How to diagnose ventricular shunt infections?

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ESCMID Study Group for Infectious Diseases of the Brain – ESGIB
Disclosure of speaker’s interests

<table>
<thead>
<tr>
<th>(Potential) conflict of interest</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td>Potentially relevant company relationships in connection with event</td>
<td>No</td>
</tr>
</tbody>
</table>

- Sponsorship or research funding
- Fee or other (financial) payment
- Scientific committee

- Gilead
- Astellas
- Correvio
- Mylan
- Pfizer
- Shionogi
- Biomérieux
Menu

Clinical cases
- Ventriculo-atrial shunt infection
- Ventriculo-peritoneal shunt infection

Biological tests for diagnosis of ventricular shunt infections
- Blood
- CSF

Imaging studies
- Brain imaging
- Others

Messages
Ventricular shunts
- Permanent catheters
- Proximal end = cerebral ventricle
- Distal end = peritoneal, atrial, or pleural
- Pressure-regulating valve
- +/- Reservoir for percutaneous access
Native Valve Endocarditis Due to *Corynebacterium striatum*: First Reported Case of Medical Treatment Alone

A 24-year-old man was admitted to the hospital because of a persistent unexplained fever. His medical history was remarkable for congenital hydrocephalus that led to complete paraplegia and required an ventriculoatrial shunt at the age of 2 months. The shunt catheter was replaced when he was 16 years old because the distal extremity had migrated into the pulmonary artery. He had had an isolated fever 7 weeks before the current admission.

*C. striatum* was isolated in three sets of blood cultures. A trans-thoracic echocardiogram revealed a 10-mm vegetation on the pulmonary valve that was close to the distal extremity of the ventriculoatrial shunt catheter and that was fluttering in the pulmonary artery. A transesophageal echocardiogram confirmed the pulmonary valve vegetation and did not reveal vegetation on the catheter.
43-year old man

- Commercial truck driver
- Ventriculoperitoneal shunt at birth
- 3 week-history of minor abdominal pain + nausea
- No fever
- Abdominal tenderness
- WBC 8,000/mm³
- CRP 22 mg/L
II. What are the Typical Cerebrospinal Fluid Findings in Patients with Healthcare-Associated Ventriculitis and Meningitis?

Cell Count, Glucose, and Protein Recommendations

13. Abnormalities of CSF cell count, glucose, and/or protein may not be reliable indicators for the presence of infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).

14. Normal CSF cell count, glucose, and protein may not reliably exclude infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).

Tunkel AR et al. Clin Infect Dis 2017
Basel, Switzerland, 1996-2006

Adults & children (>12 year-old)

CSF shunts infections (n=78)
- Ventriculoperoitoneal (n=65)
- Ventriculoatrial (n=7)

Route of infection
- Intra-operatively (n=56)
- Contiguous (n=21)
- Hematogenous (n=1)
Table 3. Laboratory analysis of CSF samples from patients with CSF shunt–associated infection.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leukocyte count</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;5 × 10^6 cells/L, no. (%) of episodes</td>
<td>48/60 (80)</td>
</tr>
<tr>
<td>Median value, ×10^6 cells/L (range)</td>
<td>61 (0.3–5010)</td>
</tr>
<tr>
<td><strong>Granulocyte count</strong></td>
<td></td>
</tr>
<tr>
<td>≥1 × 10^6 cells/L, no. (%) of episodes</td>
<td>46/60 (77)</td>
</tr>
<tr>
<td>Median value, ×10^6 cells/L (range)</td>
<td>32 (0–3006)</td>
</tr>
<tr>
<td><strong>Lactate level</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;1.9 mmol/L, no. (%) of episodes</td>
<td>34/42 (81)</td>
</tr>
<tr>
<td>Median value, mmol/L (range)</td>
<td>4 (1–14)</td>
</tr>
<tr>
<td><strong>Total protein level</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;0.45 g/L, no. (%) of episodes</td>
<td>36/62 (58)</td>
</tr>
<tr>
<td>Median value, g/L (range)</td>
<td>0.8 (0.1–36)</td>
</tr>
<tr>
<td><strong>CSF-to-blood glucose ratio</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.5, no. (%) of episodes</td>
<td>16/31 (52)</td>
</tr>
</tbody>
</table>
Characteristics and Treatment Outcome of Cerebrospinal Fluid Shunt–Associated Infections in Adults: A Retrospective Analysis over an 11-Year Period

Anna Conen,1 Laura Naemi Walti,1 Adrian Merlo,2 Ursula Flückiger,1 Manuel Battegay,1 and Andrej Trampuz1,3

A

P = .016

P < .001

P = .745

CSF leukocyte count (×10^6 cells/L)

Ventricular

Lumbar

Valve

8.5 (0.3-2020)

573 (1-5010)

484 (3-2750)

n=40

n=22

n=11

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B

\[ P = .002 \]

\[ P = .001 \]

\[ P = .597 \]

CSF granulocytes (%)

Ventricular  
Lumbar  
Valve

Site of CSF collection

n=40  n=22  n=11

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\[ P = .783 \]

\[ P = .042 \]

\[ P = .052 \]

$\begin{array}{c}
\text{Ventricular} \\
\text{Lumbar} \\
\text{Valve}
\end{array} \]

$\begin{array}{c}
\text{CSF lactate (mmol/l)} \\
2.6 \ (1.2-13.8) \\
6.0 \ (1.4-14.3) \\
3.8 \ (1.5-8.3)
\end{array} \]

\[ n=40 \quad n=22 \quad n=11 \]
16. CSF cultures are the most important test to establish the diagnosis of healthcare-associated ventriculitis and meningitis (strong, high).

17. If initial CSF cultures are negative in patients with CSF shunts or drains with suspected infection, it is recommended that cultures be held for at least 10 days in an attempt to identify organisms such as *P. acnes* (strong, high).
18. If a CSF shunt or drain is removed in patients suspected of having infection, cultures of shunt and drain components are recommended (strong, moderate).

19. If a CSF shunt or drain is removed for indications other than infection, cultures of shunt or drain components are not recommended (strong, moderate).
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CSF overall 66%

<table>
<thead>
<tr>
<th>Site of specimen collection</th>
<th>Positive culture (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound swab (n = 28)</td>
<td>93%</td>
</tr>
<tr>
<td>Shunt tip (n = 55)</td>
<td>78%</td>
</tr>
<tr>
<td>CSF from shunt valve (n = 11)</td>
<td>91%</td>
</tr>
<tr>
<td>Ventricular CSF (n = 40)</td>
<td>70%</td>
</tr>
<tr>
<td>Lumbar CSF (n = 22)</td>
<td>45%</td>
</tr>
<tr>
<td>Blood culture (VA shunt) (n = 6)</td>
<td>83%</td>
</tr>
<tr>
<td>Blood culture (VP shunt) (n = 47)</td>
<td>11%</td>
</tr>
</tbody>
</table>
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Anna Conen, Laura Naemi Walti, Adrian Merlo, Ursula Fluckiger, Manuel Battegay, and Andrej Trampuz

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Overall (n = 78)</th>
<th>Earlya (n = 48)</th>
<th>Delayeda (n = 22)</th>
<th>Latec (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>29 (37)</td>
<td>19</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>14 (18)</td>
<td>9</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>7 (9)</td>
<td>5</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td>3 (4)</td>
<td>2</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>3 (4)</td>
<td>3</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Nonfermenters</td>
<td>2 (3)</td>
<td>...</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus species</td>
<td>1 (1)</td>
<td>...</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>12 (15)</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Culture negative</td>
<td>7 (9)</td>
<td>6</td>
<td>1</td>
<td>...</td>
</tr>
</tbody>
</table>

a <1 Month after shunt surgery.
b 1–12 Months after shunt surgery.
c >12 Months after shunt surgery.

Sonication of catheter tips for improved detection of microorganisms on external ventricular drains and ventriculo-peritoneal shunts

Gregory F. Jost\textsuperscript{a,*}, Morten Wasner\textsuperscript{a}, Ethan Taub\textsuperscript{a}, Laura Walti\textsuperscript{b}, Luigi Mariani\textsuperscript{a}, Andrej Trampuz\textsuperscript{c}

### Data from patients with ventriculo-peritoneal shunts

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, sex</th>
<th>Dx</th>
<th>Shunt (days)</th>
<th>Sonication VCT (organism/CFU)</th>
<th>Sonication PC (organism/CFU)</th>
<th>CSF culture (organism/quantity)</th>
<th>Meningitis by CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75, M</td>
<td>Infection</td>
<td>24</td>
<td>CoNS/&gt;100</td>
<td>CoNS/57</td>
<td>CoNS/++</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>20, M</td>
<td>Infection</td>
<td>283</td>
<td>CoNS/&gt;20</td>
<td>CoNS/&gt;1000</td>
<td>CoNS/++</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>62, M</td>
<td>Infection</td>
<td>552</td>
<td>\textit{E. coli}/&gt;14000</td>
<td>\textit{E. coli}/&gt;10\textsuperscript{5} \textit{Kle. ox}/&gt;10\textsuperscript{5}</td>
<td>\textit{E. coli}/+++</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>50, M</td>
<td>Infection</td>
<td>NA</td>
<td>\textit{P. aerug}/400</td>
<td>NA</td>
<td>\textit{P. aerug}/+++</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>60, M</td>
<td>Infection</td>
<td>8</td>
<td>\textit{E. coli}/100</td>
<td>NA</td>
<td>\textit{E. coli}/+</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>43, F</td>
<td>Infection</td>
<td>NA</td>
<td>CoNS/&gt;1000</td>
<td>CoNS/&gt;1000</td>
<td>NA</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>28, M</td>
<td>Dysfunction</td>
<td>32</td>
<td>\textit{S. aureus}/&gt;1000</td>
<td>NA</td>
<td>Sterile</td>
<td>No</td>
</tr>
<tr>
<td>8a, 8b</td>
<td>70, M</td>
<td>Dysfunction</td>
<td>1085, 105</td>
<td>CoNS/(-)</td>
<td>NA</td>
<td>Sterile</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>83, M</td>
<td>Dysfunction</td>
<td>365</td>
<td>CoNS/(-)</td>
<td>NA</td>
<td>Sterile</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>67, F</td>
<td>Dysfunction</td>
<td>264</td>
<td>Sterile</td>
<td>NA</td>
<td>Sterile</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>35, M</td>
<td>Dysfunction</td>
<td>NA</td>
<td>CoNS/(-)</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>70, F</td>
<td>Pinealis cyst</td>
<td>107</td>
<td>\textit{P. acnes}/&gt;1000</td>
<td>NA</td>
<td>Sterile</td>
<td>No</td>
</tr>
</tbody>
</table>
20. Blood cultures are recommended in patients with suspected ventriculocisternal shunt infections (strong, high).

21. Blood cultures may be considered in patients with ventriculoperitoneal and ventriculopleural shunts (weak, low).
Table 6. Source of positive cultures in various types of cerebrospinal fluid shunt.

<table>
<thead>
<tr>
<th>Source</th>
<th>Ventriculo-atrial (48)</th>
<th>Ventriculo-peritoneal (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>95 (42)</td>
<td>20 (10)</td>
</tr>
<tr>
<td>CSF (ventricular or lumbar)†</td>
<td>58 (26)</td>
<td>79 (14)</td>
</tr>
<tr>
<td>Urine</td>
<td>16 (19)</td>
<td>0 (11)</td>
</tr>
<tr>
<td>Shunt fluid</td>
<td>83 (6)</td>
<td>100 (7)</td>
</tr>
<tr>
<td>Wound</td>
<td>62 (8)</td>
<td>100 (5)</td>
</tr>
</tbody>
</table>
30. An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of healthcare-associated bacterial ventriculitis and meningitis (weak, moderate).

31. An elevated serum procalcitonin may be useful in differentiating between CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection (weak, low).
32. Nucleic acid amplification tests, such as PCR, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low).

33. Detection of β-D-glucan and galactomannan in CSF may be useful in the diagnosis of fungal ventriculitis and meningitis (strong, moderate).
Polymerase Chain Reaction for the Rapid Detection of Cerebrospinal Fluid Shunt or Ventriculostomy Infections

- Alabama, USA
- Retrospective analysis of 86 CSF (shunt taps) with suspicion of CSF shunts infection

- 16S rRNA + specific primers
  - 18 (21%) culture + / PCR +
  - 30 (35%) culture - / PCR –
  - 42 (49%) culture – PCR +

- Among the 56 PCR +
  - *S. aureus*, n=40
  - *C. acnes*, n=30
IV. What is the Role of Imaging in Patients with Suspected Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

34. Neuroimaging is recommended in patients with suspected healthcare-associated ventriculitis and meningitis (strong, moderate).

36. In patients with infected ventriculoperitoneal shunts and abdominal symptoms (eg, pain or tenderness), an ultrasound or computed tomography (CT) of the abdomen is recommended to detect CSF loculations at the shunt terminus (strong, moderate).
Proposed algorithm for decision making in management of abdominal pseudocyst secondary to ventriculoperitoneal shunt
Management of infections associated with neurosurgical implanted devices

Anna Conen\textsuperscript{a}, Christoph A. Fux\textsuperscript{a}, Peter Vajkoczy\textsuperscript{b} and Andrej Trampuz\textsuperscript{c}

**Shunt-associated infection**

**Diagnostic:**
- CSF sample (valve puncture)
- Blood cultures

- No ventriculitis / meningitis / abscess
- No dysfunction
- No erosion (intact skin and gut)

**AND**
- Early infection

**AND**
- Microorganisms known to be susceptible to anti-biofilm antibiotics

**Empirical antimicrobial therapy in case of pathological CSF results**
- Vancomycin IV PLUS
- Ceftriaxone or cefepime/cefazidime IV (according to local surveillance data)

**Yes**

- Shunt retention or immediate reinsertion possible

- 12 weeks anti-biofilm treatment (usually 2 weeks IV then 10 weeks oral treatment)

**Adapt antimicrobial treatment to culture results**

**No**

- Remove shunt, treat infection, insert intercurrent EVD/ELD if necessary

- Reinsert shunt once infection is cleared, usually after 7-21 days (dependent on microorganism, extent of infection, CSF results)

- CSF culture + at reinsertion: 12 weeks anti-biofilm treatment
- CSF culture - at reinsertion: 4 weeks anti-biofilm treatment

Diagnostic Approach to Health Care- and Device-Associated Central Nervous System Infections

Clinical Algorithm

Recent Surgery or CNS Device Placement (e.g. EVD)
- Unresponsive or Comatose
  - Clinical Signs & Symptoms
    - Persistent or Recurrent Fever
    - New significant or increasing leukocytosis
  - Evaluate for systemic infection and other causes of clinical signs and symptoms; send CSF concomitantly if high suspicion
- Responsive or Awake
  - Clinical Signs & Symptoms
    - Persistent or Recurrent Fever
    - New significant or increasing leukocytosis
    - New seizures
    - Nausea
    - New or worsening headache
    - Neurological Decline
  - Evaluate for systemic infection and other causes of clinical signs and symptoms; send CSF concomitantly if high suspicion

Remotely Placed Permanent Devices (e.g. shunt)
- Clinical Signs & Symptoms
  - Persistent or Recurrent Fever
  - New significant or increasing leukocytosis
  - New seizures
  - Nausea
  - New or worsening headache
  - Neurological Decline
  - Evaluate for systemic infection plus brain imaging
    - High suspicion CNS infection
      - Abnormal imaging
      - Abnormal clinical signs
      - No other cause of illness identified
      - Send CSF from EVD or shunt if present; lumbar puncture if EVD or shunt not present
      - Treatment and additional studies (e.g., brain imaging) based on CSF findings and clinical course
    - Intermediate suspicion CNS infection
      - Borderline clinical symptoms
      - Normal imaging
      - No other cause of illness identified
      - Start antibiotics based on CSF findings
    - Low suspicion CNS infection
      - Normal imaging
      - Other likely cause of illness identified (e.g., pneumonia)
      - Treatment based on CSF findings
      - Treat other causes; consider CSF if no improvement
Infection of cerebrospinal fluid (CSF) shunts is a common occurrence and can often be difficult to diagnose using standard analysis of shunt fluid. This article presents the first case report on the diagnosis of a CSF shunt infection on FDG PET scan. A 26-year-old female underwent ventriculoperitoneal shunt placement after developing a pseudomeningocele subsequent to a suboccipital craniectomy for Chiari malformation. Two months later, the patient presented with abdominal pain and non-specific symptoms and was found to have a perisplenic abscess for which she was adequately treated. Failure of her symptoms to solve and an initial negative shunt CSF analysis prompted the search for other sources of infection. An FDG PET scan performed a week later found evidence of increase tracer uptake around the distal tip of the catheter and a repeat shunt CSF analysis showed evidence of CSF infection. FDG PET may be useful in diagnosing shunt related infections in case of high clinical suspicion when standard diagnostic modalities fail to diagnose hardware infection.
Conclusion: Diagnosis of CSF shunt infection is tricky!

- Clinical presentation often non-specific

- CSF difficult to interpret
  - Different yields with different sites of sampling
  - Thresholds poorly defined (cells, protein, glucose, lactate)
  - Literature data limited
  - Prolonged culture (10 days) ↔ *C. acnes*
  - PCR

- Blood cultures for suspicion of ventriculoatrial shunt infection

- Sonication if shunt explanted?

- Imaging studies
  - Brain imaging if suspicion ‘moderate’ or ‘high’
  - Abdominal CT or US if ventriculoperitoneal shunts
  - PET/CT?