Case Presentation

Supervisor: VS洪世文
Presenter: PGY 賴詩涵
102/05/18

Patient's profile

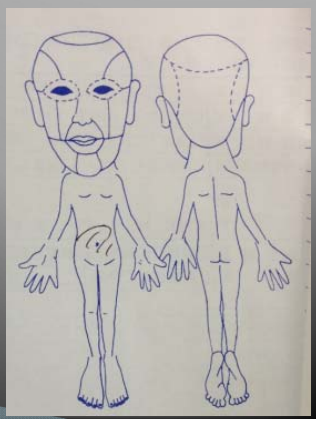
- 67 y/o female
- Admission date: DAY1 (18:54分)
- Chief complaint: Fever with chillness this afternoon
- T/P/R=38.3/75/22, BP=130/56 mmHg, SpO2:100%,, Triage: III
- Cough(+/-), rinorrhea(+) for 2 weeks, vomiting many times(food), diarrhea(-)

Past History

- Allergy: NKA
- DM
- HTN
- Old CVA with left hemiplegia s/p VP shunt, bedridden for 6 years
- TOCC: travel Hx(-), occupation(-)
- cluster Hx(-), contact Hx(-)

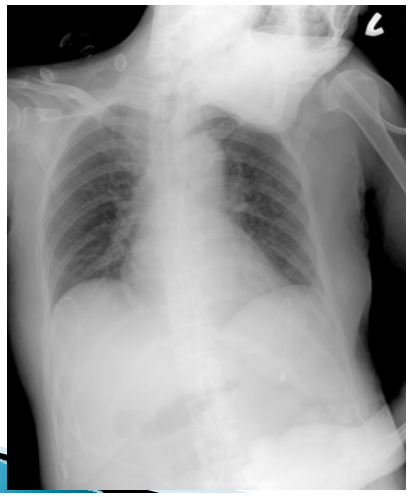
Physical Examination

- Cons: E4V2M4
- Neck: supple
- Chest: clear BS
  - RHB, no murmur
- Abdomen: soft,
  - No abd tenderness
  - No rebound tender
  - No muscle guarding
- Extremity: warm, spasm, no cellulitis, no skin rash

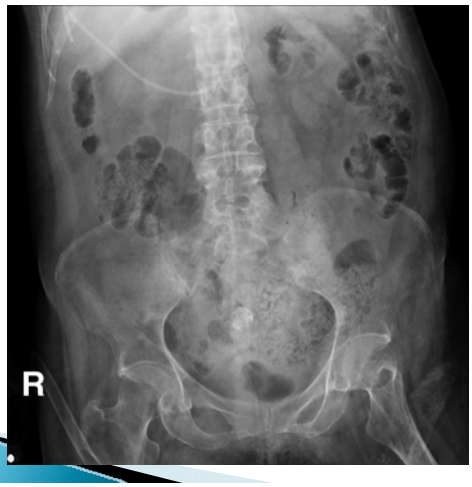


Impression?

CXR



KUB



Lab - DAY1

Blood

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
CBC/Platelet/DC	**********					
WBC	13.9	X1000/ul	3.800	10.000	*H	8.9
RBC	5.06	million	3.800	5.000	*H	
Hb	14.0	gm/dl	11.000	16.000		14.1
Ht	42.4	%	35.000	48.000		
MCV	83.8	fl	81.000	98.000		
MCH	27.7	pg	27.000	32.000		
MCHC	33.0	%	32.000	36.000		
RDW	14.7	%	11.500	14.500	*H	
Platelet	231	x1000/ul	140.000	450.000		221

Biochemistry

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
GOT(AST)	13	U/L	5.000	35.000		11
T-Bilirubin	0.5	mg/dL	0.200	1.300		0.1
BUN	19	mg/dL	8.000	20.000		15
Creatinine	0.59	mg/dL	0.500	1.300		0.65
eGFR	101.98					91.20
Lipase	26	U/L	13.000	60.000		
CRP	0.228	mg/dL	0.000	0.500		0.787

Lab - DAY1

U/A

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
Sediment	**********					**********
RBC	0-1	/HPF	0.000	2.000		0-1
WBC	8-15	/HPF	0.000	5.000		>100
Epithelial cell	0-1	/HPF	0.000	5.000		1-2
Cast	Not Found	/LPF				Not Found
Cast-amount	-					-
Crystal	Amphos	/HPF				Not Found
Cry-amount	+					-
Bacteria	+++					+++
Others	Not Found					Yeast-Like

PH=7.364
PCO2=48.9 mmHg
PO2=18 mmHg
BE=2 mmol/L
HCO3=27.9 mmol/L
TCO2=29 mmol/L
SO2=25 %
NA=134 mmol/L
K=4.6 mmol/L
HCT=42 %PCV
HB=14.3 g/dL

Influenza A, B (negative)

day3-> abdomen echo: negative finding

Blood culture : (negative)

What's your next step?

DAY1 Tentative diagnosis

Fever, cause? Suspect UTI

↓

cefmetazole

↓

day2 fever on and off->review Past hx-> MK102, U/C=yeast, B/C- GPB,(within 6 months) r/o nosocomial infection->ATB: Tatumcef ı clindymycin ı Tamiflu

Day 3 Abdomen echo: negative finding, persistent fever

↓

Day 4 CSF aspiration-

DAY4 Aspiration-CSF

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
Glucose	80	mg/dL	40.000	70.000	*H	61
Total-protein	38.0	mg/dL	15.000	45.000		24.0

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
CSF	**********					**********
Color	Colorless					Colorless
Appearance	Clear					Clear
Pandy's test	Trace					Trace
RBC	3	x10/9ul				10
WBC	39	x10/9ul	0.000	5.000		20
L:N	55%:45%		0.000	5.000		75%:25%

DAY4 DX: VP shunt infection

- Consult NS 陳

=>先內科治療,惡化再開刀remove VP shunt

- Consult INF陳

=>keep ceftazidime, wait for CSF culture

➡ Fever subsided at day5 PM

day6 CSF AEROBIC CULTURE:
Organism:
Escherichia coli --- Heavy

Present Illness

day1 → ER: suspect UTI----→ cefmetazole

Day2-3 → Fever on and off, FUO --→ Abd echo(negative finding)→改 ATB: Tatumcef+ Clindmycin

day4 → FUO, CSF analysis: WBC:39, L/N=55/45, GNB: positive
Consult NS(原VS陳):先內科治療,惡化再開刀remove VP shunt
Consult Inf 陳: keep ceftazidime, wait for CSFculture

day6 → CSF: E.coli, keep ceftazidime(4/29-5/12), B/C*II(negative)

day11 → F/U CSF, improved, WBC:39->13, L/N=95/5, GNB: negative, culture: negative

day13 → Admission

Tentative diagnosis

- VP shunt infection, E.coli, UTI related
- DM
- HTN
- old CVA , hydrocephalus s/p V-p shunt

DAY11 repeat CSF f/u

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
CSF	**********					**********
Color	Colorless					Colorless
Appearance	Clear					Clear
Pandy's test	Negative					Trace
RBC	3	x10/9ul				3
WBC	13	x10/9ul	0.000	5.000		39
L:N	95%:5%		0.000	5.000		55%:45%

day12: CSF GRAM'S STAIN: No bacteria was found.

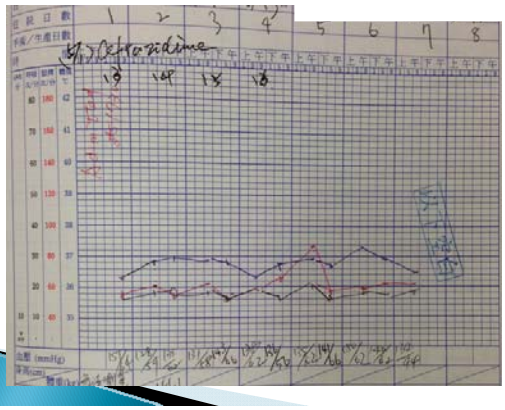
day13:CSF SPECIMEN:
ACID- FAST STAIN: Negative
CSF culture: Negative

DAY14 Lab data follow up

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
Hb	12.6	gm/dl	11.000	16.000		14.0
WBC	6.3	x1000/ul	3.800	10.000		13.9
Differential count	**********					**********
Segmented Neutro.	69.0	%	37.000	75.000		86.0
Lymphocyte	22.3	%	20.000	55.000		7.0
Monocyte	5.7	%	4.000	10.000		3.0
Eosinophil	2.7	%	0.000	5.000		1.0
Basophil	0.3	%	0.000	2.000		0.0
Platelet	295	x1000/ul	140.000	450.000		231

檢驗項目名稱	檢驗值	檢驗值單位	最小參考值	最大參考值	Hi,Lo值	前次檢驗值
BUN	18	mg/dL	8.000	20.000		19
Creatinine	0.48	mg/dL	0.500	1.300	*L	0.59
eGFR	129.40					101.98
Na	139	meq/L	133.000	145.000		136
K	4.5	meq/L	3.300	5.100		5.4
Cl	105	meq/L	96.000	108.000		
CRP	<0.100	mg/dL	0.000	0.500		0.228

Clinical Course DAY13-



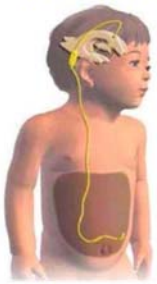
Infections of central nervous system shunts and other devices

Discussion

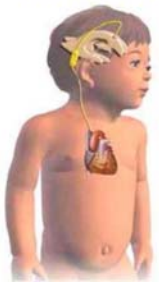
From uptodate

Types of shunts –Internalized shunts

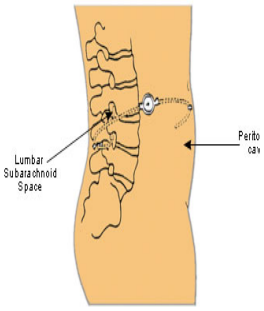
VP SHUNT



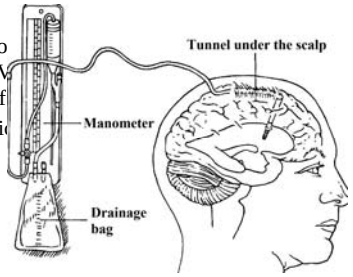
VA SHUNT

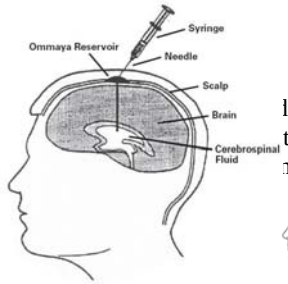


LP shunt

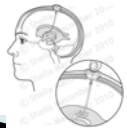


- Externalized devices (ventriculo
  external ventricular drains or EV
  typically placed in the setting of
  for ICP monitoring and therapeuti





levices such as Ommaya
tion of antimicrobial drugs or
also become infected.



INCIDENCE AND RISK FACTORS

Device	The rate of infection
internalized	5 to 15 %
externalized	**5 to 10 %.**

- the initial month after placement.
- Factors associated with increased risk of infection include :
- *Intraventricular hemorrhage*
- *Subarachnoid hemorrhage*
- *Cranial fracture with CSF leak*
- *Craniotomy*
- *Ventriculostomy catheter irrigation*
- *Duration of catheterization (eg, higher risk if device remains in place longer than three to five days)*

MICROBIOLOGY AND PATHOGENESIS

Type of infection	Early infection with skin flora	direct contamination of the distal end of the shunt or hematogenous seeding.
Rate	most common type	10 to 15 % of shunt infections
Cause	via breakdown of the wound or overlying skin.	Distal end shunts - bowel perforation or peritonitis Contamination of externalized devices -cateter irrigation
Timly	at the time of surgery or postoperatively	months after shunt placement
organisms	◦About **1/2** of all shunt infections coagulase-negative staphylococci and about **1/3 of** cases are due to Staphylococcus aureus . ◦Diphtheroids (such **as Propionibacterium acnes** and **Corynebacterium jeikeium**) may also be pathogenic.	streptococci, gram-negative bacteria (including Pseudomonas aeruginosa), anaerobes, mycobacteria and fungi.

CLINICAL MANIFESTATIONS

- Shunt infections can present with few or no symptoms.
- Meningeal symptoms may not be observed
- Fever may or may not be present.

CLINICAL MANIFESTATIONS

- Symptoms may also present with localization to the distal internal (VP or VA shunts) or external end of the shunt:

Infected site	Sympton
Ventriculoperitoneal (VP) shunt infections	**peritonitis**, including fever, abdominal pain, and anorexia.
Ventriculoatrial (VA) shunt infections	fever and evidence of bloodstream infection, from an infected thrombus at the catheter tip. →Endocarditis, septic pulmonary emboli , glomerulonephritis
Distal external shunt infections	soft tissue infection with swelling, erythema, tenderness or purulent drainage.

DIAGNOSIS

- If clinical manifestations suggest the possibility of infection, a diagnostic evaluation should be initiated with cerebrospinal fluid analysis, blood cultures, and imaging.
- **Cerebrospinal fluid**
- **Blood cultures**
- **Imaging**

Cerebrospinal fluid

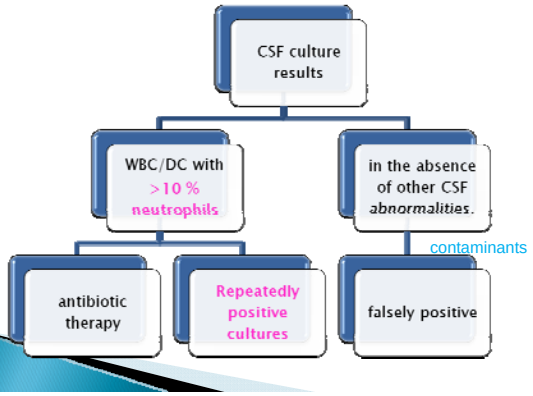
CSF aspiration	**Direct aspiration of the shunt is preferred** or lumbar puncture
CSF examination	white cell count with differential, glucose and protein concentrations, Gram stain, and culture.
Interpretation of CSF parameters	no single clinical or laboratory parameter, including fever, leukocytosis, pleocytosis, or CSF protein and glucose, can reliably predict or exclude a shunt infection.
CNS device-related infections	less inflammation than bacterial meningitis; minic postoperative inflammation.

Cerebrospinal fluid

- The white cell differential may be a useful clue.

WBC/DC with >10 % neutrophils → 90 % sensitive for predicting infection; the NPV= 0.99.

Cerebrospinal fluid



Blood cultures

- Blood cultures should be obtained along with CSF analysis when shunt infection is suspected.
- Their yield is much higher in the setting of ventriculoatrial shunts (VA) than ventriculoperitoneal (VP) shunts (95 versus 23 % in one series).

Imaging

- Neuroimaging studies can be useful to look for evidence of ventriculitis or CSF obstruction.
- Abdominal imaging (computed tomography or ultrasound) may be useful to identify CSF loculations at the distal end of VP shunts.

TREATMENT

- Management of CNS shunt infection should include removal of the device, external drainage, parenteral antibiotics, and shunt replacement.
  - intraventricular antibiotics may be useful if device removal is not feasible
- **Device removal**
- **Antibiotic therapy**
- **Intraventricular antibiotics**

Device removal

- In one retrospective review of 50 CNS shunt infections, for example

Management	shunt removal	external drainage	antibiotics	shunt replacement	Response rates
22	○	○	○	×	95
17	○	×	○	○	65
11	×	×	○	×	35

Acta Neurochir (Wien). 1981;59(3-4):157-66.

The management of cerebrospinal fluid shunt infections: a clinical experience.

James HE, Walsh JW, Wilson HD, Connor JD.

Antibiotic therapy

- Parenteral antibiotic selection should be guided by the results of CSF Gram stain and culture.
- Pending these results, empiric therapy with vancomycin and an agent to cover gram-negative pathogens.
  - **For adults**, an agent to cover nosocomial gram-negative pathogens (ceftazidime, cefepime, or meropenem) is appropriate.
  - **For children**, an agent to cover endogenous gram-negative pathogens (eg, cefotaxime) is appropriate.
- Subsequent antibiotic therapy should be tailored to culture and susceptibility results.

Antibiotic therapy

- **For gram-positive isolates**, vancomycin monotherapy should be continued for methicillin-resistant pathogens, while methicillin susceptible pathogens should be managed with nafcillin or oxacillin.
- Oral rifampin is not routinely added to the above regimens, but may augment treatment in the setting of refractory cases.
- Linezolid and quinupristin-dalfopristin have also been used to treat CNS shunt infections, although they are not first-line therapy .

Intraventricular antibiotics

- This treatment modality is potentially toxic and requires careful preparation and delivery to avoid contamination.
- It may be useful in the following settings:
  - Failure of parenteral therapy to sterilize the CSF
  - Presence of highly resistant organisms sensitive only to antibiotics with poor CSF penetration
  - Circumstances in which shunt devices cannot be removed (including infected Ommaya reservoirs)

Intraventricular antibiotics

- There are no antibiotics that have been approved (FDA) for intraventricular use.
  - The greatest clinical experience has been with vancomycin and gentamicin
  - In one study colistin 10 mg was administered every 12 hours intrathecally without an increase in observed toxicity .
  - Penicillins and cephalosporins should not be given by the intraventricular route because of significant neurotoxicity.
- There is no standardized approach to intraventricular antibiotic dosing.

Recommended dosages of antimicrobial agents administered by the intraventricular route

Antimicrobial agent	Dose
Vancomycin	5-20 mg/day*
Gentamicin	1-2 mg/day in children; 4-8 mg/day in adults*
Tobramycin	5-20 mg/day
Amikacin	5-50 mg/day△
Polymyxin B	2 mg/day in children; 5 mg/day in adults◇
Colistin	10 mg once daily or 5 mg every 12 hours
Quinupristin/dalfopristin	2-5 mg daily
Teicoplanin	5-40 mg daily§
Amphotericin B	0.1-1 mg daily¥

There are no specific data that define the exact dose of an antimicrobial agent that should be administered by the intraventricular route.
* Most studies have used a 10 mg or 20 mg dose.
• Usual daily dose is 1-2 mg for infants and children and 4-8 mg for adults.
△ The usual daily intraventricular dose is 30 mg.
◇ Dosage in children is 2 mg daily.
§ Dosage of 5-10 mg every 48-72 h in one study [Cruciani, M, et al. Clin Infect Dis 1992; 15:285].
¥ Murphy, K. et al. Childs Nerv Syst 2000; 16:4. Shapiro, S. Pediatr Neurosci 1989; 15:125.
Adapted with permission from: Tunkel, AR, Hartman, BJ, Kaplan, SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004; 39:1267.

1. Empiric initial doses are outlined in the table.
2. Subsequent dosing to ensure adequate CSF concentrations has been guided by calculation of the "inhibitory quotient".

Antibiotic duration

Situation	managment
Normal CSF chemistries and CSF cultures (+) for coagulase(–) staphylococci , device is removed	If cultures are negative on the third day after removal → shunt may be replaced
coagulase (–) staphylococci and concomitant abnormal CSF chemistries	antibiotics should be administered for the total time the device remains in place and for at least one additional week following removal. (The CSF should be sterile prior to shunt replacement .)
Shunt infections with more virulent pathogens such as S. aureus and gram-negative bacilli warrant longer therapy;	S. aureus –at least 10 days GNB –14 to 21 days (The CSF should be sterile for 10 days prior to shunt replacement.)
If the device is not removed	antibiotics should be administered for at least 7 to 10 days after sterilization of the CSF

Any CSF parameter can predict shunt infection?

Laboratory Investigation

J Korean Neurosurg Soc 51 : 328-333, 2012

Increased Vascular Endothelial Growth Factor in the Ventricular Cerebrospinal Fluid as a Predictive Marker for Subsequent Ventriculoperitoneal Shunt Infection : A Comparison Study among Hydrocephalic Patients

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Objective : The aim of this study is to determine the association between the cerebrospinal fluid (CSF) biomarkers and inflammation, and the predictive value of these CSF biomarkers for subsequent shunt associated infection.
Methods : We obtained CSF samples from the patients with hydrocephalus during ventriculoperitoneal (VP) shunt operations. Twenty-two patients were enrolled for this study and divided into 3 groups: subarachnoid hemorrhage (SAH)-induced hydrocephalus, idiopathic normal pressure hydrocephalus (INPH) and hydrocephalus with a subsequent shunt infection. We analyzed the transforming growth factor-β1, tumor necrosis factor-α, vascular endothelial growth factor (VEGF) and total tau in the CSF by performing enzyme-linked immunosorbent assay. The subsequent development of shunt infection was confirmed by the clinical presentations, the CSF parameters and CSF culture from the shunt devices.
Results : The mean VEGF concentration (±standard deviation) in the CSF of the SAH-induced hydrocephalus, INPH and shunt infection groups was 236±138, 237±80 and 627±391 pg/mL, respectively. There was a significant difference among the three groups (p=0.01). Between the SAH-induced hydrocephalus and infection groups and between the INPH and infection groups, there was a significant difference of the VEGF levels (p<0.01). However, the other marker levels did not differ among them.
Conclusion : The present study showed that only the CSF VEGF levels are associated with the subsequent development of shunt infection. Our results suggest that increased CSF VEGF could provide a good condition for bacteria that are introduced at the time of surgery to grow in the brain, rather than reflecting a sequel of bacterial infection before VP shunt.

When to remove VP shunt?

BMC Infectious Diseases

BioMed Central

Research article

Open Access

A retrospective study of central nervous system shunt infections diagnosed in a university hospital during a 4-year period

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Published: 08 March 2006

*BMC Infectious Diseases*2006, 6:43 doi:10.1186/1471-2334-6-43

Abstract

Background: Ventriculoperitoneal (VP) shunts are used for intracranial pressure management and temporary cerebrospinal fluid (CSF) drainage. Infection of the central nervous system (CNS) is a major cause of morbidity and mortality in patients with CSF shunts. The aim of the present study was to evaluate the clinical features, pathogens, and outcomes of 22 patients with CSF shunt infections collected over 4 years.

Methods: The patients with shunt insertions were evaluated using; age, sex, etiology of hydrocephalus, shunt infection numbers, biochemical and microbiological parameters, prognosis, clinical infection features and clinical outcome.

Results: The most common causes of the etiology of hydrocephalus in shunt infected patients were congenital hydrocephalus-myelomeningocele (32%) and meningitis (23%). The commonest causative microorganism identified was *Staphylococcus (S.) aureus*, followed by *Acinetobacter spp.*, and *S. epidermidis*.

Conclusion: In a case of a shunt infection the timely usage of appropriate antibiotics, according to the antimicrobial susceptibility testing, and the removal of the shunt apparatus is essential for successful treatment.

Table 3: Microbiologic profile of CSF shunt infections attacks

Organism	Incidence (%)
Staphylococcus aureus	6 (30)
Acinetobacter spp.	4 (20)
Staphylococcus epidermidis	3 (15)
Pseudomonas aeruginosa	2 (10)
Klebsiella pneumoniae	1 (5)
Escherichia coli	1 (5)
Enterobacter aerogenes	1 (5)
Enterococci D group	1 (5)
Flavobacterium odoratum	1 (5)
Total	20 (100)

Table 4: Previously published microbiologic profile of CSF shunt infections[a]

Organism	Incidence (%)
Staphylococcus epidermidis	32–70
Staphylococcus aureus	12–48
Streptococcal species	6–10
Enteric Gram- negative bacilli	6–20
Anaerobes	6

[a] Pooled data [3,11,15,16]

1.Infection remains the most serious complication of VP shunt placement.
2. Catheter should be inserted under aseptic techniques and should not be replaced unless it is clinically demonstrated such as CSF shunt dysfunction etc.
3.In case of a catheter infection, it is both necessary to remove the shunt and commence the systemic antibiotic treatment.
4. Timely usage of appropriate antibiotics according to the antimicrobial susceptibility testing is essential for successful treatment.

Back to our patient

VP shunt infection, E.coli, UTI related

↓

ATB: ceftazidime(4/29-5/14)
S/S improved, keep VP shunt

↓

Prevent recurrent UTI, VP shunt infection

Thank you for attention!