MACROLIDE-RESISTANT *MYCOPLASMA PNEUMONIAE* PNEUMONIA

KHOA DICH VU HO HAP

Epidemiology and Clinical Manifestations of Children With Macrolide-Resistant *Mycoplasma pneumoniae* Pneumonia in Taiwan

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- Mycoplasma pneumoniae (MP): important respiratory pathogen in children that cause many upper and lower respiratory tract diseases, including wheezing, coryza, bronchopneumonia.
- 10–30% of community-acquired pneumonia (CAP) in children.

- Macrolide resistant rates of MP range from 0% to 30% in Europe, 8% in United States, 30% in Israel, and up to 90% in mainland China (3-2012). The percentage of MR strain in Taiwan is 23% in this study.

METHOD

-3/2010 to 12/2011

- <18 years old

- Admitted for CAP at the National Taiwan University Hospital and hospitals in the Taiwan Pediatric Infectious Disease Alliance.

- 412 specimens CAP

60 (15%): MP (+) by real-time PCR

14/60 (23%): MPRM presented point mutation (all A2063G) in 23S rRNA.

46 MLs (MLs group)

RESULTS

- All MLr strains in this study had point mutation at nucleotide A2063G of domain V of the 23S rRNA gene

→ the highest resistance to macrolides.

- The febril duration after azithromycin use for children with MRMP pneumonia was significantly longer than in children with the MLs strain (3.2 days vs. 1.6 days, P 0.02).

- Tetracyclines or fluoroquinolones for suspected MPRM strain even before DNA sequencing in the MPRM group.

→ MR of febrile duration after shifting antibiotics was significantly shorter (0.2 days vs. 1.8 days, P 0.04).

- In a study analysing 13 strains of MR*MP in Japan, 10 (77%) of the* strains possessed an A-to-G transition at position 2063. Other mutations included: A-to-C transversion at position 2063, A-to-G transition at position 2064 and C-to-G transversion at position 2617.
- A mutation A-to-G transition at position 2063 showed very high levels of MR. The majority of the strains isolated in Shanghai and Beijing.

Rapid Effectiveness of Minocycline or Doxycycline Against Macrolide-resistant Mycoplasma pneumoniae Infection in a 2011 Outbreak Among Japanese Children

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METHOD

- 1- 12/2011: 258 with MP pneumonia
- Chest radiography, real-time PCR, antibody titer
- Treated: minocycline (MIN), doxycycline (DOX), or tosufloxacin (TFX)
- Mutations of the 23S rRNA identified by DNA sequencing.

RESULTS

- related to school age ($P < 0.01$)
- 176 (87.1%) MRMP:

  MIN or DOX (n=125)

  TFX (n=15)
- MIN or DOX
- ✓ significantly more effective within 24 hours
- ✓ decreasing numbers of MP DNA copies 3 days after initiation than TFX ($P \leq 0.05$).

Clinical efficacy of macrolide antibiotics against genetically determined macrolide-resistant Mycoplasma pneumoniae pneumonia in paediatric patients.

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METHOD

- 30 children with MP pneumonia
  - MPRM: 21 patients, point mutation
  - Control patients: 9 patients, no point mutations
- PCR and serology
- After treatment, identified number of MP copies by DNA sequencing

RESULT

- Control patients: 9 patients, no point mutations: number of MP in nasopharyngeal samples decreased rapidly 48 h after initiation of macrolide treatment.

RESULT

- MR patients:
  - the number of MP 48h after initiation of macrolide treatment - higher in samples.
  - In 15/21: fever persisted >48 h after the initiation of macrolide;
  - Treatment: minocycline =>fever disappeared within 48h

CASE REPORT

Severe community-acquired pneumonia caused by macrolide-resistant *Mycoplasma pneumoniae* in a 6-year-old boy

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- 6 year old Chinese boy: fever, non-productive cough for 3 days.
- Admitted to Tuen Hospital: May 2010, HK.
- Good past health, nor history of animal, bird contact, recent travel out of HK.
- Physical exam: multiple small cervical lymph node
- Chest exam: right lower zone crackle
- Chest X gray: consolidation of right lower lobe
- Blood test: normal WBC, elevated CRP (133mg/L)

- Treatment: cefotaxim + clarithromycin
- 2nd day of admission: fever + respiratory symptoms persisted => vancomycin
- 3 rd day: erythematous maculopapular, blanchable, non puritic skin rash, spread to face and limbs, no mucosal or other target lesion.

- Repeat Xgray: right pleural effusion, WBC: normal => meronem + azithromycin
- Culture: respiratory + blood: no organisms
- Urine for *Legionella* antigen, nasopharyngeal aspirate (NAP) for *Influenza A and B* antigen, PCR *Mycobaterium tuberculosis: (-)*

- NAP *MP* PCR: (+), pleural fluid specimen for *MP: (-)*
- Serology by coleletced days 2nd and 15th with tiltre rose 1:40 to 1:10240
- DNA analysed: an A-to-G trasition at posittion 2063 of 23S rRNA gene

=> 15th day: oral doxycyclin (2 mg/kg) X 10

=>fever resolved by next day

=>discharged after 17 days.

CONCLUSIONS

- Prolonged fevers may occur in children with MR isolates who are treated with macrolide.
- an A-to-G transition at position 2063 of 23S rRNA gene

⇒ high level of macrolide resistance

- Alternative treatments for macrolide-resistant strains (uptodate 3-2013)
  - Tetracyclines (eg, doxycycline 2 to 4 mg/kg per day in one or two divided doses [maximum daily dose 100 to 200 mg] for 10 days)
  - Fluoroquinolones should only be used in children younger than 18 years if the benefits of therapy exceed the risks.
    - 10 mg/kg per dose every 12h for 10 days for infants ≥6 months and children <5 years
    - 10 mg/kg per dose every 24 hours for 10 days for children ≥5 years, with a maximum daily dose of 500 mg