DR-TB

Case-based discussion

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DES Maladies Infectieuses
04/10/2024

european respiratory society every breath counts

Case 1 – history

- 39 years old, male
- BMI 22 kg/m^2
- Small **weight loss**
- **Productive cough** for last 3 months, recently treated with large-spectrum antibiotic treatment for pneumonia (levofloxacin) with no response

What else would you like to know?

Case 1 – history

- 39 years old, male
- BMI 22 kg/m^2
- Recent, small **weight loss**
- **Productive cough** for last 3 months, recently treated with large-spectrum antibiotic treatment for pneumonia (levofloxacin) with no response

- No known comorbidities
- No allergies
- No previous TB treatment
- No immigration history, occasional short travels for tourism (India, South Africa)
- Active smoker (10 pack-year), moderate drinker (5 alcohol units/week), occasional use of injectable recreational drugs
- Recent unprotected sex with different partners

Case 1 – Diagnostic work-up

Full blood count and biochemistry

- Full blood count: normal
- Electrolytes, renal function: normal
- ALT: 90 U/L (3 x ULN), AST: 62 U/L (2 x ULN)
- Bilirubin (total, direct), HbA1c, Serum albumin: normal

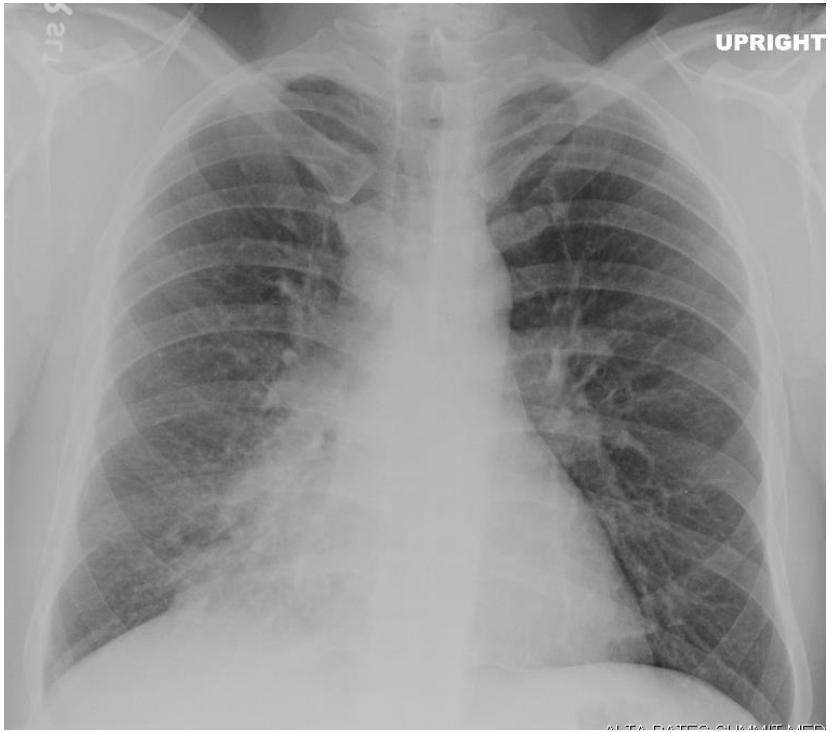
Serology

- HIV: negative, HBV: all negative
- **HCV: positive, HCV-RNA: 5.7 log copies/mL; HCV genotype: 3**

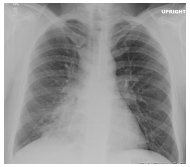
Case 1 – Imaging

Any other imaging?

- Abdomen US: no signs of liver cirrhosis, no focal lesions in the liver
- Fibroscan: F1 (minimal fibrosis)



Case 1 – Diagnostic work-up (2)



Microbiology

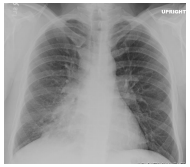
- Sputum smear (x3): positive (+)
- Sputum cultures for mycobacteria: ongoing

Anything else?

GeneXpert MTB/RIF Ultra on sputum: MTB detected, *rpoB* mutation detected

GeneXpert MTB/XDR on sputum sample: MTB detected; isoniazid: *inhA* & *katG* mutation; no mutations conferring resistance to FQ & second-line injectables

Case 1 – Diagnostic work-up (3)

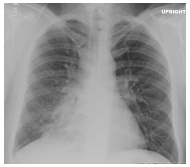


GeneXpert MTB/XDR on sputum sample: MTB detected; isoniazid: *inhA* & *katG* mutation; no mutations conferring resistance to FQ & second-line injectables

Deeplex (targeted NGS) on sputum sample:

- MTB detected
- **Confirms mutations**: *inhA* promoter (-15 C/T), *katG* (S315T) & *rpoB* (S450L)
- **Other mutations**: *embB* (M306V) & *pncA* (V180I)
- **Wild type:** *gyrA*, *gyrB*, *Rv0678*, *atpE*, *pepQ*, *rplC*, *rrl*, etc

Case 1 – Management



And now?

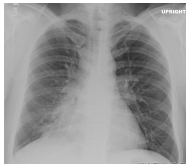
Pre-treatment evaluations:

- ECG: sinus rhythm, QTcF 484 ms
- Clinical assessment of signs/symptoms of peripheral neuropathy (BPNS), optic neuritis (visual acuity/colour perception)

TB treatment:

- Start with **BPaLM** (Bdq 400 mg daily [then 200 mg x 3/week] + pretomanid 200 mg/d + Lzd 600 mg/d + moxifloxacin 400 mg/d) -> *delamanid may be a reasonable alternative to pretomanid [BDLM]*
- Target treatment duration: **6 months**

Case 1 – Management (2)



Anything else?

HCV & TB treatment:

- There are no major known DDI between DAA for HCV and second-line TB drugs (conversely to rifamycins!)
- WHO recommends concomitant treatment of the two diseases -> timing unclear

March 2024

World Health Organization

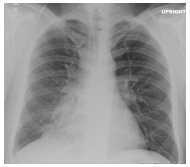
Co-administration of treatment for drug-resistant tuberculosis and hepatitis C

Rapid Communication

Therefore:

- After 4 weeks (?), start HCV treatment (after checking: https://hep-druginteractions.org/checker)
- Sofosbuvir/velpatasvir for 12 weeks (or glecaprevir/pibrentasvir but may increase Bdq and pretomanid blood levels)

Case 1 – Treatment monitoring

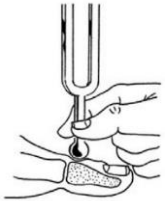


- Monthly **blood tests**: full blood count, electrolytes, liver function
- Monthly **sputum smear/culture**
- Monthly **visual acuity/color vision testing**
- Monthly **BPNS**
- Monthly **ECG**

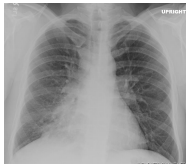
- HCV viral load (12 wks after end of HCV treatment)

Subjective symptom screening

- Pain, aching, or burning in feet, legs
- “Pins and needles" in feet, legs
- Numbness in feet, legs



Case 1 – and then…

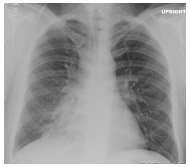


Follow-up visit (3 months):

- Blood tests:
  - Transaminases stable at 3xULN (M1), then decreasing (M2) & normal (M3)
  - Other blood tests: ok
- Microbiology:
  - Drug susceptibility testing: HRZE: resistant to all; Bdq, FQ, delamanid & pretomanid, linezolid, etc: susceptible
  - Sputum smear: positive at M1 and M2, negative at M3
  - Sputum culture: positive at M1, ongoing at M2
- ECG: QTcF 478 (M1), 485 (M2), 504 (M3)
- BPNS, visual acuity/colour vision: normal

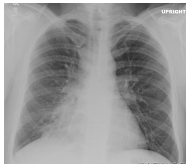
What would you do?

Case 1 – QT prolongation



- Test electrolytes (correct if needed)
- **Stop Mfx** (continue BPaL [or BDL])
- Repeat ECQ weekly
- Reintroduce Mfx when QTcF decreased; if needed, consider replacing Mfx with Lfx

Case 1 – but of course…

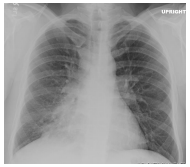


Follow-up visit (at 4 months):

- HCV treatment finished; HCV-RNA undetectable
- Blood tests:
  - All ok
- Microbiology:
  - Sputum smear: negative at M4
  - Sputum culture: negative at M2
- ECG: QTcF 472
- Visual acuity/color vision: normal
- BPNS: numbness (Grade 2) in left foot, paresthesia (Grade 3) in both feet

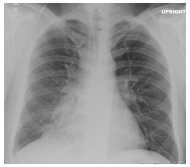
What would you do?

Case 1 – Peripheral neuropathy



- Exclude other causes of PN
- Electromyography – not so helpful for clinical decision making
- Administer pyridoxin if helpful for other causes
- **Stop Lzd** (continue (BPaM)
- Administer symptomatic treatment (gabapentin, pregabalin, etc – NOT together with Lzd)
- Two options:
  - Permanently discontinue Lzd (recommended), likely no need to replace it
  - Reintroduce at lower dose when PN resolved

Case 1 – Conclusion



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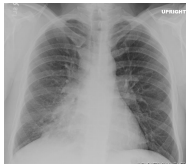
Sustained treatment success with **no sequelae** and **no post-TB lung disease**

Case 1 – EXTRA



What about people who were in contact with this patient?

ERS

ESCMID

Thank you!