Follow-up papers - Vascular general

Upper limb ischemia in a patient with Wegener’s granulomatosis

Miguel Maia*, Pedro Brandão, Pedro Monteiro, Paulo Barreto, Daniel Brandão, Joana Ferreira, Sandrina Braga, Guedes Vaz

Centro Hospitalar de Vila Nova de Gaia, Departamento de Angiologia e Cirurgia Vascular, Rua Conceição Fernandes, 4430-502 Vila Nova de Gaia, Portugal

Received 22 May 2008; received in revised form 13 August 2008; accepted 22 August 2008

Abstract

Objective: We report a clinical case of a small-vessel vasculitis with ischemia of the left upper limb. Case: A patient diagnosed with Wegener’s granulomatosis and involvement of the left axillary and brachial arteries. A left axillary-radial bypass with reversed left great saphenous vein was performed. Results: After a period of 36 months of follow-up the patient is asymptomatic with complete healing of the trophic lesions. Conclusion: Classic Wegener’s granulomatosis is a form of vasculitis that primarily involves the upper and/or lower respiratory tract and kidney. The amount of clinical symptoms is enormous and the diagnosis, arduous. In the literature there are only a few clinical cases referring to limb ischemia in a setting of Wegener’s granulomatosis. This is a unique case report of upper limb ischemia due to involvement of a medium–large size artery in a patient with Wegener’s granulomatosis.

Keywords: Small-vessel vasculitis; Wegener’s granulomatosis; Upper limb ischemia

1. Introduction

Wegener’s granulomatosis is a granulomatous, necrotizing and non-infectious small-vessel vasculitis with preferential involvement of the upper respiratory tract, lungs and kidneys [1, 3, 4].

The diagnosis of Wegener’s granulomatosis is very complex. The inflammatory process associated may involve various territories conditioning multiple clinical presentations.

Digital ischemia due to Wegener’s granulomatosis is extremely rare [4]. In known literature, there are only a few cases of limb ischemia and there are no reports of upper limb ischemia due to involvement of a medium–large size artery [4].

This is, to our knowledge, a unique case report of symptomatic upper limb ischemia with involvement of a medium–large size artery in a patient with Wegener’s granulomatosis.

2. Clinical case

A 55-year-old male with a history of non-insulin-dependent diabetes mellitus (for 10 years), hypercholesterolemia and former tobacco abuse (12 cigarettes/day for 20 years, stopped 20 years ago). Intravenous drug use was denied.

The patient presented in August 2004 with fever, weight loss (about 10 kg in 30 days), malaise, myalgias, polyarthritis, non-productive cough and occasional epistaxis, which started two weeks before.

He was first admitted in a small District Hospital under the care of the Internal Medicine Department. Chest radiographs and the thoracic computed tomography scan revealed bilateral lung parenchymal nodular densities with cavitations associated with a small pleural effusion, which was related to the inflammatory process (Fig. 1).

The blood analysis revealed a high white blood cell count (15,720/mm³; normal range: 3,800–10,600/mm³; polymorphonuclear, 86.1%), elevated erythrocyte sedimentation rate (59 mm/h; normal range: 0–20 mm/h) and a high serum C-reactive protein concentration (2.41 mg/dl; normal range: 0.01–0.5 mg/dl). Other analytical parameters were within normal range. Urinary sediment was normal.

The patient underwent a bronchoscopy and broncoalveolar lavage that showed an increase cellular number (4.04×105/ml) with: neutrophils: 4%; eosinophils: 2%; lymphocytes: 44%; monocytes/macrophages: 50%.

The first interpretation was pulmonary tuberculosis, so the patient was admitted and initiated empiric standard medication (Isoniazid: 300 mg/day; Rifampicine: 600 mg/day; Pirazinamid: 1200 mg/day; Etambutol: 1200 mg/day) with no success.

The patient was then transferred to a Central Hospital under the care of the Pneumology Department. Serologic examination revealed: serum anti-neutrophil cytoplasmic antibodies (ANCA): negative; antiproteinase three ANCA: negative; anti-nuclear antibodies: negative; rheumatoid factor: negative; anti-cardiolipin antibodies IgG: negative; anti-cardiolipin...
antibodies IgM: negative; anti-β₂-glycoprotein I IgG and IgM: negative; anti-Sm: negative; anti-SSA: negative; anti-SSB: negative.

Complement factors, IgG, IgA and IgM were within normal range. Serum α1-antitrypsin levels and tumor markers were normal.

Virus serology was positive for Cytomegalovirus IgG, Herpes Simplex type I IgG and Epstein Barr Virus IgG.

Because of ulceration in the nasal mucosa, the patient was submitted to a nasopharyngeal biopsy which revealed marked epithelium ulceration with vasculitis, compatible with Wegener’s granulomatosis.

A pulmonary biopsy was proposed, but the patient declined it.

Supported by the clinical and laboratory findings, the diagnosis of Wegener’s granulomatosis was established and the patient started cyclophosphamide (2 mg/kg/day) combined with prednisolone (1 mg/kg/day) and had an excellent clinical response.

The patient was first evaluated by our department of Angiology and Vascular Surgery in April 2005. He complained of left upper limb claudication as well as lack of muscular strength in both left arm and forearm for five months. He also complained of left upper limb coldness and rest pain during the previous 48 h. The patient presented ulceration of the 2nd through 5th left fingers, with focal necrosis, dating back to the last 15 days (Fig. 2). Capillary refilling time was severely prolonged. There were no palpable pulses and no Doppler signals in the brachial, radial or
cubital arteries. Contralateral upper limb examination was normal.

Electrocardiogram and echocardiography were normal.

The serum levels of protein C, protein S and antithrombin were normal. Testing for Factor V Leiden and Lupic anticoagulant factor was negative.

The patient underwent an angiographic examination that revealed left axillary artery occlusion (Fig. 3) and left brachial artery thrombosis (Fig. 4).

A left axillary-radial bypass with reversed left great saphenous vein was performed, without complications. Removed thrombus was sent for anatomopathological analysis. Systemic anticoagulation therapy with heparin (5000 IU/ev; bolus) was administered during the procedure.

In the early postoperatory, the patient had palpable brachial and radial pulse and bi-phasic cubital flow at Doppler examination.

During hospitalization the patient was medicated with prednisolone (10 mg/oral/day), enoxaparin (60 mg/s/12–12 h), clopidogrel (75 mg/oral/day) and paracetamol (1 g/oral/8–8 h). The patient initiated oral warfarine at the 4th postoperative day.

Transthoracic echocardiography was normal. Electrocardiogram was repeated and was again normal. Renal function was always normal throughout hospitalization. Anatomopathological analysis of the removed thrombus revealed organized blood clots.

At the discharge, by the 6th postoperative day, the patient remained asymptomatic with left brachial systolic blood pressures: Left brachial: 120 mmHg; Left radial: 120 mmHg; Left cubital: 100 mmHg; Right brachial: 120 mmHg; Right radial: 120 mmHg; Right cubital: 115 mmHg.

The patient maintained anticoagulation with warfarine, acetylsalicylic acid (150 mg/oral/day), prednisolone (10 mg/oral/day), metformin hydrochloride (850 mg/oral/day), glitazide (80 mg/oral/day), and pantoprazole (40 mg/oral/day).

Three months after the procedure, the patient was asymptomatic with complete healing of trophic lesions. Thoracic radiography showed resolution of pulmonary infiltrates.

At the present time the patient is asymptomatic with left brachial and radial palpable pulses. Doppler ultrasonography has been periodically performed and has not yet shown any evidence of hemodynamically significant stenosis.

3. Discussion

Vasculitis can result from primary vasculitis or from secondary involvement by surrounding inflammation [11]. Certain conditions can promote the occurrence of secondary vasculitis. Therefore, hypersensitivity to drugs, infectious diseases, rheumatoid arthritis, LUPUS, cancer and inflammatory bowel disease should be excluded in the study of a vasculitis [11].

Parietal inflammation can lead to endoluminal obstruction and tissue ischemia [2].

Several attempts were made to establish a unanimous classification for the extensive group of vasculitis [11]. The classification of the American College of Rheumatology, in 1990, and the recommendations of the Consensus of Chapel Hill, in 1994, are the currently accepted proposals [5, 14].

Small-vessel vasculitis refers to the preferential involvement of vessels smaller than arteries such as arterioles, capillaries and venules [1, 2]. However, it is important to realize that, despite this preferential involvement, small-vessel vasculitis can affect medium or even large-sized arteries overlapping with the clinical spectrum of medium and large-vessel vasculitis [1].

ANCA-associated vasculitides are the most common primary systemic small-vessel vasculitides in adults [1]. The three major ANCA-associated small-vessel vasculitides are: Wegener’s granulomatosis, microscopic polyangiitis and Churg-Strauss syndrome. Wegener’s granulomatosis differs from the other two by the presence of necrotizing granulomatous inflammation in the absence of asthma [1, 3].

Most patients with Wegener’s granulomatosis have anti-PR3 cytoplasmic ANCA [1, 9, 11, 13]. However, it is very important to realize that 5–10% of patients with typical Wegener’s granulomatosis are ANCA negative. Therefore ANCA seronegativity does not rule out Wegener’s granulomatosis, as ANCA seropositivity is not absolutely diagnostic of an ANCA-associated vasculitis [1]. Moreover, in limited forms of Wegener’s granulomatosis up to 40% of patients have remained ANCA negative throughout their disease.

In 1990 the American College of Rheumatology established criteria for the classification of Wegener’s granulomatosis [14]. In the traditional format classification, four criterions were selected: abnormal urinary sediment (red cell casts of five red blood cells per high magnification field), abnormal findings on chest radiograph (nodules, cavities or fixed infiltrates), oral ulcers or nasal discharge, and granulomatous inflammation on biopsy. The presence of two or more of these four criterions was associated with a sensitivity of 88.2% and a specificity of 92.0% [14]. Afterwards a fifth criterion was added: hemoptysis. The modified classification has a sensitivity of 87.1% and a specificity of 93.6% [14]. In this clinical case, three of the four classical criterions and four of the five modified criterions were observed.

Though <20% of patients have kidney involvement at the time of diagnosis, approximately 80% will develop glomerulonephritis during the course of their disease [1]. In this clinical case there was no significant renal involvement at the time of diagnosis and during clinical observation.

Certain non-specific constitutional signs and symptoms are often associated with Wegener’s granulomatosis such as fever, anorexia, weight loss, fatigue, tremors, night sweats, non-productive cough, chest discomfort, myalgias and arthralgia [1, 8]. Often, there is sinus pain associated with purulent or bloody nasal discharge and nasal mucosa ulceration [1, 15].

The occurrence of limb ischemia is very rare in the context of a small-vessel vasculitis [1]. Involvement of a medium—
large size artery by the inflammation process is extremely rare in a small-vessel vasculitis.

There are only a few cases described of limb ischemia associated with Wegener’s granulomatosis and there are no references of upper limb ischemia due to involvement of a medium–large size artery [4, 6, 7, 10, 12].

Besides precise anamneses and careful physical examination, the diagnosis process should include the use of complementary exams. Tissue biopsy, and further anatoomopathological analysis, can decisively contribute to final diagnosis, demonstrating the inflammatory process and typical necrotizing granulomatosis [1]. Biopsy should be performed on tissues with acute inflammation. Nasopharyngeal tissue is preferred, but in the absence of involvement or inconclusive results one should opt for biopsy of pulmonary parenchyma or renal tissue. In this clinical case, a nasal mucosa biopsy was conducted. The result supported the diagnosis of Wegener’s granulomatosis. To confirm the diagnosis it was proposed a pulmonary parenchyma biopsy which the patient declined.

In this clinical case, serological analysis has remained normal without elevation of serum ANCA. However, it is important to stress that elevation of serum ANCA does not imply Wegener’s granulomatosis and in some studies about 10% of patients with diagnosed Wegener’s granulomatosis (by internationally accepted criteria) were ANCA negative [1].

Typical clinical signs and symptoms associated with the presence of characteristic lung densities and subsequent anatoomopathological confirmation supported the proposed diagnosis of Wegener’s granulomatosis.

The patient had a favorable response after starting the proposed medication, diminishing the initial signs and symptoms. However, eight months later, he developed left upper limb ischemia. A left axillary-radial bypass with reversed left great saphenous vein was performed without any complications. During hospital observation the most frequent causes of peripheral ischemia were extensively investigated and excluded. Unfortunately, no artery wall was sent for anatoomopathological examination to confirm parietal inflammation, but such a procedure is highly recommended in similar cases.

The choice for an axillary-radial bypass using the great saphenous vein was made because of the technical readiness and recognized durability when using an autologous vein as conduit for a peripheral bypass. The endovascular treatment was turned down either because the limited experience of its use in peripheral ischemia in a setting of vasculitis or because of the unawareness of the medium–long-term biological effects between the synthetic material of the stent and the potentially inflamed vessel wall.

Three years after the procedure the patient remains asymptomatic. Radial and cubital systolic blood pressures are similar in both upper extremities. Ultrasound examination, with color flow Doppler and Doppler spectral analysis is within normal parameters, without turbulence or evidence of hemodynamically significant stenosis.

Because of the excellent outcome in this patient, we can conclude that in the rare cases of limb ischemia due to involvement of a medium–large size artery in a patient with a small-vessel vasculitis, performing a bypass using an autologous material, such as the great saphenous vein is a safe, viable and durable alternative.

References