

## Case report

# Subacute bacterial endocarditis presenting as polymyalgia rheumatica or giant cell arteritis

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### ABSTRACT

**Objective.** To report on several patients with subacute bacterial endocarditis who were initially presumed, incorrectly, to have polymyalgia rheumatica or giant cell arteritis.

**Methods.** We report 3 cases of subacute streptococcal endocarditis mimicking giant cell arteritis in 2 cases and polymyalgia rheumatica in one. We reviewed the literature through Medline search of French and English-language articles published between 1966 and 2005 and found 5 similar cases.

**Results.** Shoulder and/or pelvic girdle pain was associated with neck or back pain in all patients. Scalp tenderness, bilateral jaw pain, amaurosis fugax were present in 2 patients. One patient had no fever. Two patients were treated with corticosteroids with initial good clinical response in one. Appropriate antibiotic therapy resulted in the rapid disappearance of rheumatic complaints in 2 patients and achieved a definitive cure of endocarditis in all cases.

**Conclusion.** Rheumatologic symptoms may hinder the correct diagnosis of infective endocarditis in patients who present with a clinical picture suggesting polymyalgia rheumatica or giant cell arteritis. In such cases, blood cultures should be systematically drawn.

### Introduction

Polymyalgia rheumatica (PMR) is an inflammatory disorder often associated with giant cell arteritis (GCA). It is characterized by pain and morning stiffness of the shoulders and pelvic girdle, constitutional symptoms such as fever, weight loss, fatigue, and biological inflammation. Subacute bacterial endocarditis (SBE) is a systemic infectious disease. Musculo-skeletal symptoms, related to embolic and/or immunological processes, occur in up to half of the cases and may be prominent causes of misdiagnosis and delayed

specific therapy. We describe herein three patients with SBE mimicking PMR and/or GCA.

### Case reports

#### Case n°1

A 57-year-old man was admitted on July 1998 with a 2-month history of symmetrical and proximal myalgias, with progressive worsening of morning stiffness involving shoulders and hips, and transient lumbar pain. He also complained of migratory arthralgias of the left ankle, right wrist, and bilateral jaw tenderness. His medical history consisted of a probable Sydenham's chorea at 10-years of age, unexplored episodes of melena in 1994 and February 1998, hypercholesterolemia treated with simvastatin and type 2 diabetes mellitus since the age of 50. He had noticed unusual fatigue and 2 kg weight loss within 2 weeks. Aching persisted after simvastatin withdrawal. Pain decreased slightly on Ibuprofen therapy. On admission, temperature was 37.6°C. Physical examination displayed a grade 2/6 systolic murmur at the left sternal border.

Laboratory tests showed: leukocyte count 9.3 G/L with 6.8 neutrophils, haemoglobin 12 g/L, platelet count 289 G/L, erythrocyte sedimentation rate (ESR) 70 mm after the first hour, C reactive protein (CRP) 82 mg/L. Serum creatinine and urine sediment were normal. Tests for rheumatoid factor, antinuclear and anti neutrophil cytoplasmic antibodies (ANCA), cryoglobulin gave negative results. Chest radiograph showed mild heart enlargement. EKG was normal. A transthoracic echocardiography was claimed shortly after admission.

After 5 days of residential observation, a subcutaneous nodule of the left forearm appeared. Histological study of its biopsy revealed leucocytoclastic vasculitis involving dermal and hypodermal small vessels, without any immune deposits.

The temporal artery biopsy was normal, as well as the retinal fundoscopy. The abdominal computerized tomography scan (CT scan) showed a 13 cm height homogeneous splenomegaly and no diverticular abscess. Colonoscopy displayed sigmoid diverticulae.

Systematical blood cultures grew *enterococcus faecalis*. Trans-esophageal echocardiography demonstrated a large vegetation (15 x 18 mm) on the anteromedial mitral leaflet. Combination of amoxicillin and gentamycin was started, converted to amoxicillin monotherapy after 14 days. Blood cultures drawn after 4 days of therapy were sterile. Myalgias disappeared within 3 days. CRP normalized within 10 days. On October 20th 1998, transesophageal echocardiography showed minimal residual mitral regurgitation with no vegetation. After a 2 years follow-up the patient remains healthy.

#### Case n° 2

A 61 year-old man had a mitral regurgitation known for about 10 years. On July 1992, he complained of pain in the right shoulder which became bilateral after 3 weeks, accompanied by upper dorsal pain, fever (38 to 39 °C), chills, night sweats and 6 kg weight lost. After an external consultation, PMR was considered. Piroxicam 20 mg/d and then prednisone 40 mg/d were prescribed with a slight pain decrease but persistent fever. He was hospitalized in September. Physical examination displayed a temperature of 39 °C, a grade 3/6 holosystolic murmur at the apex of the heart, decayed teeth and severe parodontopathy, amyotrophy of the scapular girdle and pain during arm lifting. Laboratory tests showed: leukocyte count 11.6 G/L with 8.4 neutrophils, 1.28 monocytes, haemoglobin 11 g/dL, ESR 56 mm, fibrinogen 4.9 g/L and polyclonal hypergammaglobulinemia (21g/L). Serum creatinine, urine sediment, muscular and liver enzymes were normal. Tests for rheumatoid factor, cryoglobulinemia were negative. Shoulders and cervico-dorsal spine radiographs, cervical bone CT-scan, bone scintigraphy showed mild degenerative C4-C5 discopathy. An electromyogram was normal. The chest X ray revealed a moderate heart shadow enlargement.

Three blood cultures grew *Streptococcus mitis*. Transthoracic echocardiography displayed a mild mitral regurgitation without vegetation. Transesophageal echocardiography revealed an irregular thickening of the anteromedial mitral leaflet. Steroids were stopped. A combination of penicillin and netromycin was instituted, switching to oral regimen of ampicillin after 2 weeks. All symptoms disappeared within 3 days. Echocardiography showed persistent thickening of the mitral leaflet. The patient died 4 years later from metastatic lung cancer.

#### Case n° 3

A 65-year-old man was admitted in April 2000 with a 6-month history of fatigue accompanied by anorexia, 6 kg weight loss, low grade fever (38 °C), remitting bilateral and asymmetrical arthralgias involving metacarpophalangeal joints and wrists followed by symmetrical shoulder and hip pain with morning stiffness, partly responsive to non-steroidal anti-inflammatory drugs. Physical examination displayed a grade 1/6 systolic murmur at the apex. The temporal pulses were preserved with no thickening or induration of the arterial wall. Ophthalmological examination was normal. The patient had undergone several colonoscopies. The last one, in January 2000, allowed the resection of a small low grade dysplastic caecal polyp. Thoraco-abdominal CT scan was normal. Trans-thoracic echocardiography displayed a mild mitral regurgitation. Recent onset of striking headaches with scalp tenderness and sudden blurred vision suggested GCA. Prednisone (70 mg/d) was started with a rapid improvement of rheumatologic symptoms and recovery of vision.

Laboratory tests showed: ESR 45mm, CRP 86 mg /L, leukocyte count 10.5 G/L with 9.3 neutrophils and 1.1 lymphocytes, haemoglobin 12 g/L. Serum creatinine and urine sediment were normal. Erythrocyte Coombs test was positive and rheumatoid factor present. Cryoglobulinemia and ANCA were negative. Temporal artery biopsy displayed a mild intimal fibrosis. Blood cultures grew *streptococcus bovis* (*S. equis*). Trans-esophageal echocardiography displayed one vegetation (7 x 2.7mm) on the anteromedial mitral leaf-

let and two on the posterolateral (4.5 mm). A new colonoscopy was normal. Combination of amoxicillin and gentamycin was initiated. Blood cultures drawn after 6 days were negative. Temperature and CRP normalized within 5 days. Echocardiography indicated a total disappearance of vegetations 3 months later.

#### Discussion

We report 3 patients, aged from 57 to 65 years, who presented with symptoms mimicking PMR and/or GCA, characterized by proximal arthro-myalgias, axial pain and elevated ESR. Cephalic symptoms were present in cases n° 1 and 3. Patient n° 1 had no fever. All patients had been treated with non-steroidal anti-inflammatory drugs and 2 with prednisone, with partial or complete clinical response. However, all had prior known valvular disease. SBE is an infectious process involving, predominantly, heart valves that may present as a mosaic of symptoms due to septic-embolic and immunological phenomenon. Apart from classical nephrologic, central nervous system or cutaneous signs (1), musculo-skeletal manifestations have been described in 17% to 44% of the cases (2-6). In Churchill's serie, rheumatologic complaint was predominant in 27% of cases and the only presenting feature in 15% (3). The main reported manifestations were arthralgia, myalgia, arthritis, back pain with or without osteomyelitis (2-6). Their equivocal significance might result in misdiagnoses, the most common of these being rheumatic fever (2, 3-5), gout, spondylarthropathy, rheumatoid arthritis (3) and degenerative sciatica (3, 4). Recently, arthralgias represented 24% to 74 % of the rheumatologic symptoms observed in SBE (3, 5, 6). The shoulders, knees and hips were the most frequently involved (3, 4, 6), with a usual asymmetrical pattern that is rarely encountered in authentic PMR (7). Arthritis was less frequent, noted in 12% to 33% of the rheumatologic symptoms of SBE (3-6). Proximal and lower extremity joints were most commonly involved with a mono or oligoarticular pattern (4, 5). Headaches, although present in half of the patients with SBE (8), rarely had the usual characteristics of those

observed in GCA i.e. recent, localized, associated with scalp tenderness and temporal induration (9). They resulted from varied conditions such as cerebral infarct, rupture of a mycotic aneurysm, intracerebral abscess or meningitis (1). As illustrated by one of our cases (n° 3), patients aged over 50 years that present with a new headache and elevated ESR in the course of SBE, fulfill three of the ACR-criteria and may be classified as having GCA (9). The other confusing symptoms of SBE are abrupt central nervous system deficit and amaurosis fugax or sudden blindness. They usually result from cerebral embolism in SBE and from vasculitis in GCA. Ocular manifestation occur much more frequently in GCA than in SBE. Whereas on the opposite, the reported prevalence of cerebral involvement is said to be 3% to 7% of GCA (10) and as high as one third of the SBE cases (1). The possible association of SBE with renal involvement, cutaneous vasculitis (as observed in patient n°1) (6), and immunological anomalies such as rheumatoid factors (present in up to 50% of cases) (3), cryoglobulinemia (4, 6), ANCA (11) or ANA (3), might further lead to misdiagnosis, more specifically towards systemic vasculitis. In fact, symptoms evoking PMR/GCA are rarely encountered in SBE (3, 6). SBE has been cited as a relevant differential diagnosis in patient with proximal polymyalgia (7, 12). However, we only found 5 previous specific reports of SBE mimicking PMR/GCA (12-16) and one case of isolated jaw claudication (2). To our knowledge, scalp tenderness, observed in case n° 3, was not previously reported in SBE. In the French nationwide prospective study on GCA that included 400 patients with PMR/GCA (17), one case of SBE was initially misdiagnosed as PMR because of low-grade fever, back pain, elevated ESR and response to corticosteroids. In Spomer *et al.*'s case, neck, shoulders and leg pain raised the hypothesis of PMR until positivity of blood and synovial fluid cultures (14). In the most recent report, a typical pattern of PMR appeared in contrast to a severe malaise. After an M-mode echogram had been performed and revealed a normal condition, prednisone 15mg/d was started but proved unsuccessful. A

temporal artery biopsy was verified and prednisone was increased to 40mg/d. All the blood cultures eventually grew *haemophilus paraeinflezae* and a new echocardiogram disclosed vegetations (12). Grétilat *et al.*'s case presented with cervical and lumbar pain without fever and increased ESR. The presence of a disrupted internal elastic lamina on temporal artery biopsy led to an inefficient prednisone therapy with secondary onset of arthralgias, headaches, fever and subsequent positive blood cultures (15). Two other reports of streptococcal SBE suggested GCA with bitemporal headaches, blurred vision and even bitemporal inflammatory nodules. In both cases, temporal artery biopsy showed a large exudative vessel wall and perivascular infiltrate with endoluminal thrombosis and microorganisms after a gram stain (13, 16).

Pathophysiology of SBE includes circulating immune complexes, vasculitis and embolic phenomena that are probably, variously, involved in rheumatological symptoms of SBE, although the kidney and skin usually provide the main expressive manifestations (3). According to the symmetrical pattern of pain, an embolic pathophysiology could not be evoked for our patients. Joint and muscle pain appeared more commonly among patients with a brief duration of illness and did not correlate with immunoglobulins levels (5). Increased levels of macrophage-derived cytokines are shared by both streptococcal or enterococcal SBE and PMR/GCA (18, 19) and might be involved in the pathogenesis of inflammatory arthro-myalgias.

Among patients with rheumatic and systemic symptoms, valvular heart disease, previously known or not, must lead to an early evocation of SBE and a checking of blood cultures. Inflammatory disorders requiring corticosteroids such as GCA or PMR, should be considered and treated only after SBE has been completely ruled out.

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