

16. **Morgenthaler NG**, Struck J, Christ-Crain M, *et al.* Pro-atrial natriuretic peptide is a prognostic marker in sepsis, similar to the APACHE II score: an observational study. *Crit Care* 2003;**9**:R37–45.
17. **Morgenthaler NG**, Struck J, Alonso C, *et al.* Assay for the measurement of copeptin, a stable peptide derived from the precursor of vasopressin. *Clin Chem* 2006;**52**:112–9.
18. **Struck J**, Morgenthaler NG, Bergmann A. Copeptin, a stable peptide derived from the vasopressin precursor, is elevated in serum of sepsis patients. *Peptides* 2005;**26**:2500–4.
19. **Morgenthaler NG**, Struck J, Thomas B, *et al.* Immunoluminometric assay for the midregion of pro-atrial natriuretic peptide in human plasma. *Clin Chem* 2004;**50**:234–36.
20. **Niederman MS**, Mandell LA, Anzueto A, *et al.* Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am J Respir Crit Care Med* 2001;**163**:1730–54.
21. **Müller B**, Suess E, Schuetz P, *et al.* Circulating levels of pro-atrial natriuretic peptide in lower respiratory tract infection. *J Intern Med* 2006;**260**:568–76.
22. **Prat C**, Lacombe A, Dominguez J, *et al.* Midregional pro-atrial natriuretic peptide as a prognostic marker in pneumonia. *J Infect* 2007;**55**:400–7.
23. **Mortensen EM**, Coley CM, Singer DE, *et al.* Causes of death for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team cohort study. *Arch Intern Med* 2002;**162**:1059–64.
24. **Yende S**, D'Angelo G, Kellum JA, *et al.* Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. *Am J Respir Crit Care Med* 2008;**177**:1242–7.
25. **Jochberger S**, Morgenthaler NG, Mayr VD, *et al.* Copeptin and arginine vasopressin concentrations in critically ill patients. *J Clin Endocrinol Metab* 2006;**91**:4381–6.
26. **Jochberger S**, Mayr VD, Luckner G, *et al.* Serum vasopressin concentrations in critically ill patients. *Crit Care Med* 2006;**34**:293–9.
27. **Without R**, Busch C, Fraunberger P, *et al.* Plasma atrial natriuretic peptide and brain natriuretic peptide are increased in septic shock: impact of interleukin-6 and sepsis-associated left ventricular dysfunction. *Intensive Care Med* 2003;**29**:1696–702.
28. **Gegenhuber A**, Struck J, Poelz W, *et al.* Midregional pro-A-type natriuretic peptide measurements for diagnosis of acute destabilized heart failure in short-of-breath patients: comparison with B-type natriuretic peptide (BNP) and amino-terminal proBNP. *Clin Chem* 2006;**52**:827–31.
29. **McLean AS**, Huang SJ, Nalos M, *et al.* The confounding effects of age, gender, serum creatinine, and electrolyte concentrations on plasma B-type natriuretic peptide concentrations in critically ill patients. *Crit Care Med* 2003;**31**:2611–8.

## Pulmonary puzzle

### Three diagnoses become one: a woman with ground-glass attenuation develops fever

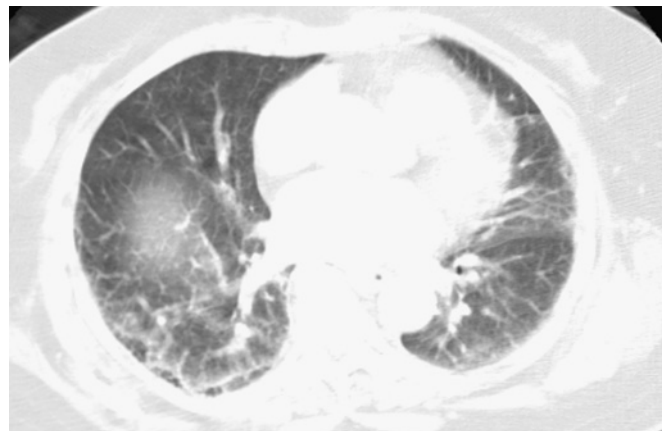
#### CLINICAL PRESENTATION

In 2002 a 73-year-old woman (non-smoking, medical history of allergic rhinitis) was referred to a rheumatologist because of synovitis of the metacarpophalangeal and proximal interphalangeal joints of both hands which had slowly developed over 3 months. Late-onset rheumatoid arthritis was suspected. Morning stiffness, rheumatoid nodules, erosions of cartilage or bone, rheumatoid factor and antibodies to cyclic citrullinated peptides were absent. Prednisone (2.5–5 mg daily) and non-steroidal anti-inflammatory drugs were started.

In 2004 she was referred to a respiratory physician for analysis of a persistent dry cough and pleural effusion. CT scans of the lungs (six scans between 2004 and 2009, see representative scan in figure 1) revealed fleeting bilateral multifocal consolidations with ground-glass attenuation. Bronchoscopic examination was normal. The lavage fluid showed 39% macrophages, 58% lymphocytes and 2% neutrophils. Diffusing capacity (transfer factor) was low while spirometry was normal. These findings were interpreted as lung disease secondary to rheumatoid arthritis. Because polyarthritis had responded to low-dose glucocorticoid treatment and the pulmonary lesions appeared stable over time, this low-dose regimen was maintained over the years.

In 2005 diabetes mellitus type 2 was diagnosed which was treated with oral blood glucose lowering agents (metformin 500 mg twice daily) resulting in adequate control (glycosylated haemoglobin 7.1%). No diabetic retinopathy was present. In 2006 she developed painful polyneuropathy. The neurologist ascribed polyneuropathy to diabetes mellitus and started amitriptyline. No further tests were ordered.

In 2008 she developed persistent fevers, elevated inflammatory parameters (peak erythrocyte sedimentation rate 106 mm/h, C-reactive protein 135 mg/l) and normocytic anaemia (haemoglobin 8.7 g/dl (5.3 mmol/l)). Elaborate testing failed to provide new insights. These tests included serial blood cultures, tests for tuberculosis, syphilis, borrelia, hepatitis, HIV, bone marrow biopsy, CT scans of chest and abdomen, positron emission tomography, leucocyte scan, bronchoalveolar lavage and temporal artery biopsy.



**Figure 1** CT scan of the lungs of a 73-year-old woman with ground-glass attenuation and fever.

#### QUESTION

A woman with presumed rheumatoid arthritis, associated lung disease, diabetes mellitus and polyneuropathy develops fevers of unknown origin. Which alternative diagnosis is possible based on the clinical information and the CT image (figure 1) and which tests would you order to confirm this?

See page 270 for answer

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