

Good morning pharmacists!

Case nr 1

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Conflict-of-interest disclosure

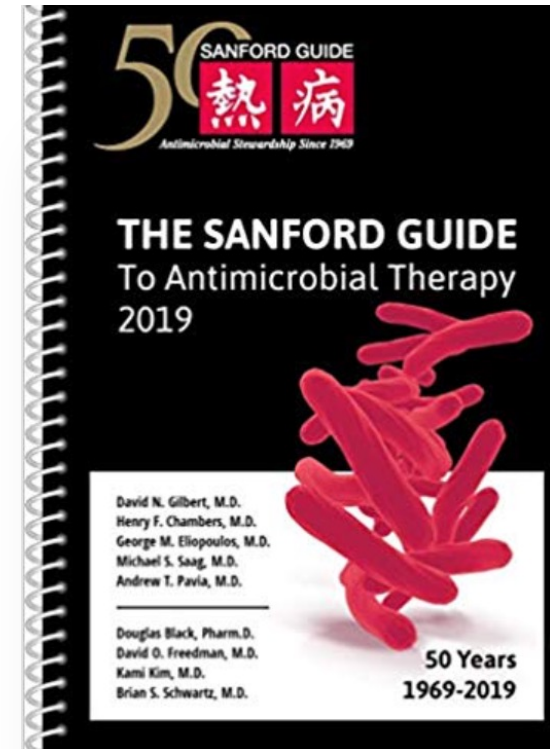
- Nothing to declare

89 years old woman

- 24.11.19. Hospitalised to the department of cardiology

Complaints:

- fever (39⁰C), dizziness
 - No dyspnoea, dysuria, diarrhoea, nausea, headache
 - Venous leg ulcers
- 60kg



At the day of admission

Medical history

- Hypertension
- Heart failure
- Type 2 diabetes
- Chronic renal failure (eGFR ~30)
- Chronic venous leg ulcers, recurrent soft tissue infections – 1 week ago treated with amoxicillin-clavulanic acid tablets

Medication at home:

- T. Metoprolol 50mg od
- T. Furosemide 60mg od
- T. Linagliptin 5mg od

At the day of admission

Relevant analyses

- Influenza A, B and RSV RNA negative
- WBC 11.4 (3.5-8.8 E⁹/L)
- CRP 49 (<5 mg/L)
- Procalcitonin 0.16 (<0.05 µg/L)
- Creatinine 158 (45-84 µmol/L)
- eGFR (CKD-EPI) 25 (>90 mL/min/1,73m²)
- Albumine 24 (35-52 g/L)
- Urine: leucocytes, nitrites (negative)

Other tests

- Chest X-ray: no signs of pneumonia
- BP 94/41 mmHg

Q1. What could be the initial diagnosis of infection?

- A. Pneumonia
- B. Soft-tissue infection
- C. Urinfection
- D. Infection with unclear location
- E. Influenza
- F. RSV virus

Influenza A, B, RSV RNA negative
WBC 11.4 (3.5-8.8 E⁹/L)
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Creatinine 158 (45 .. 84 µmol/L)
eGFR (CKD-EPI) 25
Chest X-ray: no signs of pneumonia
BP 94/41 mmHg
Fever (39°C)
No dyspnoea, dysuria, diarrhoea,
nausea, headache
Venous leg ulcers

Q2. Empiric therapy at the day of admission was started with?

- Current diagnosis: infection with unclear location
 - A. Cefuroxime
 - B. Penicillin-G
 - C. Nitrofurantoin
 - D. Amoxicillin-clavulanic acid
 - E. Meropenem
 - F. TMP/SMX

WBC 11.4 (3.5- 8.8 E9/L)
CRP 49 (<5 mg/L)
Procalcitonin 0.16 (<0.05 µg/L)
Creatinine 158 (45-84 µmol/L)
eGFR (CKD-EPI) 25

Q3. What i/v dose of Amoxicillin-clavulanic acid would you suggest?

- A. 1000/200mg q8h
- B. 1000/200mg initially then 500/100mg q12h
- C. 500/100mg q24h
- D. 1000/200mg initially then 500/100mg q24h
- E. 500/100mg q12h

High amoxicillin doses if patient has renal failure
– risk of cristalluria

WBC 11.4 (3.5-8.8 E⁹/L)
CRP 49 (<5 mg/L)
Procalcitonin 0.16 (<0.05 µg/L)
Creatinine 158 (45 - 84 µmol/L)
eGFR 25 mL/min/1,73m²

Day 1-3

- CRP increased 62 -> 223mg/l
- Diagnosis still unclear: Infection of the leg ulcer? Pneumonia?

Q4. Which pathogen was growing from the leg ulcer culture?

A. *Haemofilus influenzae*

B. *Streptococcus pneumoniae*

C. *Staphylococcus aureus*

D. *Streptococcus pyogenes*

All skin ulcers become colonized,
subsequent infection may be local or
progress to bacteremia
Polymicrobial, incl skin microflora,
aerobic and anaerobic gram-negative bacilli

Day 1-3

- *Staphylococcus aureus* was **MSSA** (methicillin-susceptible)
- Amoxicillin-clavulanic acid is ongoing treatment

Q5. Which antibiotics would be acceptable as primary regimen

- A. Vancomycin 15mg/kg iv q8-12h (MRSA regimen)
- B. Oxacillin 2gm iv q4h
- C. TMP-SMX 8mg TMP/kg/day divided q12h
- D. Cefazolin 2gm iv q8h

Day 4

- CRV rised to 278mg/l; antibacterial treatment changed to ertapenem
 - **Q6 What would be the suitable dose for our patient?**
- A. 30 mg/kg/day divided q12h (paediatric dose)
- B. Loading dose 1gm iv q24h, followed by 0.5gm q24h (reduced dose if eGFR < 30)
- C. 1gm iv q24h (normal renal function dose)
- D. 1gm iv q12h

CRP 278 (<5 mg/L)
eGFR 25 mL/min/1,73m²

SMPC: There are inadequate data on the safety and efficacy of ertapenem in patients with severe renal impairment to support a dose recommendation. Therefore, ertapenem should not be used in these patients

Day 5-7

- CRV decreased -> 220 -> 107 mg/L
- Day 5: generalised epileptic seizure (< 1min) -> im diazepam
 - MRT from the head - no changes
 - Fever 37.9°C
- Day 6: no seizures, fever 37.7°C
- Day 7: several seizures -> im diazepam -> iv valproic acid 800mg bolus
- > infusion 60mg/h
- Epileptic status suspected -> transferred to ICU

Day 7 at the ICU

- Comatose
- No neurological infection diagnosed
- **Q7.** Which medicines could have seizures as side effect:

- A. Metoprolol
- B. Furosemide
- C. Linagliptin
- D. Ertapenem
- E. Valproic acid

Seizures have been reported in patients treated with ertapenem. Seizures occurred most commonly in elderly patients and those with pre-existing CNS disorders and/or compromised renal function.

Albumine 24 (35 .. 52 g/L), ertapenem protein binding 95%

Day 7 at the ICU

- eGFR 33 mL/min/1,73m² → ertapenem dose increased from 500mg od to 1gm od
- CRP 34 mg/L
- Procalcitonin 0.08 µg/L

Valproate level at the ICU

- Valproate levels (infusion 80mg/h -> 120mg/h (max daily dose))
 - Day 7: 23.2 (ref 50-100 mg/L)
 - Day 8: 24.1 mg/L
 - Day 9: 38.9 mg/L

- Patient still unconcious

- **Q8. Why valproic acid concentration is low? Any interactions?**

- A. Metoprolol
- B. Furosemide
- C. Linagliptin
- D. Ertapenem
- E. Valproic acid

Decreases in valproic acid levels that may fall below the therapeutic range have been reported when valproic acid was co-administered with carbapenem. The lowered valproic acid levels can lead to inadequate seizure control; therefore, concomitant use of ertapenem and valproic acid/sodium valproate is not recommended and alternative antibacterial or anti-convulsant therapies should be considered.

Days 10-11

- CRP 25
- Ertapenem stopped
- Day 11: „seizures“ stopped
- Valproate level 52 mg/L (ref 50-100 mg/L)
- Day 12: patient was discharged from the ICU to the department of internal medicine for follow up