Multivessel Percutaneous Treatment of Takayasu Arteritis

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We report the case of a female patient with obstructive lesions in the right and left carotid, right renal, left subclavian and left common iliac arteries which were percutaneously treated.

Takayasu arteritis (TA) is a chronic vasculitis which affects especially the aorta and its main branches, resulting in varied ischemic symptoms due to stenotic lesions or thrombus formation1-6. Percutaneous treatment with stent implantation is feasible for the correction of stenoses of the coronary and carotid arteries, as well as of peripheral lesions, and has been increasingly considered in the management of Takayasu arteritis7-10.

Case report

Twenty-five-year-old female Indian patient, born in and coming from an Indian reserve of the Kaingang tribe. She sought medical attention with a complaint of severe holocranial headache, accompanied by nausea and vomiting. In August, 2002 the patient had an episode of acute pulmonary edema (APE); she sought medical attention and was diagnosed with systemic hypertension (SH). She was referred for investigation of the possible causes of APE.

Physical examination revealed a patient in good general conditions. Cardiac auscultation showed regular rhythm and a grade 3/6 diastolic murmur of regurgitation in the aortic area. Pulmonary auscultation showed decreased breath sounds. Reduced left carotid pulse and water-hammer radial pulse in the right upper extremity were observed. The left radial, brachial, dorsalis pedis and posterior tibial pulses were not palpable. Blood pressure (BP) was 200x40 mmHg in the right arm, and it could not be measured in the left arm due to the absence of pulse. Bilateral carotid systolic murmur with fremitus on the right side, right femoral artery murmur and abdominal murmur were detected. The funduscopy revealed arteriolar narrowing, increased arteriolar reflex and pathologic arteriovenous crossings.

The electrocardiogram showed sinus rhythm, heart rate of 75 beats per minute, left atrial and ventricular overload and alterations in ventricular repolarization (Fig. 1).

The chest radiograph showed enlarged cardiac silhouette, elongated and dilated ascending aorta, with no signs of pulmonary congestion.

Laboratory tests showed: BUN 53mg/dl (15-45), creatinine 1.39mg/dl (0.6-1.4), erythrocyte sedimentation rate (ESR) 101mm/h (10-20mm/h), C-reactive protein 30 (up to 6.0), mucoprotein tyrosine 8.8 mg/dl (1.7 a 5.1).

Carotid ultrasound revealed diffuse and extensive thickening of the walls, causing a 70% stenosis of the lumen of the left common carotid artery.

Fig. 1 - Electrocardiogram – left chamber overload and alterations in ventricular repolarization.

Takayasu disease was suspected, and to confirm the hypothesis of other arterial lesions the patient underwent coronary angiography, aortography, and peripheral arteriography, which demonstrated normal coronary arteries, severe lesion in the left common carotid artery, mild lesion in the right common carotid artery, occlusion in the proximal third of the left subclavian artery, a 60% lesion in the ostium of the right renal artery, severe lesion in the ostium of the left renal artery, and occlusion in the proximal third of the left iliac artery. Left ventricle with diffuse hypokinesia and ejection fraction (EF) of 33% were observed. The aortography showed ectasia of the aorta and moderate to severe aortic regurgitation (Fig. 2).

In August, 26th, 2002, the patient underwent a successful

Key words

Takayasu arteritis, indian, stent, intravascular ultrasound, extracardiac interventional.
Case Report

Tumelero et al
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Arq Bras Cardiol 2006; 87 : e182-e188

in the postimplantation, an adequate juxtaposition of the endoprosthesis shaft.

After a two-year follow-up on an outpatient basis with an asymptomatic course, the patient was seen again in January, 2005 with decompensation of blood pressure (BP 180/100 mmHg), and ESR of 53 mm/h. She was on acetylsalicylic acid 200 mg, amlodipine 10 mg, captopril 150 mg, clopidogrel 75 mg, furosemide 40 mg, and sinvastatin 20 mg daily. The patient was referred to renal and carotid angiography which demonstrated unchanged successful stent implantation (performed in August, 2002) and severe lesion (80%) in the right renal artery, which was treated with a 6.5 mm x 12 mm Herculink (Guidant, CA, USA) stent implantation (Fig. 7). She was discharged with no symptoms and on the same medication.

In the 32-month follow-up since the initial diagnosis, a reduction in the inflammatory activity was observed, as demonstrated by the reduction in ESR (9 mm/h) and in C-reactive protein (<0.6), in addition to the unchanged results of the percutaneous procedures. However, progression of the untreated lesion in the renal artery was observed, despite preserved renal function (creatinine 0.96, BUN 33).

In April, 2005 the patient was asymptomatic, with reduction of the clinical and echocardiographic signs of aortic regurgitation, with controlled blood pressure (BP = 140/60 mmHg) and reduction in the number of antihypertensive drugs, with daily doses of captopril 75 mg, amlodipine 10 mg, and hydrochlorothiazide 25 mg.

Discussion

Takayasu arteritis (TA), described by Mikito Takayasu in 1908, is a chronic, idiopathic, inflammatory vasculitis that affects large and medium arteries, particularly the thoracic aorta and its major branches and the main pulmonary arteries,
in addition to the coronary arteries. The initial phase of this vasculitis is characterized by the thickening of the aorta wall with or without alterations in the arterial lumen. In this phase, however, the absence of luminal alterations does not exclude the diagnosis of TA.

The inflammatory process is destructive/degenerative and, in a late phase, leads to alterations in the arterial lumen characterized by stenosis, occlusion/thrombosis, atypical coarctation, dilation and/or aneurysms. Frequently, stenosis and obstruction predominate, but dilation and aneurysms are not rare. The epidemiology of TA shows a rare condition, with an incidence of 1.2 to 2.6 cases/million/year and which mainly affects young women in Japan, United States and Mexico, although some studies show similar frequencies as regards gender, especially in Southeast Asia. Lower rates are observed among white European or North American descendants. The location in the aortic arch is more frequently found in patients in Japan, whereas a more extensive disease affecting the abdominal and thoracic aorta predominates in India, Thailand and Mexico. Although the literature indicates a higher prevalence of TA among Asians and Central/South American populations, the authors did not find specific reports of prevalence studies of TA among the Amerindian population.

This is probably an autoimmune disease, since the association of arteritis with the haplotype HLA A24-B52-DR2 was demonstrated. We should point out that several ethnic groups have different HLA alleles associated with TA. Patients with these HLA have a tendency to an accelerated

Fig. 3 - Herculink stent implantation in renal artery lesion; pre and postintervention.

Fig. 4 - Smart stent implantation in carotid artery lesion; pre and postintervention.
inflammatory process and also to a higher resistance to steroid therapy when compared to those who do not have these HLA. Heterogeneous characteristics in its presentation, progression and response to therapy are observed.

According to Sharma et al\textsuperscript{11} (modified by Ishikawa\textsuperscript{12}), the clinical diagnosis of Takayasu disease consists of three major criteria (lesion in the left mid subclavian artery, lesion in the right mid subclavian artery, and characteristic signs and symptoms with duration greater than one month), and ten minor criteria (increased erythrocyte sedimentation rate, pain or tenderness in the carotid artery, high blood pressure, aortic regurgitation or ectasia of the aortic ring, lesion in the pulmonary artery, lesion in the left mid common carotid artery, distal lesion in the brachiocephalic trunk, lesion in the descending thoracic aorta, lesion in the abdominal aorta, and lesion in the coronary artery). For a high probability of diagnosis (92.5% and 95% sensitivity, and 95% and 96% specificity, according to the Indian or Japanese grouping, respectively), two major criteria, one major criterion plus 2 minor criteria, or 4 minor criteria are necessary\textsuperscript{11}.

In the present case, the diagnosis of TA was based on the presence of a major criterion (lesion in the left subclavian artery) and six minor criteria (ESR > 20 mm/h, systemic hypertension, aortic regurgitation, lesion in the carotid artery, lesion in the brachiocephalic trunk, and lesion in the abdominal aorta) confirmed by clinical, laboratory and angiographic tests.

Although the erythrocyte sedimentation is a well-established test to follow the activity of the disease and even considered an excellent test\textsuperscript{13} is currently been questioned, because of the histological findings of specimens obtained during surgery and of sequential angiographic studies\textsuperscript{14}. Other acute phase reactions should be valued as good activity markers and thus enable an adequate treatment. Therefore, alpha-1 acid glycoprotein, C-reactive protein, electrophoretic alpha-2 globulin, and haptoglobin levels

\textbf{Fig. 5} - Successful previous interventions remained unchanged. Lesion in the right common carotid artery.

\textbf{Fig. 6} - Herculink stent implantation in carotid artery lesion; pre and post intervention.
Angiography is the direct imaging method to evaluate the affected vessels, although several restrictions apply to its use due to the invasiveness, exposure to radiation, vessel rupture risk, bleedings and infections. However, it is the traditional modality for the diagnosis of TA. Arteriography should be indicated for all patients, not only facilitating the diagnosis, but also the assessment of severity of the disease and the choice of surgical treatment, thus being a mandatory preoperative test. Periodic angiographic studies may demonstrate an asymptomatic progression resulting in new sites of stenosis or aneurysm formation. Stenoses are usually more frequent than aneurysms.

The treatment of TA consists of the control of vascular inflammation with the use of immunosuppressors alone or in combination. However, in the chronic phase, the objective of the clinical treatment is not always achieved, and ischemia in several sites occurs, especially in the cerebral, coronary, peripheral arterial and renal territories. Diffuse, multifocal and ostial vessel involvement in TA makes the surgical revascularization difficult, in addition to being associated to a high rate of restenosis. Thus, the percutaneous correction of vessel obstructions emerges as a therapeutic possibility with no contraindication even in the presence of active arterial inflammation.

Obstructive carotid, renal and peripheral lesions in TA have been successfully treated with percutaneous angioplasty with stent implantation, which has proved safe and with a good cost-benefit ratio, thus being an alternative for patients at high surgical risk, despite the morbidity and mortality associated with the disease and the procedures. The experience with the percutaneous treatment of TA described in the literature is limited to case reports. Takahashi et al reported the first case of multiple stenting in all branches of the supraortic arch, however without the involvement of the renal arteries, with a two-year follow-up and favorable outcome.

In the case reported, angioplasty with stent implantation was successfully performed in the renal and carotid arteries. Procedures in the carotid arteries were performed with a distal embolic protection device, with the purpose of reducing the risk of stroke during endoprosthesis implantation. Endarterectomy is accepted as the standard treatment for revascularization of extracranial occlusive atherosclerotic lesions, validated by means of randomized controlled studies which demonstrated the superiority of endarterectomy over the pharmacologic treatment. However, in the past few years, the utilization of stents for the treatment of atherosclerotic stenoses of the carotid arteries has emerged as an alternative to endarterectomy. The endovascular treatment has been corroborated by randomized studies as a treatment as efficient as endarterectomy. The SAPPHIRE study designed for the treatment of patients considered at high surgical risk according to Sundt criteria demonstrated similar results for the surgical and percutaneous treatment when the distal cerebral embolic protection device was used. TA and atherosclerotic disease are known to be distinct diseases, but the risk of the surgical procedure is not reduced in TA. Additionally, although TA does not favor the presence of plaque fragments, the use of the distal protection device facilitates the procedure.
device is justified by the possibility of thrombus formation with distal embolization, which should be prevented. Thus, the patient at issue was considered at high risk due to the clinical presentation with acute pulmonary edema, aortic valve involvement, left ventricular dysfunction and poor control of blood pressure. Given the rare presentation and its pathogenicity, no studies comparing endarterectomy and stent implantation in patients with Takayasu arteritis are available. However, the clinical control of inflammation with immunosuppressors is known to provide a better prognosis for patients with this condition when undergoing the procedure.

The usefulness of intravascular ultrasound (IVUS) for this disease remains unknown. Information on the visualization of the involvement and possible remodeling of the arterial wall, especially of its extension, provided by IVUS and which may not be reliably obtained by angiography, helps both differentiating the etiology of the obstruction and making decisions regarding the treatment, thus enabling a better definition of the length and diameter of the endoprosthesis and presumably more favorable outcomes, especially when the use of drug-eluting stents is considered. As occurred with the coronary atherosclerotic disease, the routine utilization of stents may contribute for a better understanding of TA. Stent implantation in the right common carotid artery was monitored by intravascular ultrasound to evaluate the characteristics and composition of the obstructive lesion. The renal arteries were treated at different moments, but always showed significant clinical manifestation. Current studies on the treatment of renal artery stenosis, mainly on percutaneous revascularization, comprise patients undergoing the procedure for the management of systemic hypertension and take into account the probability of improvement of blood pressure and/or renal preservation. Unfortunately, many studies suggest that revascularization of the renal artery for the treatment of atherosclerotic stenosis of the renal artery seldom cures systemic hypertension; cure rates of percutaneous transluminal angioplasty, stent implantation, and surgery range from 6 to 21%. In this case, we observed both a better control of the blood pressure and preservation of the renal function. Regarding recanalization of the left subclavian artery, success is highly related to specific characteristics of the chronic occlusions and technical aspects. Characteristics related to the lesion are the total occlusion time, the extension of the lesion and the morphological aspect, unknown under the angiographic and intravascular ultrasound aspects. The ability to cross the lesion with the guidewire is the determinant technical factor for success. In this case, the guidewire could not cross the occlusion. The chronic process installed and the diffuse disease associated with the aggressive inflammatory activity contribute for the failure of the recanalization. In chronic occlusions of the coronary arteries, in addition to specific guidewires, other techniques are used, such as rotational atherectomy, laser and radiofrequency. Despite being useful in a small group of procedures, these techniques are not superior to the use of specific hydrophilic guides. Additionally, the inflammatory character of TA may contribute to increase the rates of complications, the most important of which is arterial perforation. The left common carotid, renal and aorta arteries were assessed by intravascular ultrasound using 30-MHz and 9-MHz probes, respectively. The arteries treated were patent and showed no proliferative lesions.

We conclude that the management of TA with immunosuppressive clinical treatment associated with percutaneous revascularization is a short and mid-term option for patients with significant extracardiac arterial lesions. The progression of the disease, even with the use of immunosuppressive therapy, should be considered. Except when recurrence is verified, the steroid dose should be continuously decreased, with discontinuation between six and 12 months. A possible alternative to be evaluated is the use of stents coated with drugs which inhibit endothelial proliferation by means of cytostatic and cytotoxic mechanisms, such as sirolimus and paclitaxel, currently used in the treatment of atherosclerotic coronary lesions. Patients with more prominent endothelial proliferation, such as those with diabetes mellitus and chronic renal failure are proved to obtain greater benefits. Even with higher costs of the procedure, the association with the use of intravascular ultrasound may be useful to differentiate atherosclerosis from specific characteristics of TA, thus adding information and guiding the percutaneous treatment.

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