Dr Marie Bruyneel and Deborah Konopnicki

BVIKM/SBMIC
November 8th, 2012

PNEUMONIA IN A PRESUMED IMMUNOCOMPETENT PATIENT

Men, 54 years

Emergency room on end october 2009

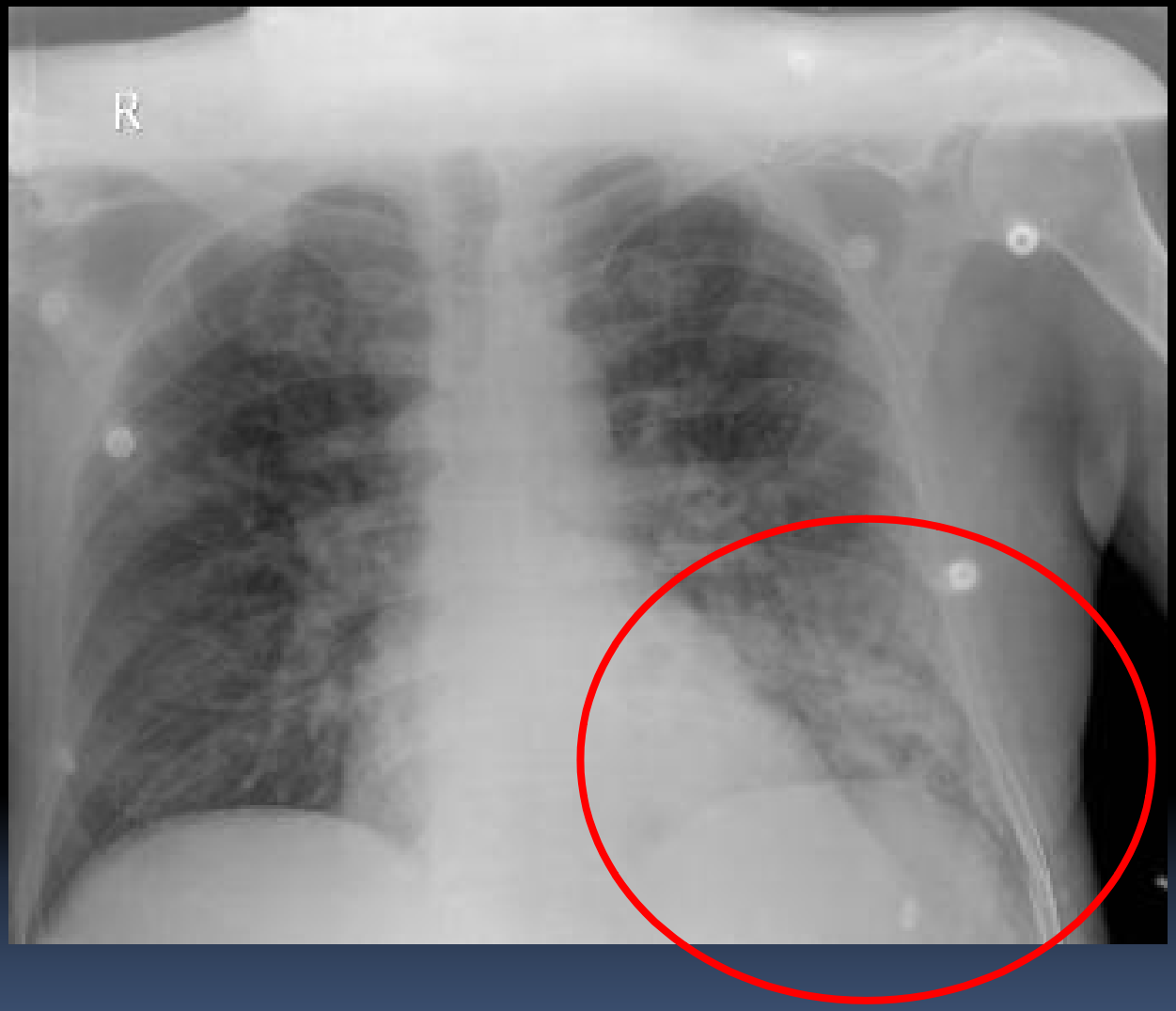
- Sent by his family doctor for Influenza A H1N1?
- Viral syndrom, cough, fever →39° (7j)
  - No improvment with oral antibiotics
  - Hallucination for 2 days
  - Lost 8 kg since 1 month

- From Poland, in Belgium since 2009
- Building worker, 5 beers/day, smoker (34 PY).

- Physical examination:
  - Restless, difficult to examine
  - 38°C
  - SAO2 91%

- Blood test:
  - Whites cells 10700, 83% PN
  - CRP: 218 mg/dL
  - K+:2.6mEq/L
  - plateletts: 131.000
  - Moderate liver tests abnormalities

- 2 Blood cultures



1. Pneumonia
2. Alcohol withdrawal syndrom

Start
Amoxicilline +
Clavulanate
1g qd

Evolution

- Unfavorable
- Fever →39,5°; hypoxemia PaO2=55 mm Hg
- CRP: 360 mg/dL after 4 days of ABtherapy

  - Repeated blood cultures remain negative
  - Nasopharyngal swabs:
    - Rapid Ag detection for Influenza, RSV, adénovirus –
    - Viral culture – repeatdly
  - Urine culture -
  - Sputum (saliva): levures (candida albicans)
- shift **Piperacillin+Tazobactam** 4X4 g/j
- Mouth candidosis R/**fluconazole**
- Type II diabetes (HbA1c 6.2%) R/ **glucophage**

What diagnostic prodecure would you rank first?

1 - Skin test for tuberculosis

2 - Serum Aspergillus antigen (galactomannan test)

3 - Chest CT and bronchoalveolar lavage

4 - Transbronchic biospsies

5 - Honestly, I have no idea

What diagnostic prodecure would you rank first?

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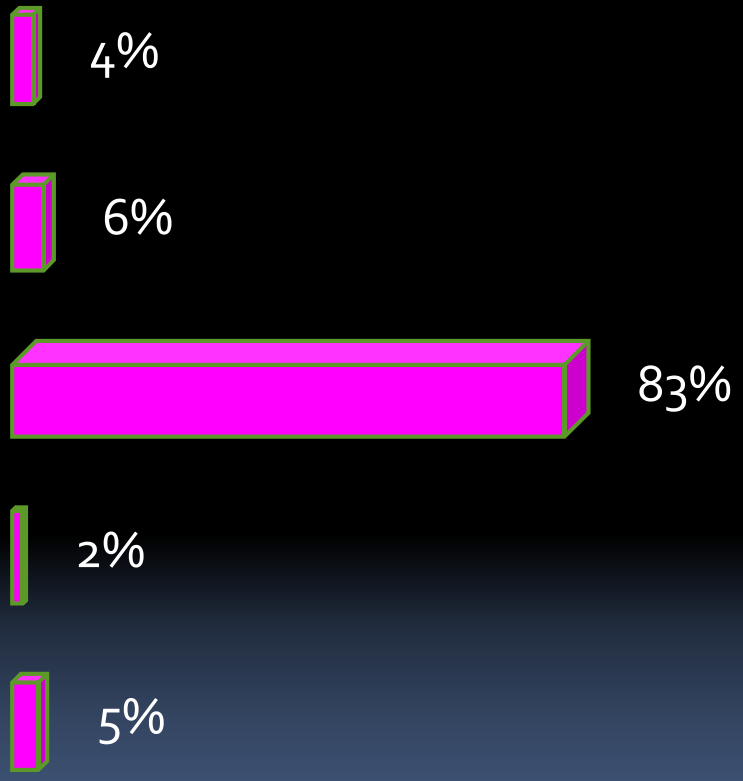
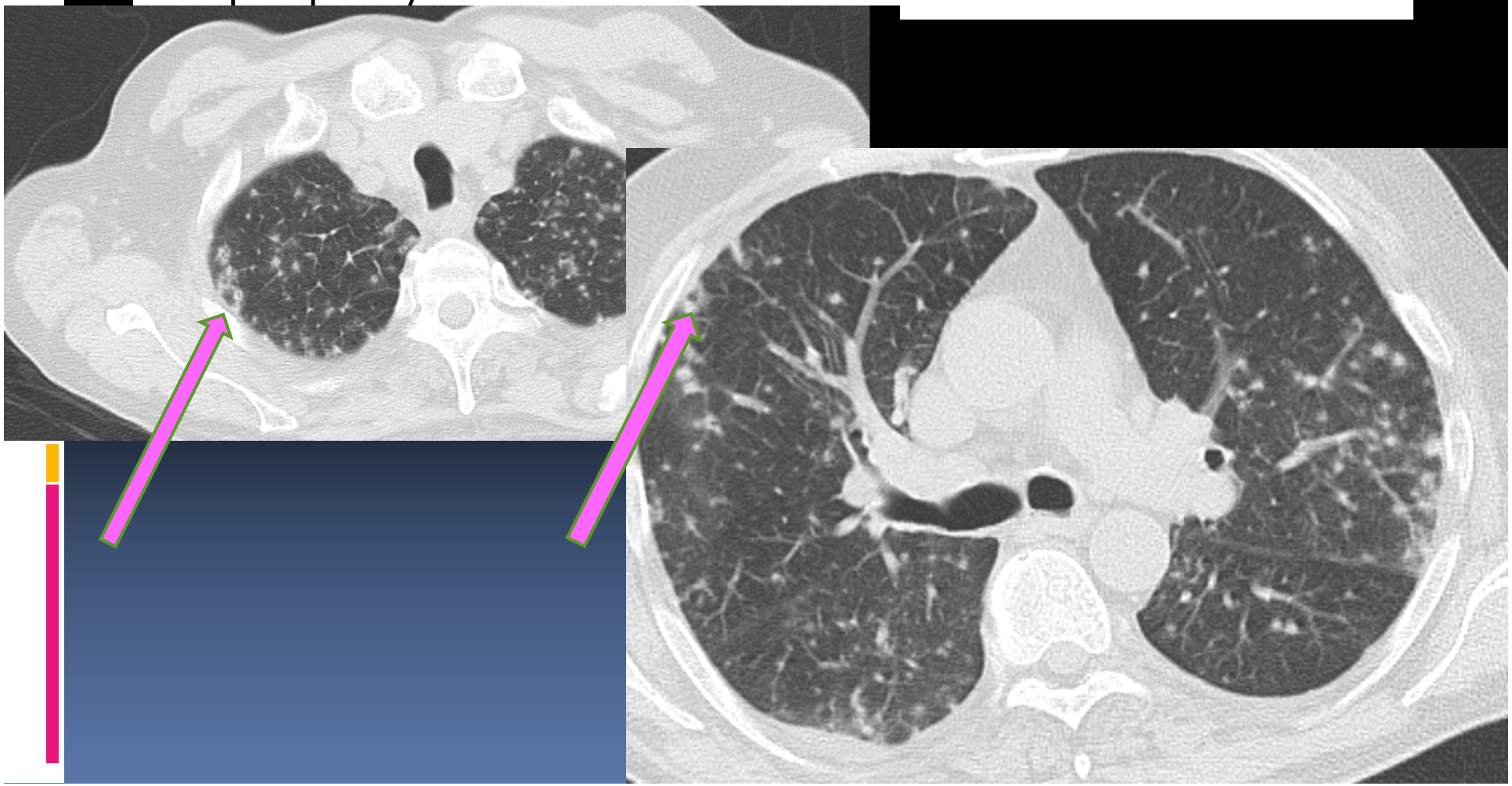


Thorax CT

Mediastinal adenopathies. Pneumonia of the left inferior pulmonary lobe and pleural reaction. Numerous nodulary infiltrates with blurred limits in the 2 lungs, in particular in the periphery zone. Nodular lesions some with excavation.



Among the diagnoses proposed by the radiologist, which one is your choice?

1 - Mycobacterial infection

2 - Invasive aspergillosis

3 - Actinomycosis

4 - Coccidioidomycosis

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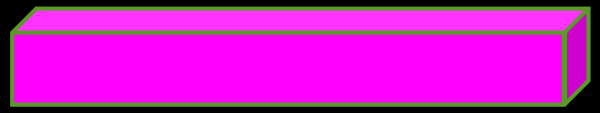
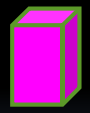


49%

2 - Invasive aspergillosis

43%

3 - Actinomycosis



6%

4 - Coccidioidomycosis

2%

Investigations (1)

- *Legionella* urinary antigen detection negative twice
- Serologies are negative for
  - Mycoplasma, Q fever
  - HIV, Hepatitis A, B and C, CMV.
  - *Chlamydophila* are elevated IgG and IgA anti LPs but controls remain stable so not in favour of acute infection
- Fan and ANCA are negative. **RF =65 (<14 UI/ml)**
- Nasopharyngal swabs:
  - PCR for influenza A- and H1N1
  - Viral culture negative

Investigations (2)

- Sputum cultures:
  - BK: direct exam negative (4X)
  - rares colonies de *Candida albicans* (5X)
  - *Aspergillus fumigatus* (Nov 6 : 4 colonies; Nov 12: 1 colony)
- Serum cryptococcal Ag and Galctomannan (2x) : negative
- Broncho-alveolar lavage (2X):
  - BK DE and PCR are negative
  - Mould cultures are negative
  - Galactomannan ag detection= 0,12.
- Transbronchic Biopsies nov 9th and dec 1st: unspecific lymphocytic infiltrate, bronchiolitis

Stop Piperacillin+Tazobactam after 7 days : CRP ↓ 66 mg/dL
Start treatment against tuberculosis mid nov

What is the PPV of BAL Galactomannan in non-neutropenic patients with Aspergillosis?

1 - <25%

2 - 25-50%

3 - 50-75%

4 - >75%

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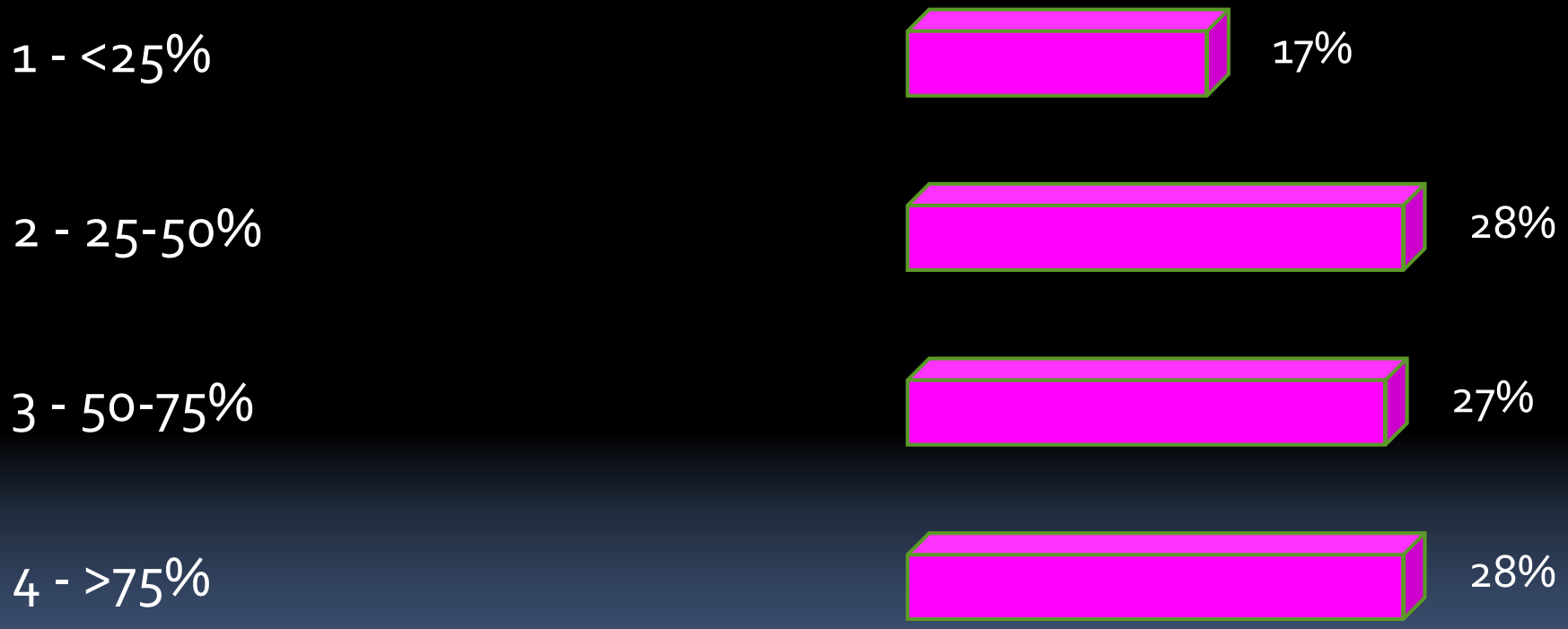

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Use of Bronchoalveolar Lavage To Detect Galactomannan for Diagnosis of Pulmonary Aspergillosis among Nonimmunocompromised Hosts▽

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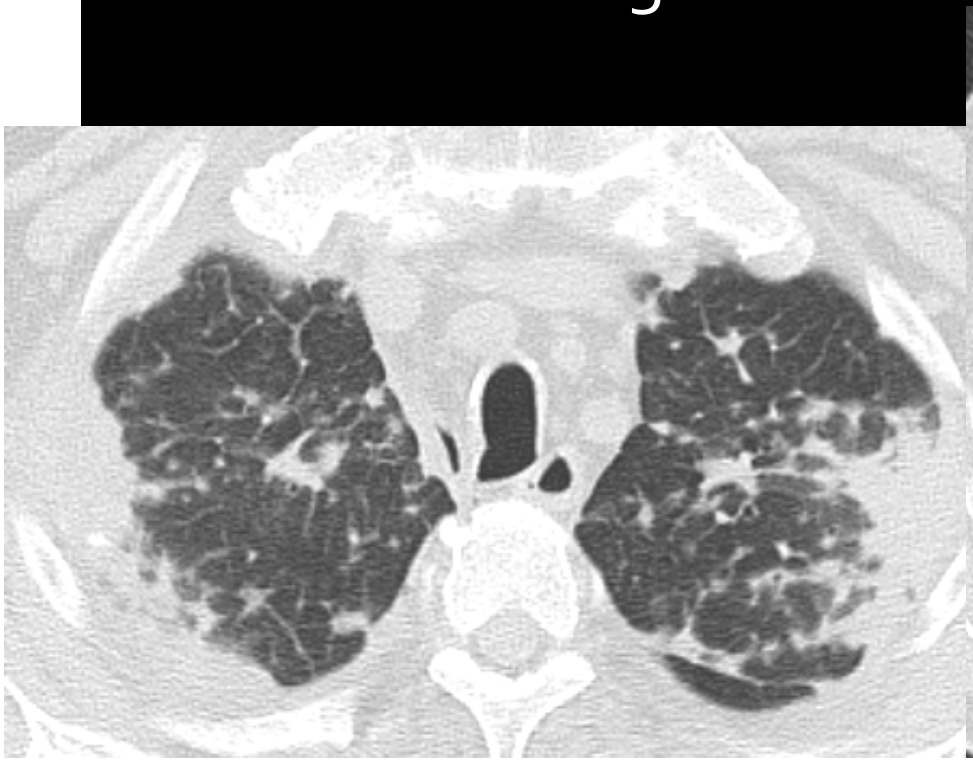
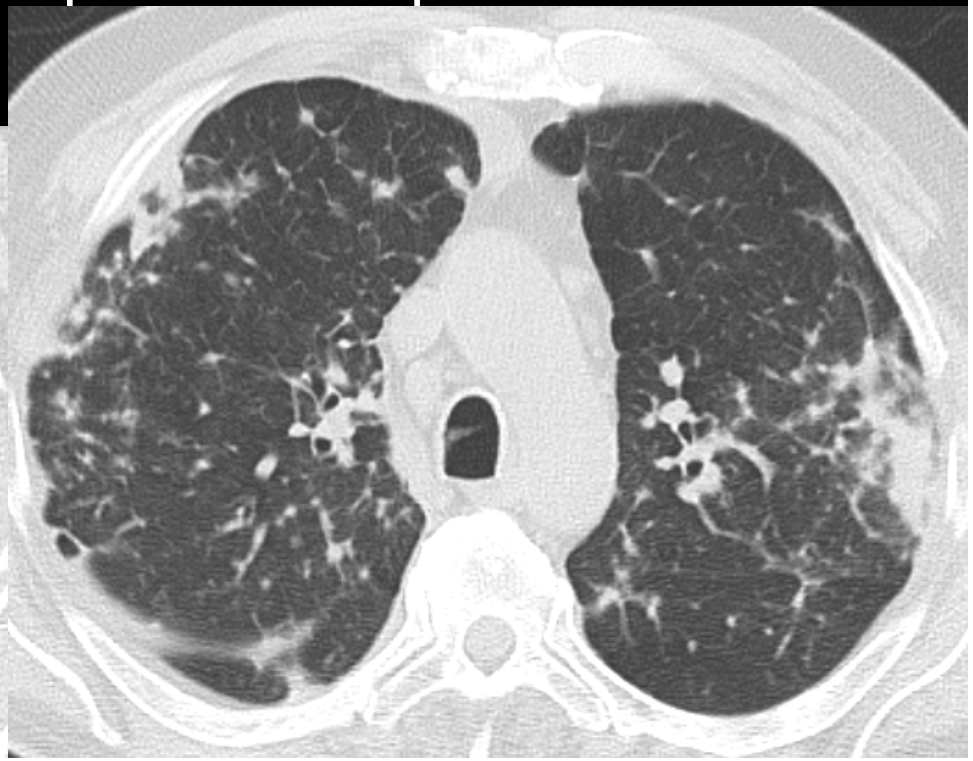
73 patients: 6 aspergillosis

BAL	GL ≥ 0.5	GL ≥ 1
Sensitivity	100%	100%
Specificity	77%	88%
NPV	100%	100%
PPV	29%	43%

Evolution: end of November

- Low grade fever: 37.5-38 °C
  Mild leucocytosis: 12,000 /µL (75% of PMN)
  Mild inflammatory syndrom: 60-80 mg/dL
- Repeated chest CT: worsened
- PET Scan: Lung bilateral captation unspecific





Evolution: end of November

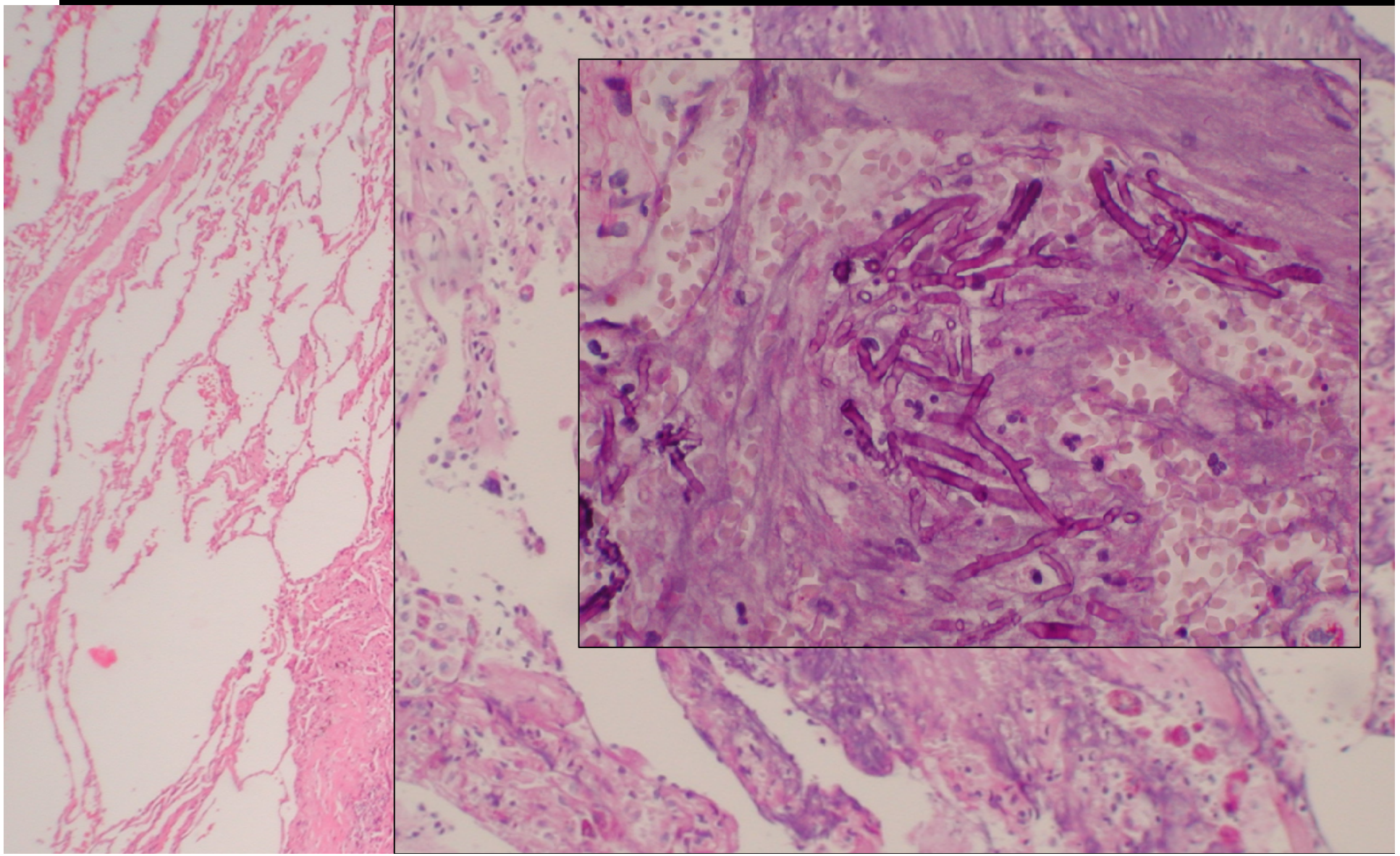
- Stop antituberculous therapy after 3 weeks
- **Vibramycin** (serologic results for *Chlamydophila*)

- Slow reaction:
  - Brain CT : maxillary sinusitis
  - Lumbar puncture: protein are slightly increased

- ? Cirrhosis (albumine 2.6, INR 1.5) but liver CT normal

- Hyperγglobulinemia M + IgG Kappa monoclonality
  - Free λ and κ ↑ (urine)
  - β 2 microglobuline↑
  - Bone marrow aspirate is normal

Thoracoscopy + pulmonary biopsies on december 7th:



Multiple lung foci of infection with pus. No lymphoma. No tuberculosis. Special colotration (PAS, Zielh and Grocott) show aspergillus within granulation tissu.

- *Start **MERONEM** 2g X3 for nosocomial lung infection (fever and inflammation) after surgery*

- *Start **Amphotericine B** 50 mg IV x1 for 3 weeks*

  *Shift in **Voriconazole** 350 mg x2/day/ 9 weeks*

Are case-report papers on invasive aspergilloses in immunocompetent patients rare?

1 - <10

2 - 10-30

3 - 30-50

4 - >50

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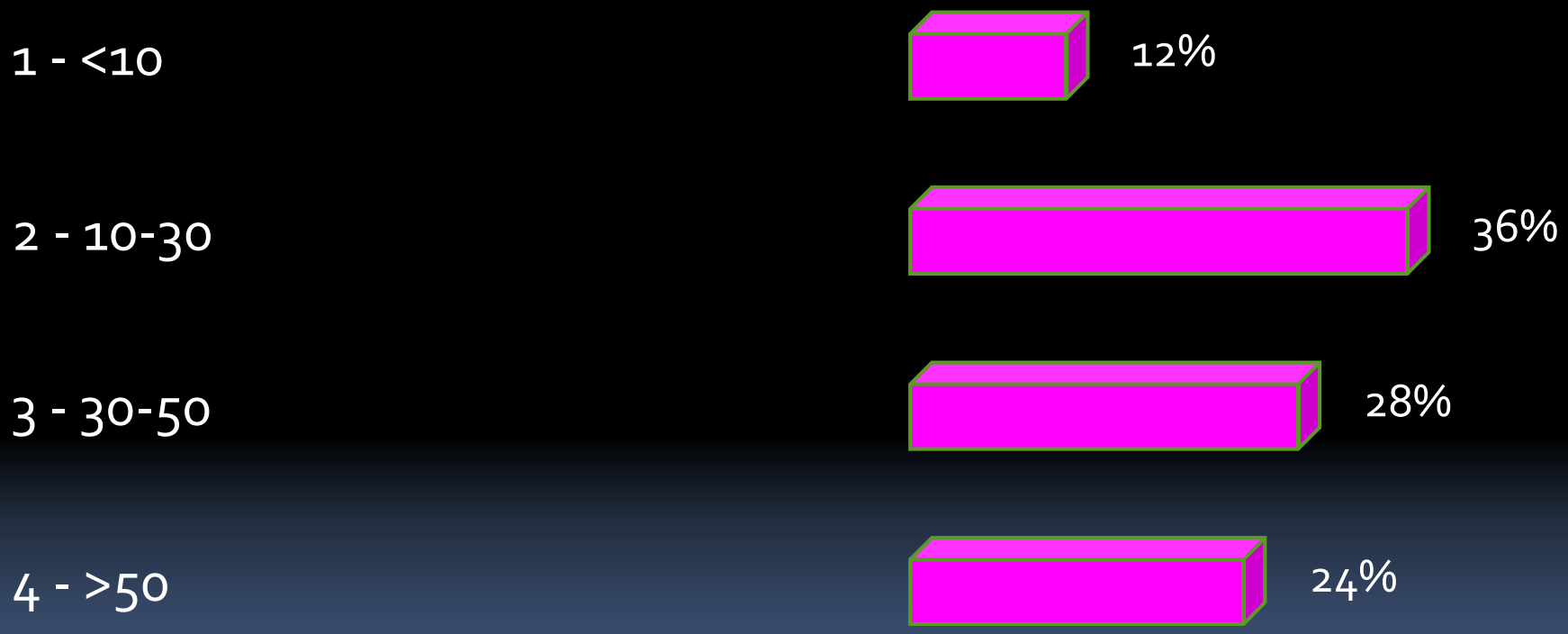

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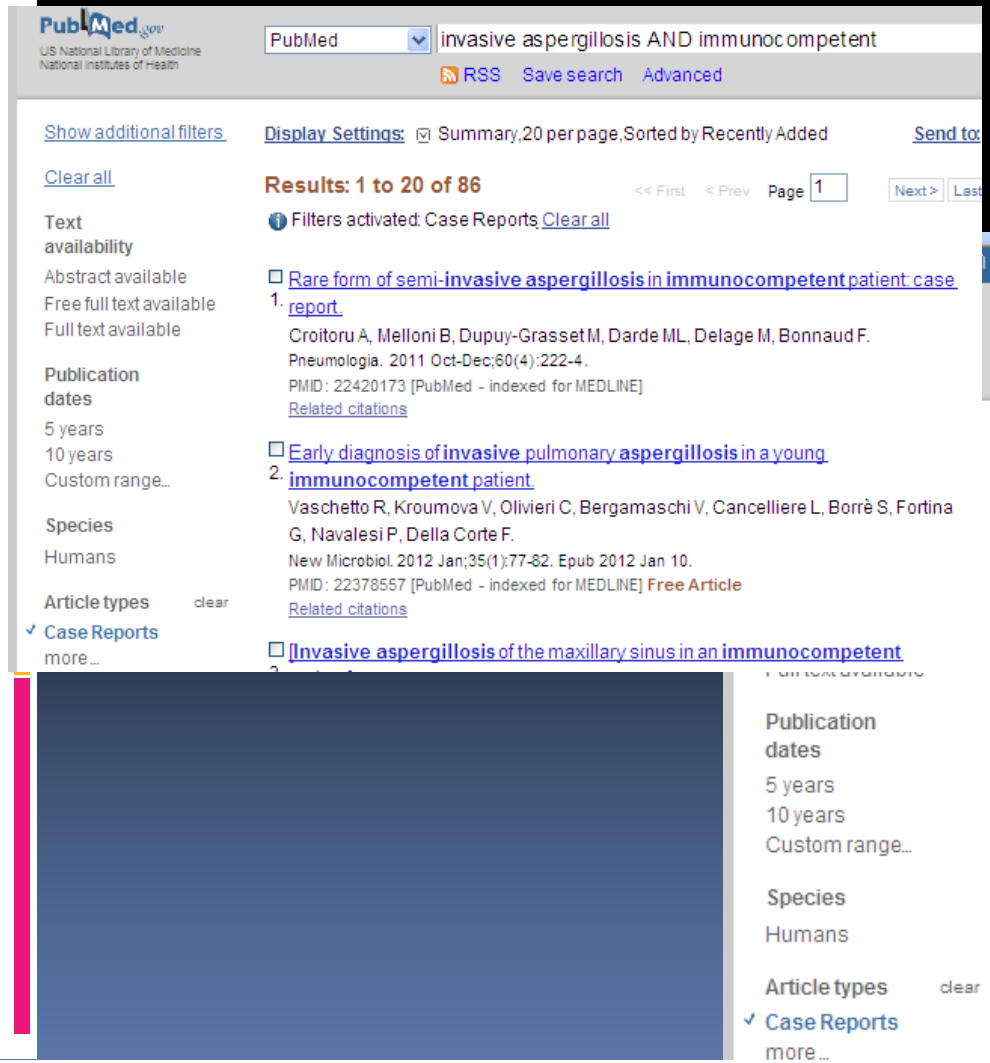
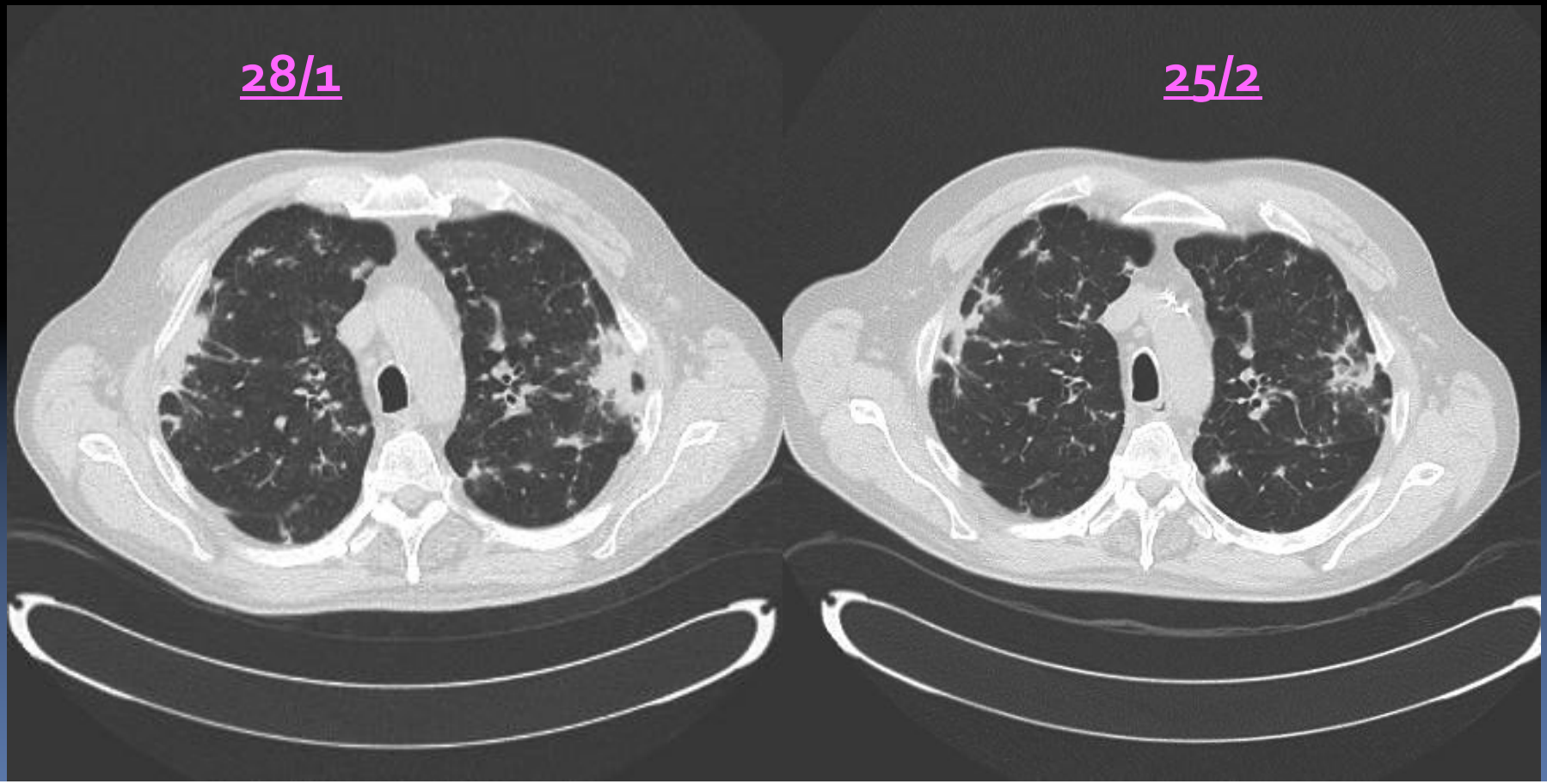


EVOLUTION

- Clinically: rapidly better (no fever, +4kg)
- Lab: GB 11300, PN 70%, CRP= 40
- CT:



Conclusion

1. Invasive pulmonary aspergillosis (favoured by viral infection?)
2. Maxillary sinusitis
3. Several mild immune defects
   - Mild diabetes II
   - Alcoholic liver dysfunction
   - Monoclonal gammopathy
4. Bacterial lung infections

Could there be a link between Influenza infection and Invasive Aspergillosis?

1. Yes but only in immuno**compromised** patients
2. Yes but only in immuno**competent** patients
3. Yes in **both** immuno- compromised and competent patients
4. No

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Invasive Aspergillosis after Pandemic (H1N1) 2009

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Abstract

Go to:

We report 2 patients with invasive aspergillosis after infection with pandemic (H1N1) 2009. Influenza viruses are known to cause immunologic defects and impair ciliary clearance. These defects, combined with high-dose corticosteroids prescribed during influenza-associated adult respiratory distress syndrome, may be novel risk factors predisposing otherwise immunocompetent patients to invasive aspergillosis.