WORKSHOP
GENERAL INTERNAL MEDICINE

Belgian Society of Internal Medicine

15th Annual Congress

67-year-old Female

Present complaints:

- Pain left lower quadrant since 3 wks
- Fatigue, sleeps more
- Muscle aches (arms & legs)

Additional symptoms:

- Weight loss (4 kgs/3wks)
- Night sweats, no fever
- Headache (right temple)

Past history

- Allergy to penicillin and cephalosporins (angio-edema)
- 1992: Vasospastic angina
- 2005: PTA and stenting RCA
- Arterial hypertension
- Hypercholesterolemia
- Pneumonia
- 2007: right CEA (stenosis 80-99%; amaurosis fugax)

A 67-year-old female with subacute left abdominal pain and fatigue

Medication

- Cardioaspirine 100 mg
- Simvastatine 40 mg
- Coruno 16 mg
- Vasexten 20 mg
- Bisoprolol 10 mg
- Teveten plus

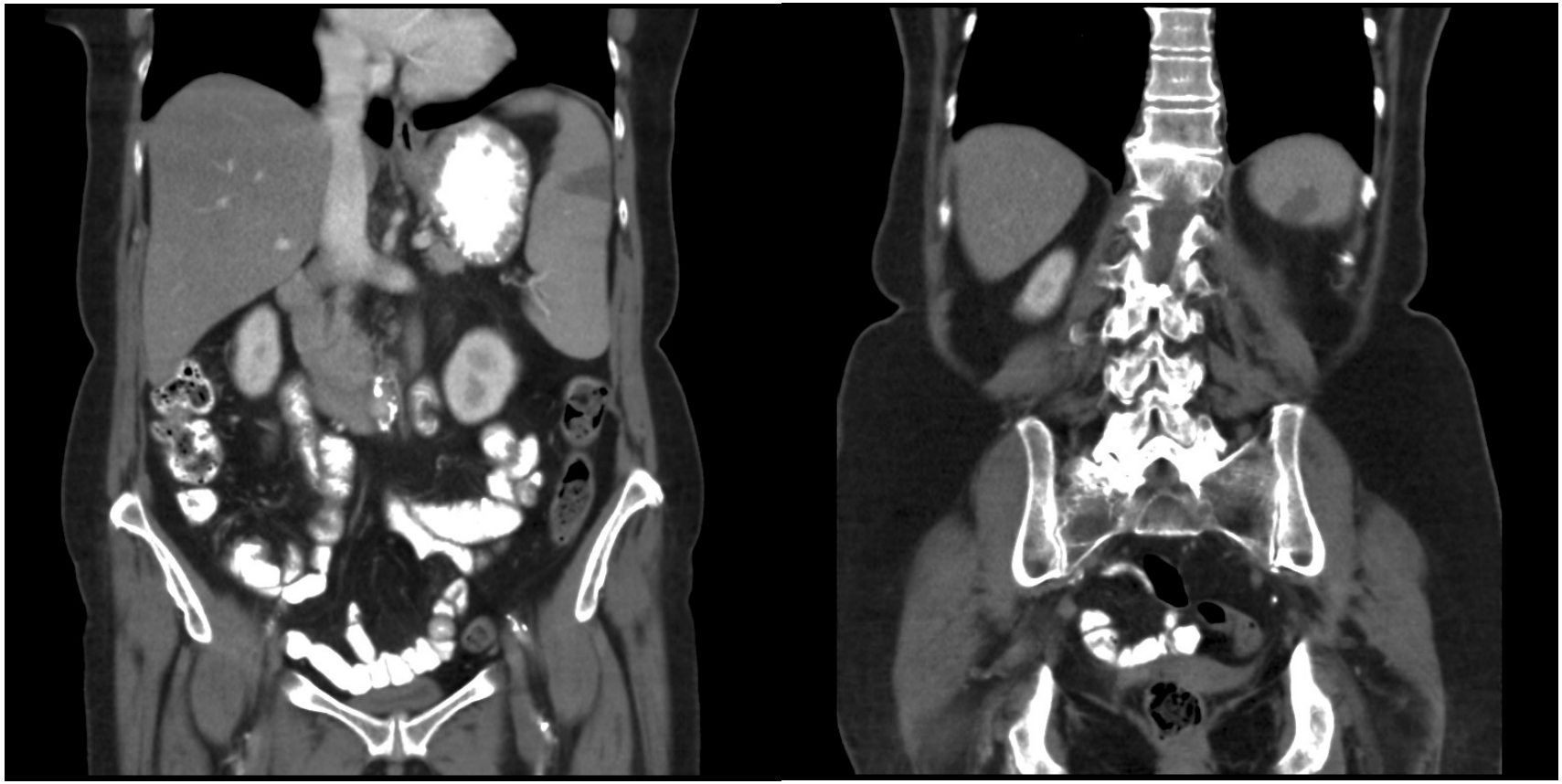
A 67-year-old female with subacute left abdominal pain and fatigue

Clinical examination

To note:

- Heart: systolic murmur apex, 2/6
- Abdomen: widespread tenderness, esp. left flank

CT abdomen



A 67-year-old female with subacute left abdominal pain and fatigue

Lab results

- C-reactive protein: 16.3 mg/L (ref.: <= 5.0)

- Alkaline Phoshatase: 469 U/L (ref.: <= 240)
- Alanine aminotransferase: 73 U/L (ref.: <= 32)
- Aspartate aminotransferase: 124 U/L (ref.: <= 31)
- Gamma-glutamyltransferase: 171 U/L (ref.: <= 35)
- Lactate dehydrogenase: 785 U/L (ref.: 240-480)

- Thrombophilia screen: highly positive IgM anticardiolipin antibody

- Normal levels of: peripheral blood count, BUN, creatinin, bilirubin, elektrolytes.

A 67-year-old female with subacute left abdominal pain and fatigue

Technical examinations

- Blood cultures: sterile
- ECG: sinus rhythm, 65 bpm, normal
- Chest X-ray: non-contributory
- Fundoscopic examination: normal
- Transoesophageal echocardiogram:
  - Mitral regurgitation ¼, possible chorda rupture of posterior mitral leaflet
  - Aortic sclerosis

Peripheral blood count, d3

- White-cell count: 8.0 x 10^9/L (ref.: 4.0-10.0)
- Differential count (%):
  - Neutrophils: 31% (ref.: 38.0-77.0)
  - Lymphocytes: 55.6% (20.0-50.0)
  - Monocytes: 11.1 % (20.-10.0)
- Atypical lymphocytes 3+

Causes of splenomegaly and subacute fever

- Infection
  - Viral (hepatitis, infectious mononucleosis, cytomegalovirus, human immunodefiency virus)
  - Bacterial (salmonella, brucella, pyogenic abscess, endocarditis)
  - Mycobacterial (tuberculosis, atypical mycobacterial infections)
  - Parasitic (malaria, toxoplasmosis)
  - Rickettsial (Rocky Mountain spotted fever)
  - Fungal (histoplasmosis)
- Inflammation
  - Systemic lupus erythematosus
  - Rheumatoid arthritis
  - Sarcoidosis
  - Serum sickness
- Malignant condition
  - Lymphomas
  - Acute and chronic leukemias
- Other hematologic disorders (acute and chronic autoimmune hemolytic anemias)

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Differential diagnosis of splenic infarction

- Myeloid disorders
  - Myeloproliferative neoplasms (myelofibrosis, polycythemia vera, essential thrombocythemia)
  - Myelodysplastic syndromes
  - Acute leukemias
- Lymphomas
- Hemoglobinopathy
- Thromboembolic events
  - Cardioembolic origin
  - Hypercoagulable states
    - Antiphospholipid syndrome
    - Malignant conditions
- Conditions with marked splenomegaly
- Wandering spleen
- Infection
  - Infective endocarditis
  - Infectious mononucleosis
  - Cytomegalovirus
  - Malaria

After: N Engl J Med;2010:363(13):1271

Viral serology

- Epstein-Barr EBNA: positive
- Cytomegalovirus
  - IgM: positive
  - IgG: positive (205 AU/ml)
  - IgG avidity: 4% (= very low, suggestive of recent primary infection)

Diagnosis & evolution

- Acute cytomegalovirus infection, with splenic infarction
- 'CMV of the granny':

  The patient had cared for her grandchildren (aged 1 & 3) who were ill a few days before getting ill herself
- Recovery was complete and uneventful.

“Feverish granny syndrome”

“Sir-
Cytomegalovirus (CMV) infection is most often found in children and young adults but is less common in older patients. We report three grandmothers with fever and malaise who may have acquired primary CMV infection from their young grandchildren.
…”

Lancet 1995 (304):1084

Case 2: 26-year-old female PhD student, referred to outpatient department

"Dear colleague,

The patient has sustained a whiplash injury after a car accident one year ago. Apart from this, she functions well.

However, she lost 30 kgs and has a fast resting heart rate (>100 bpm).

Blood analysis shows a microcytic anemia, with elevated serum ferritin, thrombocytosis, and inflammatory markers."

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Lab tests (GP)

- Erythrocyte sedimentation rate: 119 mm (0-20)
- Hemoglobin: 10.7 g/dL (12.0-16.0)
- Hematocrit: 32.7% (36.0-46.0)
- White-cell count: 10.8 10*9/L (4.0-11.0)
- Platelet count: 743 10*9/L (150-400)
- Iron: 24 µg/dL (40-150)
- Ferritin: 351 ng/mL (15-150)
- C-reactive protein: 13.85 mg/dL (0.00-0.50)
- Transaminases, renal function tests, thyroid function tests, electrolytes, glucose: normal

Additonal history

- Current:
  - Recurrent inflammation of proximal interphalangeal joints, both 1st metacarpophalangeal joints, and wrists since 6 mths
  - Shortness of breath when biking uphill
  - Apetite slightly decreased
  - No fever, night sweats, Raynaud phenomenon, photosensibility, diarrhea, nocturnal pains
- Past:
  - Mechanical-type cervicodorsalgia after traffic accident one year before
  - Erythema nodosum 2 years ago. Negative investigation in Utrecht.
- Familial:
  - Grandmother: rheumatoid arthritis
  - Father: gastrectomy for gastrointestinal stromal tumor
- Medication:
  - Redomex, Tramadol as needed

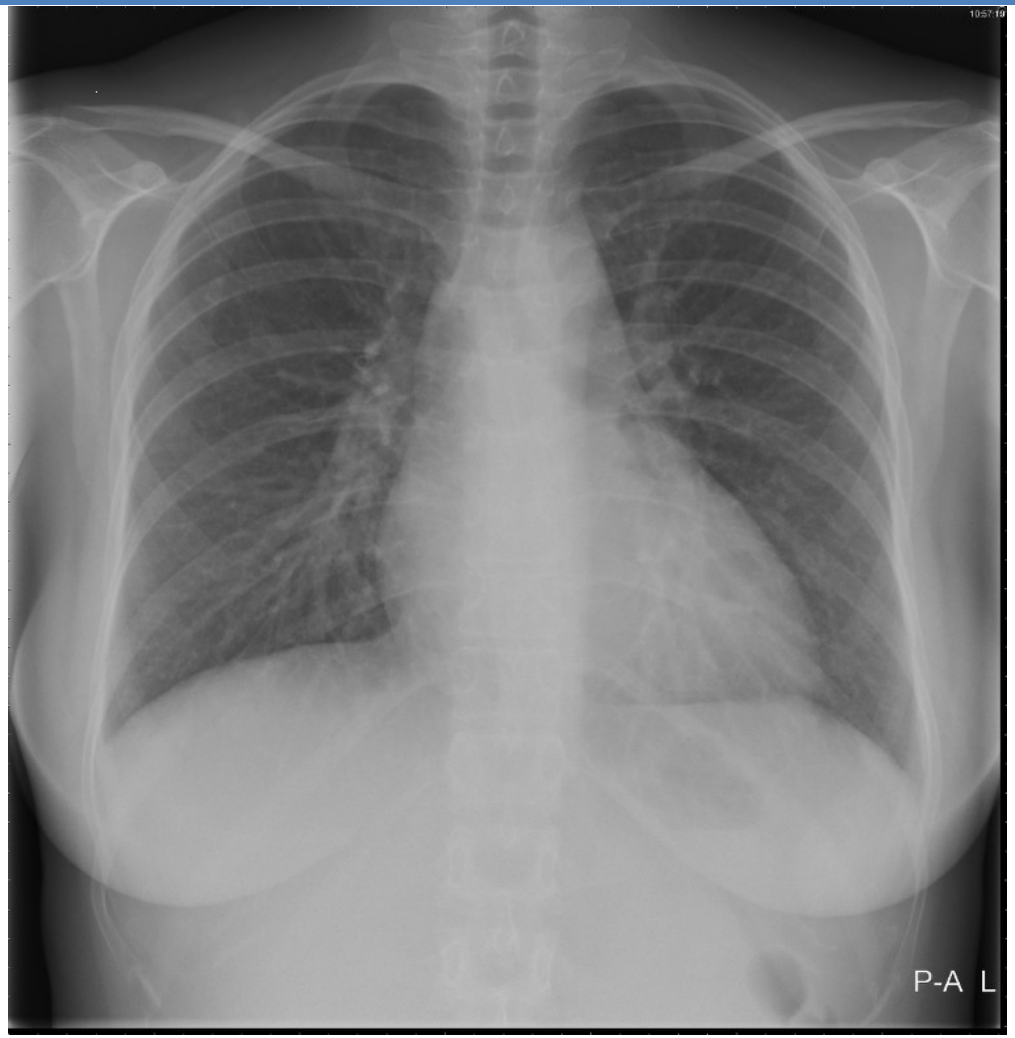
Clinical examination

- Body weight: 64.4 kg, BMI: 24 kg/m^2
- Blood pressure: 110/70 mmHg
- Heart rate: 120 bpm, regular
- Heart auscultation: systolic murmur 3/6, apex; early diastolic murmur over lower sternum
- JVP: +8 cm H_2O, positive HJR
- Normal lung auscultation
- Normal abdominal examination
- No synovitis
- No adenopathies

Tests

- ECG: sinus rhythm, 107 bpm
- Urine: protein: 0.30 g/L (0.0-0.15)
- NT-proBNP: 5564 ng/L (<=115)
- US abdomen: slightly enlarged liver
- X-ray hands: normal
- Fundoscopic examination: normal
- Lung function tests: ~ normal, besides slightly decreased diffusion capacity
- Immunology:
  - ANA: 1/80
    - Anti-ds-DNA (Farr): 9.0 IU/mL (<7.0)
    - ENA: negative
  - Complement levels: moderate C3-elevation
  - ANCA: negative
  - Lupus anticoagulans: slightly positive
  - IgG anticardiolipin antibody: 2.9 (<= 2.5)
  - IgM anticardiolipin antibody: 3.5 (<= 3.5)
- Negative cultures and viral serologies

Chest X-ray



Transthoracic echocardiography

- Moderate dilatation of left ventricle with moderately diminished systolic function (EF: 40%)
- Severe mitral insufficiency (3 to 4/4)
- Moderate aortic insufficiency (2/4)
- Severe pulmonary hypertension:
  - PAP syst. 42 mmHg + CVP
- No vegetations

MRI heart

- Dilated left ventricle with moderately severe systolic dysfunction (EF: 37.5%) and severe mitral insufficiency, most likely secondary to LV dilatation
- Normal appearance of the myocard

Transoesophageal echocardiography

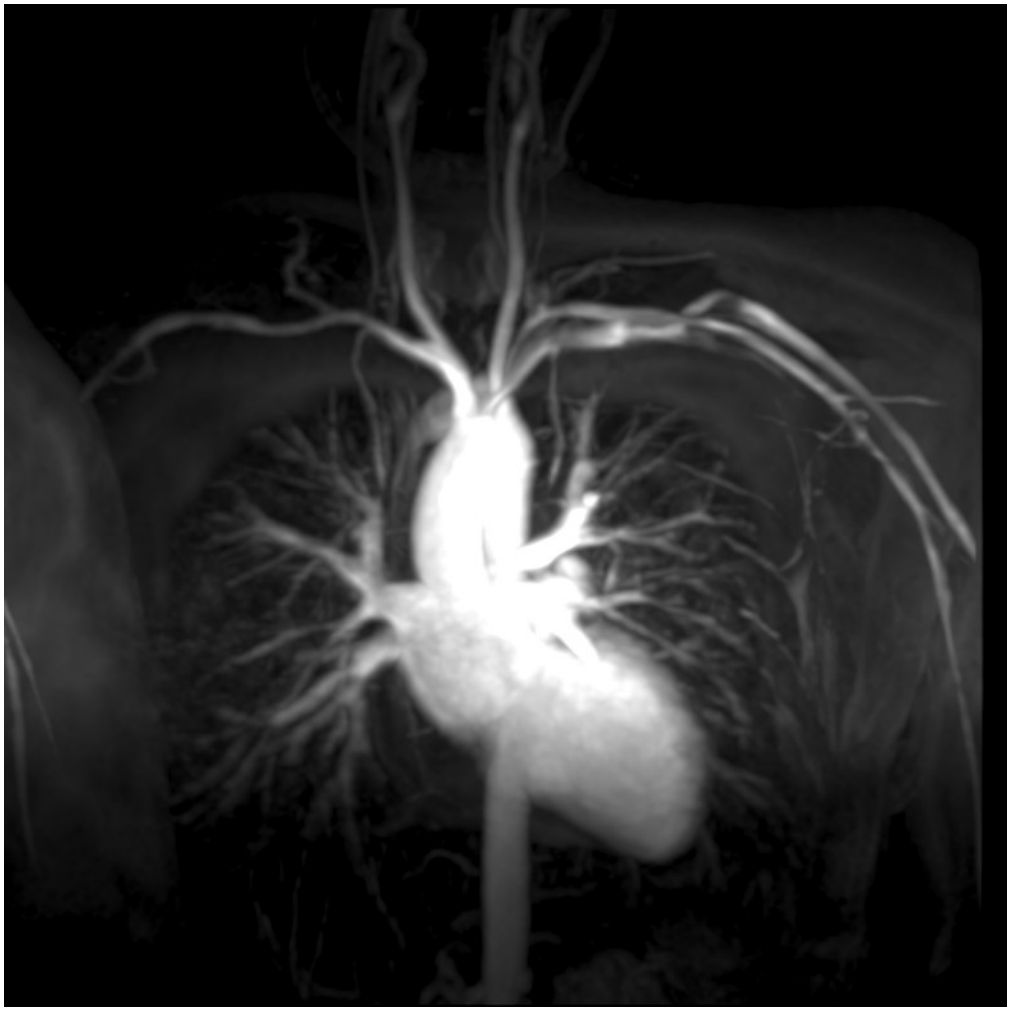
- Severe aortic insufficiency
- Moderately dilated, moderately hypocontractile LV
- Moderate to severe mitral insuffiency ¾
- Slightly thickend aortic wall (IMT: 1.6 mm)

FDG-PET-scintigraphy

- Increased captation of the bone marrow, compatible with reactive bone marrow activation
- No clear focus of arthritis or other source of infection/inflammation.

Biopsy of the myocard

- Normal findings



MRI of the aorta

- Tapering of both subclavian arteries, suggestive of Takayasu arteritis

Diagnosis, therapy and evolution

- Diagnosis:
  - Takayasu arteritis:
    - Young female
    - Chronic inflammation with profound weight loss (inflammation already present before car accident)
    - Aortic insufficiency with LV dilatation and failure, secondary mitral insufficiency
    - Tapering of both proximal subclavian arteries
    - Arthritis of finger joints
    - Erythema nodosum in past history
- Therapy:
  - Loop diuretics, betablockers, ACE-inhibition
  - Corticosteroids with prompt response (subjective and inflammatory markers)
  - Cardiac surgery with aortic valve replacement and mitral valve repair; marked thickening and inflammation of aortic wall, retracted aortic valve (Bx: intima thickening; no active aortitis (any more))

Quick overview of Takayasu 'aorta-arteritis'(TA)

- The aorta and its major branches are the prime disease targets in TA.
- Clinical symptoms of vascular inflammation and insufficiency are usually accompanied or preceded by a systemic inflammatory process.
- TA tends to affect women much more often than men (F:M=9:1), and has a predilection for Asian women. However, TA has been described in individuals of all racial and ethnic backgrounds.
- TA is associated with granulomatous inflammation within the blood vessel wall. The histopathological features of the disease closely resemble those of giant cell arteritis.
- TA leads to vascular narrowing in most blood vessels it affects. However, in the aorta, TA can cause aneurysms of the ascending aorta. These often lead to aortic regurgitation. Up to 40% of patients with TA have cardiac disease, including aortic regurgitation in 20%.
- A lesion of great concern in TA is renal artery stenosis, which can lead to renin-mediated hypertension.

Distinghuishing features of giant cell versus Takayasu arteritis

Finding	**Giant cell arteritis**	**Takayasu arteritis**
Female-to-male ratio	3:2	7:1
Age at onset	>50 years	<40 years
Ethnic ancestry	European	Asian
Histopathology	Granulomatous inflammation	Granulomatous inflammation
Primary vessels involved	External carotid artery branches	Aorta and branches
Renovascular hypertension	Rare	Common
HLA association	HLA-DR4	HLA-Bw52
Course	Self-limited	Chronic
Response to corticosteroids	Excellent	Excellent
Surgical intervention needed	Rare	Common