Giant cell arteritis as a cardiovascular entity

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Giant cell arteritis (GCA) is a relatively infrequent disorder that is underdiagnosed and little appraised in the field of general cardiology. However, it is important to be familiar with the clinical picture of this disease, especially because of the risk of developing fatal aortic aneurysms. If the disease is suspected after a thorough history and clinical examination combined with laboratory investigation, the diagnosis can be confirmed with ^{18}F -2-deoxy-glucose positron emission tomographic (FDG-PET) imaging. Early recognition of giant cell arteritis followed by prompt treatment with glucocorticosteroids will decrease the risk of developing large-vessel complications. (*Neth Heart J* 2009;17:281-3.)

Keywords: giant cell arteritis, large-vessel disease, aortitis

A 66-year-old previously healthy female patient presented with symptoms of fatigue, anorexia and low-grade fever. She had no claudication, headache or muscle weakness. She was a non-smoker, did not use any alcohol and had no family history of cardiovascular disease. On clinical examination we saw an anaemic Caucasian woman with a blood pressure of 145/75 mmHg with a regular pulse of 75 beats/min. On examination of the heart there were normal heart

sounds with a grade III early systolic murmur radiating to the carotid arteries. Peripheral pulsations were palpable and of normal volume. Examination of the lungs and abdomen was unremarkable and on inspection of the skin we found no stigmata of endocarditis. Laboratory investigation revealed a normocytic anaemia (haemoglobin 4.7 mmol/l) and an acute phase reaction with thrombocytosis (535/nl), elevated erythrocyte sedimentation rate (ESR, 128 mm/h) and elevated C-reactive protein (135 mg/l). Electrocardiogram and chest X-ray were normal. In two anaerobic bottles out of six blood cultures *Bacterium propioni acnes* was grown. Transthoracic echocardiography showed a hyperdynamic left ventricle and severe concentric myocardial hypertrophy. The ascending aorta was not dilated. The aortic valve was tricuspid with calcified cusps and a moderate aortic insufficiency. On the aortic side of the valve a possible vegetation was visualised.

The diagnosis of endocarditis of the aortic valve caused by *Bacterium propioni acnes* was made in this patient and treatment was started with intravenous penicillin and gentamycin. Despite 14 days of therapy there was no improvement in the clinical picture or laboratory results. A transoesophageal echocardiography was performed and showed no evidence of vegetations on any of the valves. The diagnosis of endocarditis was questioned and other causes of a chronic inflammatory syndrome were carefully reviewed. Subsequential laboratory analysis was negative for antinuclear antibodies, antineutrophil cytoplasmic antibodies, cryoglobulin and monoclonal antibodies. Computer tomography of the thorax and abdomen showed marked thickening of the wall of the thoracic and abdominal aorta, raising the suspicion of aortitis. ^{18}F -2-deoxy-glucose positron emission tomographic (FDG-PET) imaging disclosed a generalised, diffuse ^{18}F -2-deoxy-glucose uptake in the vessel wall of the carotid arteries, brachial arteries, thoracic and abdominal aorta and iliacal arteries (figure 1). To confirm the diagnosis of large cell arteritis, we decided to perform a biopsy of the temporal artery. Microscopic examination revealed a mononuclear infiltrate through-

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out the vessel wall with disruption of the internal elastic lamina and a profound fibrosis and oedema of the intima.

Based on the clinical picture, the results of the FDG-PET and biopsy, the initial diagnosis of endocarditis was rejected and the diagnosis of giant cell arteritis was made. The patient was treated with prednisone and within 48 hours her complaints of fatigue and anorexia improved. The ESR decreased to normal within eight weeks of therapy. Subsequent FDG-PET imaging showed a significant decrease of the inflammation of the major vessels (figure 1).

Discussion

Giant cell arteritis (GCA) is a chronic systemic vasculitis affecting large and medium-sized arterial vessels. The spectrum of systemic vasculitides are well-known entities in rheumatology and internal medicine; however, they are much less considered in the field of general cardiology. Our case report illustrates the importance of being aware of this cardiovascular disease. GCA virtually only affects people over 50 years of age and there is a geographic difference in incidence with a predominance for people of northern European descent.^{1,2} The classical and most frequent clinical presentation of GCA is that of temporal arteritis or polymyalgia rheumatica. However, in this discussion we want to focus on large-vessel involvement. At one end of the spectrum, dilatation can be a sequel to generalised aortitis. Both the thoracic and abdominal aorta can dilate to aneurysmatic proportions with a risk of dissection. At the other end of the spectrum, stenotic disease in the primary and secondary branches of the aorta may develop.³

During clinical examination bruits may be heard over the carotid, subclavian, axillary and brachial arteries. Peripheral pulses in neck or arms may be diminished or even absent and the blood pressure can be asymmetric.⁴ Patients with aortitis are often asymptomatic until they present with the typical clinical picture of an aortic dissection. Large-vessel involvement may present years after onset of GCA or even years after treatment with glucocorticosteroids.³

On laboratory examination the most important diagnostic finding is an elevated ESR of at least 50 mm/h. A mild normocytic anaemia may be present, as well as mildly elevated liver enzymes. A chest radiograph may show dilatation of the aorta. Angiography, contrast-enhanced computer tomography (CT) and magnetic resonance angiography (MRI) are important tools in diagnosing the disease and its extent.⁵ 18-FDG-PET can be an important diagnostic tool in detection and staging of the disease. Especially extra-cranial involvement of GCA can be detected by the use of FDG-PET.⁶ Despite the low sensitivity of only 58%,⁷ a biopsy of the temporal artery should always be

Figure 1. Images of a PET/CT scan (Philips Gemini XL/16 slice), 60 minutes after intravenous injection of a standard dose of 18-FDG. The first panel shows increased FDG uptake in the vessel wall of the thoracic and abdominal aorta; its secondary branches are clearly visible. The second panel shows virtually complete resolution of uptake three months after treatment with glucocorticosteroids.

performed in our opinion. It is a low-risk procedure providing important diagnostic information justifying long-term glucocorticosteroid therapy.

GCA should be differentiated from Takayasu arteritis. The latter has a different age distribution, affecting patients before the age of 40 with a higher incidence in the Asian race.⁸ The systemic response and aspecific laboratory findings of GCA make it difficult, however, to differentiate GCA from conditions such as rheumatoid arthritis, amyloidosis, systemic lupus erythematosus, but also chronic infectious diseases or even endocarditis. FDG-PET can be an important tool to differentiate giant-cell arteritis from other diseases. Our case report illustrates the value of FDG-PET and in retrospect we have to conclude that the blood cultures had been contaminated with *Bacterium propioni acnes* as this pathogen was only present in two (anaerobic) bottles out of twelve bottles in total. Moreover, the Duke criteria were not fulfilled and *Bacterium propioni acnes* is unlikely to infect native valves.

Glucocorticosteroids form the cornerstone in the treatment of GCA. Typically, the response to therapy is rapid with resolution of symptoms within 24 to 48 hours. The ESR can be useful to decide whether further reduction of dosage is appropriate. Many patients need to be treated with low-dose prednisone for one to two years to prevent relapse of the disease.¹ One should be familiar with the common side effects of glucocorticosteroids therapy. If not, it is recommended to consult a rheumatologist or internist who are more familiar with glucocorticosteroid treatment and dose adjustments.

Symptomatic stenotic disease can be treated with balloon angioplasty. Dilatation of the thoracic and abdominal aorta is usually asymptomatic and can progress to a fatal rupture. It is therefore advocated that all patients with GCA should be screened for the presence of aneurysms. Screening consists of a baseline and yearly abdominal ultrasound, chest X-ray and transthoracic echocardiography. For patients with an aortic insufficiency murmur, an ESR >100 mm/h, hypertension, hyperlipidaemia or coronary artery disease, a baseline CT or MRI angiography is recommended. Asymptomatic aneurysms should be referred for surgery following the guidelines for atherosclerotic aneurysms as there are no data available on surveillance and treatment of thoracic and abdominal aneurysms in patients with GCA.³ Mortality of patients with large-artery involvement is comparable with the group of patients without large-artery complications. It may be obvious that the subgroup of patients with a symptomatic thoracic aneurysm has a poor prognosis with a median survival of 1.1 years.⁹ ■

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