Case Report

Periaortitis Heralding Wegener's Granulomatosis

CHRISTINE de ROUX-SERRATRICE, JACQUES SERRATRICE, BRIGITTE GRANEL, PATRICK DISDIER, JEAN-MICHEL BARTOLI, XAVIER PACHE, PHILIPPE ASTOUL, LUCIENNE GARBE, ALAIN BRANCHEREAU, and PIERRE-JEAN WEILLER

ABSTRACT. We describe a 47-year-old man who successively presented atheromatous coronary artery disease, cholesterol embolism after angioplasty, periaortitis with presence of c-ANCA, and finally typical pulmonary lesions caused by Wegener's granulomatosis. This case illustrates the link between atheromatous and inflammatory process and emphasizes that periaortitis may be a feature of Wegener's granulomatosis. (J Rheumatol 2002;29:392–4)

Key Indexing Terms:
PERIAORTITIS WEGENER'S GRANULOMATOSIS ATHEROMA
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We describe a 47-year-old man who successively presented with atheromatous coronary artery disease, cholesterol embolism after angioplasty, periaortitis with presence of antineutrophil cytoplasmic antibodies (c-ANCA), and finally typical pulmonary lesions caused by Wegener's granulomatosis (WG).

CASE REPORT

A 47-year-old man was admitted to our service in 1997 for livedo with focal areas of skin necrosis of lower limbs and prolonged fever (38°C). For 20 years he had smoked a pack of cigarettes per day, and he had hypercholesterolemia, hypertension, lower limb arteritis, and coronary artery disease (first myocardial infarction occurred in 1992 and was treated by angioplasty of the left circumflex artery). He had recently presented a 2nd myocardial infarction, which was treated by right coronary artery angioplasty and anticoagulants. Laboratory evaluation found an inflammatory process [C-reactive protein (CRP) 121 mg/l; normal < 5]. Creatinine was 83 μmol/l. Chest and abdominal computerized tomographic (CT) scans revealed a mildly atheromatous abdominal aorta. All these findings strongly evoked cholesterol embolism.

In 1998 he was hospitalized for intensive abdominal pain. Abdominal CT scan showed ectasia of infrarenal aorta (diameter 27 mm) extending to the aortic bifurcation, with atheroma and a considerable retroperitoneal infiltration surrounding the abdominal aorta. This inflammatory infiltration reached the iliac arteries, surrounded the inferior mesenteric artery, but did not affect the lumbar ureters, and was typical of periaortitis (Figure 1). Chest CT scan showed centrolobular emphysema and bronchiectasis. Bone scintigraphy was normal. Laboratory variables were as follows: leukocytes 7.55×10^9/l; hematocrit 38%; erythrocyte sedimentation rate (ESR) 38 mm/h; CRP 88 mg/l; with negative antinuclear antibodies, positive antineutrophil cytoplasmic antibodies of the c-ANCA type [antiproteinase 3 (PR3) 62 IU/l (normal < 20), ELISA]. Steroid treatment was rapidly started (prednisolone 1 mg/kg/day), with improvement of abdominal pains. During the following months steroids were progressively tapered, and abdominal symptoms reoccurred with < 0.25 mg/kg/day. Abdominal CT scan evidenced no improvement of periaortitis. We added azathioprine (150 mg/day) and obtained a good response for pain, a partial response of the periaortitis, and a dramatic decrease of ANCA (anti-PR3 3 IU/l) (Figure 2).

After 6 mo of steroid and azathioprine treatment, he presented pseudomalarial fever crisis, with ESR 40 mm/h and CRP 67 mg/l. Search for an infectious process was unsuccessful. Serological tests for hepatitis B and C viruses, Epstein-Barr virus, cytomegalovirus, and herpesviruses 1 and 2 were negative. Blood cultures, urine cultures, cerebrospinal fluid culture, and bone marrow cultures remained sterile. However, we stopped the azathioprine due

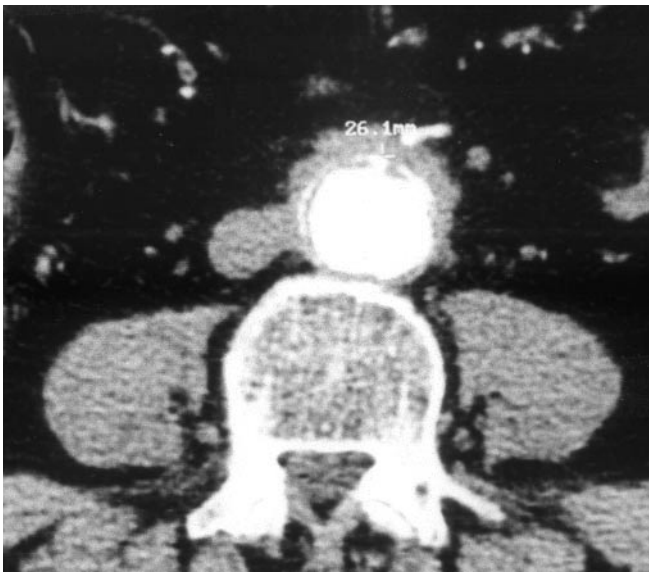

Figure 1. Abdominal CT scan with contrast injection showing an ectasia on infrarenal aorta with parietal calcifications evoking an atheromatous process and a periaortic inflammatory infiltration on lateral and anterior walls.

From the Service de Médecine Interne, Service de Radiologie, and Service de Chirurgie Vasculaire, CHU Timone; and Service de Pneumologie, Service d'Anatomie Pathologique, Hôpital Sainte Marguerite, Marseille, France.

C. de Roux-Serratrice, MD; J. Serratrice, MD; B. Granel, MD; P. Disdier, MD; P-J. Weiller, MD; X. Pache, MD, Service de Médecine Interne; J-M. Bartoli, MD, Service de Radiologie; A. Branchereau, MD, Service de Chirurgie Vasculaire, CHU Timone; P. Astoul, MD, Service de Pneumologie; L. Garbe, MD, Service d'Anatomie Pathologique, Hôpital Sainte Marguerite.

Address reprint requests to Prof. P. Disdier, Service de médecine interne, CHU Timone, 264 rue Saint Pierre, 13385 Marseille Cedex 5, France. E-mail: pdisdier@ap-hm.fr

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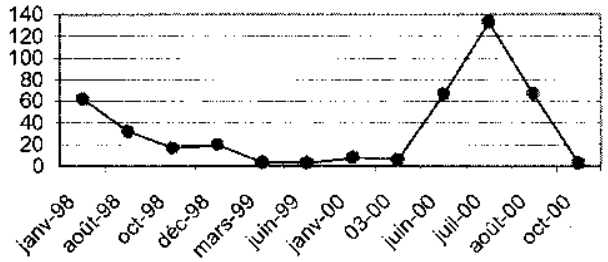

Figure 2. Course of the c-ANCA ratio (IU/l).

to this unexplained recurrent fever and ineffectiveness regarding the periaortitis. We considered surgery for the aortic lesions. However, a few weeks later, chest radiograph and CT scan revealed 2 macronodular lesions in the upper and middle right lung lobes (Figure 3) associated with alveolar opacity in the lower lobe. c-ANCA rose to 67 IU/l, so we rapidly performed lung biopsies. Histopathological analysis of biopsies showed acidophilic necrosis with giant cells, vascularitis, and inflammatory granulomas typical of Wegener's granulomatosis. Intravenous cyclophosphamide bolus (0.7 g/m^2) was given every 3 weeks. A first intravenous prednisone bolus (240 mg/day for 3 days) was given, followed by prolonged oral steroid treatment (1 mg/kg/day). After 6 months of treatment (progressive tapering of prednisone to 0.25 mg/kg/day), no relapse was noted and pulmonary lesions regressed in parallel with the disappearance of c-ANCA (Figure 2).

DISCUSSION

In our case, the usual causes of periaortitis (Takayasu's disease, temporal arteritis, Churg-Strauss syndrome, polyarteritis nodosa, Cogan's syndrome, relapsing polychondritis, Erdheim-Chester disease) were excluded. An unquestionable diagnosis of WG was made, due to positivity of c-ANCA, lung nodular excavations on imaging evaluation, and histopathological examination of surgical lung biopsies[1].

Our observation raises several questions: When did WG occur in our patient? At the onset of the clinical history (1992) there was no doubt about atheroma as a typical clinical manifestation (coronary artery disease) and several vascular risk factors were present. At the end of the history (2000), WG was evident, as laboratory markers (c-ANCA) were present, pathological examination was absolutely conclusive, and imaging strongly supported a diagnosis of WG.

Was there a cholesterol embolism in 1997? With suspicion of cholesterol embolism after a coronary angioplasty, search for c-ANCA is not currently prescribed, and moreover at this time these markers were not available.

WG is a systemic disease that predominantly affects small arteries, arterioles, and venules. Interestingly, cardiac lesions can occur in WG and include pericarditis and coronary arteritis with myocardial infarction[2]. Histopathological examination frequently showed a mixture of atheromatous changes and vasculitis processes.

Persistent ANCA after cholesterol embolism has been reported[3]. We ourselves observed a huge increase of ANCA after angiography related aortic trauma (unpublished data).

What about periaortitis? This term has been proposed for a group of diseases including idiopathic retroperitoneal fibrosis, perianeurysmal retroperitoneal fibrosis, and inflammatory aneurysm of the aorta. All these conditions are indistinguishable histopathologically (all show severe adventitial lymphocytes and plasma cell infiltration with fibrosis). Thus, the painful periaortitis of our patient, which was clearly time related with the increase in c-ANCA levels, may logically be considered to be a part of WG, although we do not routinely

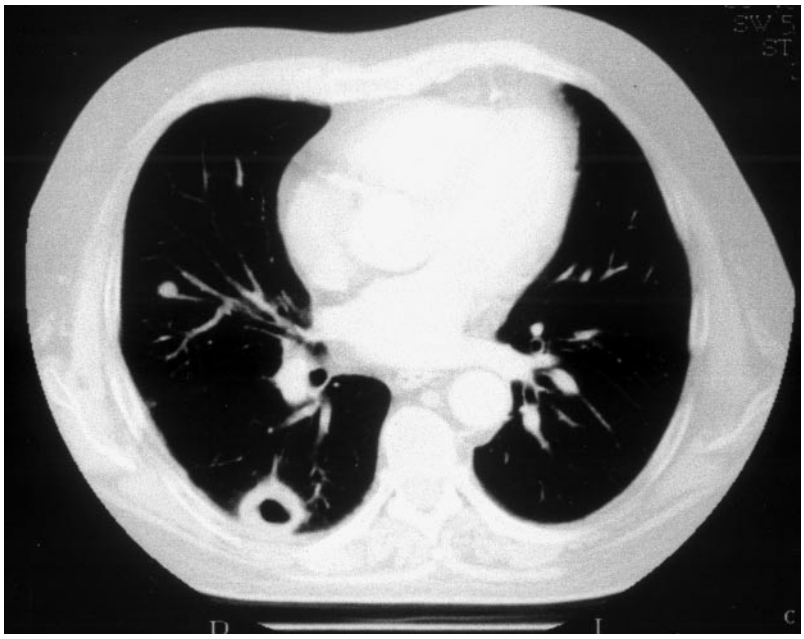

Figure 3. Thoracic CT scan in "lung window" showing a nodular lesion in middle lobe of the lung and a cavitary lesion in the lower lobe.

perform aortic biopsies. This is all the more probable considering similar cases in the literature. Fink, *et al* described a first case in 1994[4]; the diagnosis of periaortitis was based on an Indium-111 labeled leukocyte scan. A second case[5] described an intramural aortic dissection as being an early manifestation of WG. Surgical biopsies showed granulomatous vasculitis. In these 2 cases, histopathological examination of aorta confirmed the diagnosis of WG.

Our case illustrates the possible links between atheroma, cholesterol embolism disease, and WG. Although we do not rule out that our patient had had WG since the onset of his vascular symptoms, we feel there is a possible continuum between these manifestations. He developed atheroma complicated with cholesterol embolism after an angioplastic procedure; then he presented periaortitis with c-ANCA; and finally he exhibited typical symptoms of WG. The pathophysiology of such phenomena emphasizes the key role of ANCA. Recently, Palmgren, *et al*[3] described a patient with cholesterol embolism who developed persistent ANCA. Moreover, some cases of aortitis have been associated with ANCA[6], and in these cases histological analysis revealed vasavasoritis. Moreover, it has been shown in animal models that c-ANCA plays a role in WG pathogenesis.

For all these reasons, although we do not rule out a chance association, we feel that the limits between atheromatous and inflammatory processes are not as distinct as currently supposed. Our observations also emphasize that periaortitis may be a sign of WG.

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