/l
ALT (SGPT)	204	H	[7-35] iu/l
AST (SGOT)	156	H	[5-40] iu/l
Bilirubin, Total	2.1	H	[0.2-1.4] mg/dl

Urinalysis

Color	YELLOW	[YELLOW]	
Clarity	CLEAR	[CLEAR]	
PH	5.7	[4.5 - 8.0]	
Specific Gravity	1.035	[1.003 - 1.035]	
Protein	2+	[Negative]	
Blood	NEG	[Negative]	
Glucose	NEG	[Negative]	
Ketones	POS	[Negative]	
Bilirubin	NEG	[Negative]	
Urobilinogen	0.4	[0.2 - 1.0]	eu/dl
NITRATE	NEG	[Negative]	
LEUKOCYTES	NEG	[Negative]	
RBC	0 - 2	[0 - 2]	/hpf
WBC	0 - 2	[0 - 5]	/hpf
Nonrenal Epith Cells	0	[0 - 5]	/hpf
Mucous	NEG	[Negative]	

Micro - **Blood Culture** (Accessioned) - F62610

Micro - **Blood Culture** (Accessioned) - F62611

Micro – **Throat Culture** (Accessioned) - F62617

Micro – **Vaginal Culture** (Accessioned) - F62619

Learning Objectives:

1. Develop a problem list for this patient.

The physicians caring for this patient formulated a differential diagnosis, diagnostic and therapeutic plan. On hospital day 2 blood cultures are sterile and throat culture is negative. Vaginal culture is positive for many catalase positive, Gram positive cocci.

2. What organism do you expect to be isolated from the vagina?

3. Based on the data given, this patient's condition is representative of what syndrome? Support your diagnosis.

4. Is there a significance of tampon use in this patient?

5. What virulence factor does this organism produce which is believed to be responsible for the signs and symptoms in this patient?

6. One of the primary principles of therapy for this condition includes aggressive administration of intravenous fluids. Why?

7. Which of the Penicillins would be most appropriate to treat this infection (assuming this is not MRSA)?

8. In addition to the penicillin agents discussed above, it is also recommended that clindamycin be added to the antibiotic regimen. Postulate why (based on the information provided in your P&T Introduction to Antibiotics lectures).

9. Review the Case Images:

Case Images are accessed via the *LUMEN* site on Loyola.wired
Under Second Year…
To Mechanisms of Human Disease…
To Images for S.G. Cases (Second Item under "Resources" on far right of screen)

Figure 1.
Figure 2.
Figure 3.

CASE 2

A 14 month old boy was referred from another hospital for management of an infected ventriculoperitoneal shunt. The baby was born prematurely and had meningomyelocele and hydrocephalus. He underwent surgery for his first shunt when he was 7 weeks old. He had a shunt revision 6 months ago. One week prior to transfer, he was admitted to the hospital for fever and leukocytosis (white blood cell count of 15,000 /mm^3). Needle aspiration of the shunt revealed a cloudy fluid. Gram stain of the fluid revealed Gram positive cocci in clusters. The laboratory further reports that the organisms are coagulase negative.

Learning Objectives

1. What is the most likely pathogen to be recovered from his fluid culture?

2. Where are these organisms normally found in nature and how do they gain access to prosthetic devices (such as ventriculoperitoneal shunts) and intravascular catheters in patients?

3. What virulence factors does this organism possess which allows it to be an opportunistic pathogen? How does this influence treatment decisions?

4. Define “meningomyelocele”, “hydrocephalus”, and ventriculoperitoneal shunt”.

5. Review the Case Images

Figure 1.
Figure 2.
Figure 3.

To see an image of a meningomyelocele via internet go to
Utah Web Path – The Internet Pathology Library
Go to Organ System Pathology -----Central Nervous System Pathology ---Congenital Malformations ----Image 61 --- meningomyelocele gross

http://library.med.utah.edu/WebPath/CNSHTML/CNS026.html

CASE 3

An 18 year-old college student is brought to Student Health by his roommates with a 12 hour history of fever and chills followed by headache and confusion progressing over the preceeding two hours.
He has been in excellent health and takes no medications.
According to his roommates, he does not smoke or use illicit drugs. He rarely drinks beer.

On physical examination the temperature is 40.1^{o}C, pulse 110/min, blood pressure 110/70 and respiratory rate is 24/min. He is somnolent and combative when aroused.

Lung, heart, and abdominal exam are unremarkable (aside from tachycardia).
Fundoscopic examination is normal with no evidence of papilledema.
The neck is rigid. Kernig's sign is positive. Brudzinski's sign is positive. He moves all four of his extremities symmetrically and spontaneously.
The skin shows scattered petechial hemorrhages, 0.3-1.0 cm in diameter on the face, trunk, and extremities.

Lumbar puncture is done and discloses an opening pressure of 24 cm H_2O.

LABORATORY VALUES

Glu & Protein, CSF

Glucose, CSF	9	[45-75] mg/dl
Protein	110	[15-45] mg/dl
Appearance	Cloudy	

Spinal Fluid Cnt

Clarity	Cloudy	[CLEAR]
Color	Tan	[CLLESS]
Volume	2.0 ml	
RBC	0	[0] /ul
WBC	450	[0-8] /ul
Seg	94%	
Lymph	6%	

CBC w/ DIFF

WBC	15.2	H	[4.0-10.0] k/ul
RBC	3.89		[3.60-5.50] m/ul
Hgb	15.4		[12.0-16.0] gm/dl
Hct	46.2		[34.0-51.0] %
MCV	92		[85-95] fl
MCH	30.3		[28.0-32.0] pg
MCHC	33.3		[32.0-36.0] gm/dl
RDW	12.2		[11.0-15.0] %
Plt Count	94,000	L	[150-400] k/ul
Diff Type	Manual		
Bands%	45		
Bands #6.8			
Gran	30		[45-70] %
Gran #	4.5		[2.0-7.0] k/mm3
Lymph	20		[20-45] %
Lymph #	3.0		[1.0-4.0] k/mm3
Mono	5		[0-10] %

Mono #	0.8	[0.0-1.0] k/mm3
Eo	0	[0-7] %
Eo #	0	[0.0-0.7] k/mm3
Baso	0	[0-2] %
Baso #	0.0	[0.0-0.2] k/mm3

BASIC METABOLIC PNL

Sodium	139	[136-146] mm/l
Potassium	4.0	[3.3-5.1] mm/l
Chloride	105	[98-108] mm/l
CO2	19 L	[20-32] mm/l
Glucose	88	[70-100] mg/dl
Bun	24 H	[7-22] mg/dl
Creatinine	1.1	[0.6-1.4] mg/dl
Calclium	9.0	[8.9-10.3] mg/dl

EDUCATIONAL OBJECTIVES

1. What is Kernig's sign and how is it performed? What is Brudzinski's sign and how is it performed?

2. Interpret the cerebrospinal fluid analysis. Develop a differential diagnosis for the CSF findings.

3. What organism(s) would most likely be etiologic agent(s) for this patient's illness?

4. CSF Gram stain demonstrates Gram negative diplococci. Based on the data provided, what is the organism most likely causing disease in this patient? Describe additional Gram stain findings, expected morphology of the colonies, optimal growing conditions, and additional characteristics which identify the organism .

5. How is this organism transmitted? Discuss the epidemiology of this disease. What infection control measures should be instituted while the patient is hospitalized? Do most people who are exposed develop disease?

6. What virulence factor promotes the survival of this organism in the bloodstream?

7. Discuss the antibiotic treatment of this patient's infection. (do not discuss empiric therapy for this disease process,but direct your comments to the specific organism in this case). Discuss your rationale.

8. Should his roommates receive any care?

9. For which patient groups is the meningococcal vaccine recommended?

10. The patient was started on appropriate intravneous antibiotics, but over the next six hours he developed large purpuric skin lesions, refractory hypotension and died. What is this manifestation called?

11. What component of the organism is responsible for the profound systemic inflammatory response?

12. Review the Case Images:

Case 4

A 10-month-old male is brought to the pediatrician's office with a 2 day history of fever to 102^0F and of vomiting and irritability. He had been having cough and runny nose throughout the preceding week.

On physical examination the conjunctiva are normal. There is mild rhinorrhea. The pharynx is normal. Lung examination demonstrates clear breath sounds bilaterally. Abdominal exam is normal. The left tympanic membrane is slightly convex, translucent, and mobile. The right tympanic membrane is bulging, dull and opaque, with purulent fluid visible behind the membrane.

Educational Objectives

1. What is the diagnosis?

2. Viruses and bacteria both are etiologic agents of this disease process. Which bacteria are the most common causes of this infection?

Students: You will have 3 more questions regarding antibiotic therapy for this case/disease process that will be distributed to you during the Small Group Session