Multivessel Percutaneous Treatment of Takayasu Arteritis

Rogério Tadeu Tumelero, Júlio César Canfield Teixeira, Norberto Toazza Duda, Alexandre Pereira Tognon, Mateus Rossato

Hospital São Vicente de Paulo - Faculdade de Medicina da Universidade de Passo Fundo, Passo Fundo, RS, Brazil

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 formation[1-6]. 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 arteritis[7-10].

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).

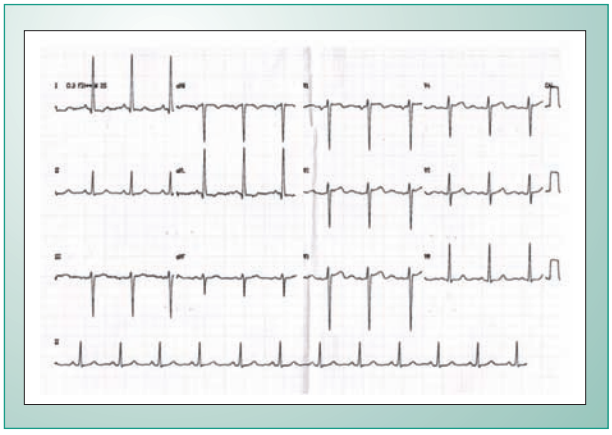

Fig. 1 - *Electrocardiogram – left chamber overload and alterations in ventricular repolarization.*

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.

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.

Mailing Address: Rogério Tadeu Tumelero •
Rua José Bonifácio, 230/302 – 99070-070 – Passo Fundo, RS, Brazil
E-mail: rttumelero@cardiol.br, rttumelero@terra.com.br
Manuscript received September 1, 2005, revised manuscript received November 8, 2005; accepted November 11, 2005.

Case Report

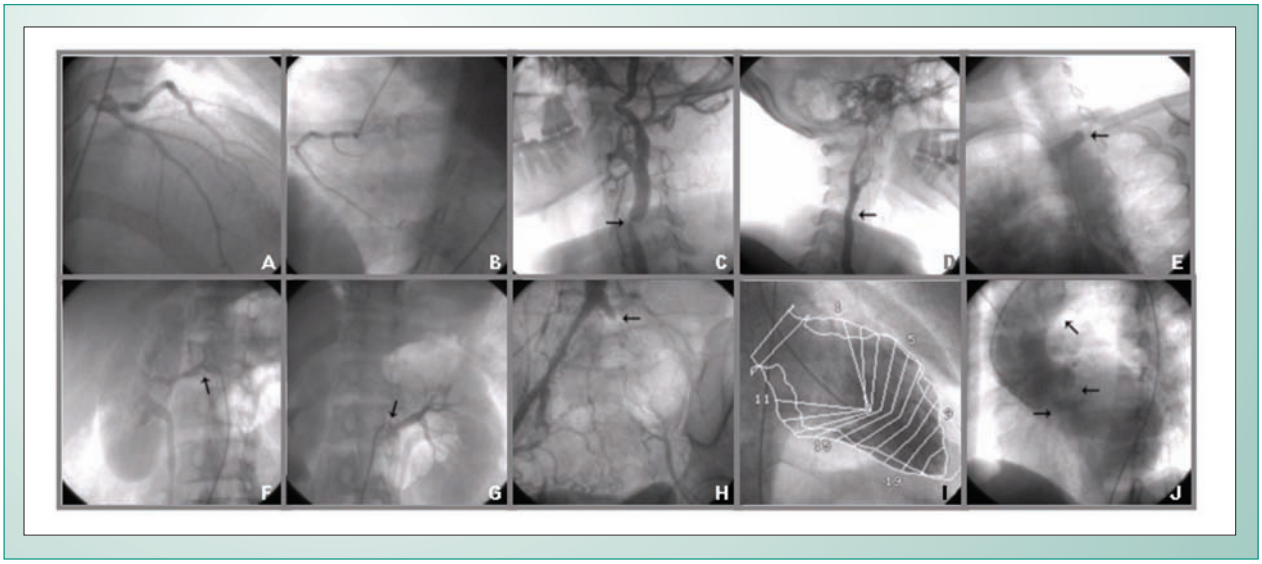

Fig. 2 - *Preinterventional angiography: A and B: left and right coronary arteries, respectively, with no obstructive lesions; C: left common carotid artery with severe obstruction; D: right common carotid artery with mild obstruction; E: left subclavian artery with occlusion in the proximal third; F and G: right and left renal arteries with moderate and severe lesions, respectively; H: left iliac artery with occlusion in the proximal third; I: left ventricle with diffuse hypokinesia; J: aortic valve regurgitation and ectasia of the ascending aorta.*

6.5 mm x 13 mm Herculink (Guidant, CA, USA) stent implantation for the treatment of the ostial lesion of the left renal artery (Fig. 3). The patient was treated on an outpatient-basis with acetylsalicylic acid 200 mg/day, clopidogrel 75 mg/day, and prednisone 80 mg/day to reduce the inflammatory activity.

A new angioplasty was performed in September, 2002, with a self-expanding 8 mm x 30 mm Smart (Cordis, FL, USA) stent implantation to treat the severe lesion in the proximal third of the left common carotid artery, using an Angioguard (Cordis, FL, USA) distal embolic protection device. She was discharged with no cardiovascular events (Fig. 4).

In October, 2002, an angioplasty was performed for recanalization of the left subclavian artery. The procedure was not successful due to the inability to cross the chronic obstruction with the guidewire. The vessels previously treated were checked, showing an unchanged angiographic result. Due to the presence of a new systolic murmur in the topography of the right carotid artery, an angiography was performed demonstrating mild to moderate (70%) progression of the ostial lesion (Fig. 5).

Since an adequate control of the inflammatory activity was not achieved (ESR 76 mm/h), cyclophosphamide 75 mg/day was added to the treatment.

In January, 2003, after a treatment cycle with cyclophosphamide, the patient underwent a successful angioplasty with a 7 mm x 18 mm Herculink (Guidant, CA, USA) stent implantation to treat the moderate lesion in the ostium of the right common carotid artery (Fig. 6). The procedure was performed using an Angioguard (Cordis, FL, USA) distal embolic protection device and was monitored with an intracardiac and intravascular ultrasound using 9-MHz and 30-MHz transducers (Boston Scientifics, MN, USA). The ultrasound revealed diffuse thickening and moderate stenosis of the right common carotid artery and, in the postimplantation, an adequate juxtaposition of the endoprosthesis shafts.

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 (9mm/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[1] , is a chronic, idiopatic[2], 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[3-5].

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[6].

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[6].

The epidemiology of TA shows a rare condition, with an incidence of 1.2 to 2.6 cases/million/year[7] and which mainly affects young women in Japan[8], United States and Mexico, although some studies show similar frequencies as regards gender, especially in Southeastern Asia. Lower rates are observed among white European or North American descendants[5]. 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[9]. 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[10] 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.*

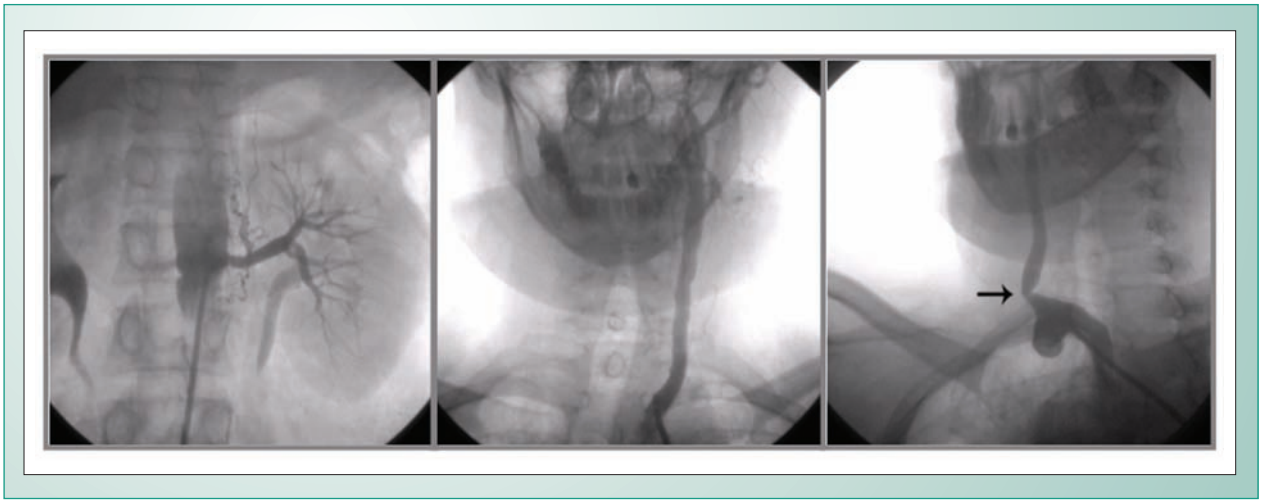

Fig. 5 - *Successful previous interventions remained unchanged. Lesion in the right common carotid artery.*

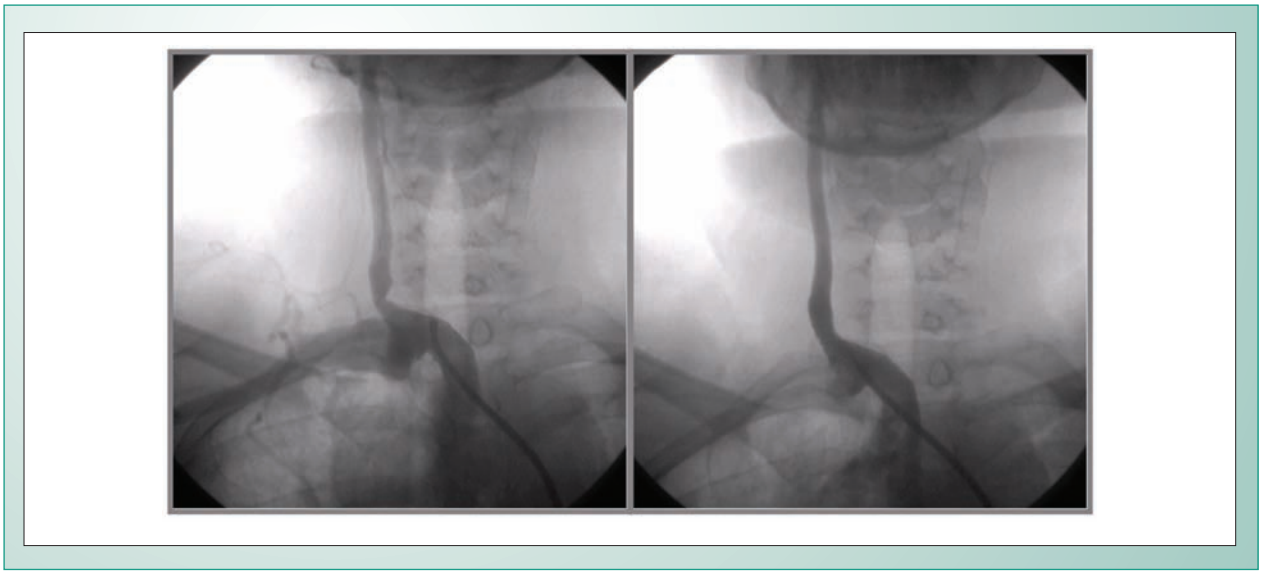

Fig. 6 - *Herculink stent implantation in carotid artery lesion; pre and postintervention.*

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[11] (modified by Ishikawa[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[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[13] is currently been questioned, because of the histological findings of specimens obtained during surgery and of sequential angiographic studies[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

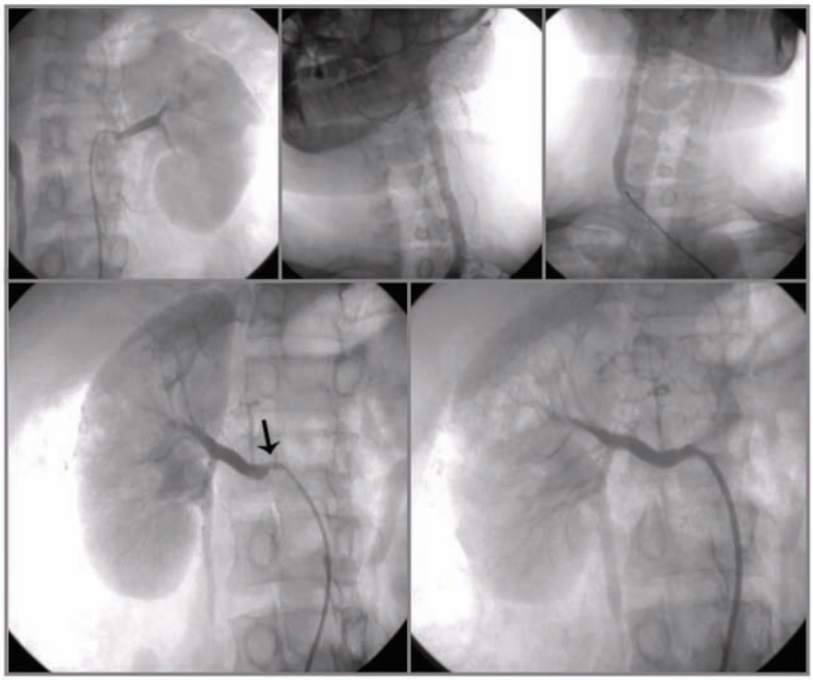

Fig. 7 - *Results of previous interventions remained unchanged and implantation of Herculink stent in renal lesion.*

could be indicators of inflammatory activity, thus facilitating therapeutic decisions.

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[6,15,16]. 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[17]. Periodic angiographic studies may demonstrate an asymptomatic progression resulting in new sites of stenosis or aneurysm formation. Stenoses are usually more frequent than aneurysms[18].

The treatment of TA consists of the control of vascular inflammation with the use of immunosupressors 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[19]. 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[20], despite the morbidity and mortality associated with the disease and the procedures[21]. 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[22].

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[23]. 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[24]. The endovascular treatment has been corroborated by randomized studies as a treatment as efficient as endarterectomy. The SAPPHIRE[23] study designed for the treatment of patients considered at high surgical risk according to Sundt[25] 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 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 pathogeny, no studies comparing endarterectomy and stent implantation in patients with Takayasu arteritis are available. However, the clinical control of inflammation with immunosupressors 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[26]. 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%[27]. 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[28]. 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[29-30]. 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 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.

References

1. Department of National Health and Population Development. Epidemiological comments. TB update 1995;22:13.
2. Hachiya J. Current concept of Takayasu's arteritis. Semin Roentgenol. 1970;5:245.
3. Cid MC, Font C, Coll-Vinent B, et al. Large vessel vasculitides. Curr Opin Rheumatol. 1998;10(1):18-28.
4. Viecili PR, Pamplona D, Cesena FHY, da Luz PL. Angina Instável devida a comunicação entre artéria coronária e artéria pulmonar direita em paciente com arterite de Takayasu. Arq Bras Cardiol 1997; 69:129-32.
5. Numano F. Differences in clinical presentation and outcome in different countries for Takayasu's arteritis. Curr Opin Rheumatol. 1997;9(1):12,-5.
6. Matsunaga N, Hayashi K, Sakamoto I, et al. Takayasu arteritis: protean radiologic manifestations and diagnosis. Radiographics. 1997;17(3):579-94.
7. Hall S, Buchbinder R. Takayasu's arteritis. Rheum Dis North Am. 1990;16(2):411-22.
8. Sato EL, Lima DN, Espirito Santo B, Hata F. Takayasu's arteritis. Treatment and prognosis in a university center in Brazil. Int J Cardiol. 2000;75:S163-6.
9. Subramanyan R, Joy J, Balakrishnan KG. Natural history of aortoarteritis (Takayasu's disease). Circulation. 1989;80(3);429-37.
10. Kimura A, Kitamura H, Date Y, et al. Comprehensive analysis of HLA genes in Takayasu's arteritis in Japan. Int J Cardiol 1996;54(Suppl): S61.
11. Sharma BK, Jain S, Suri S, et al. Diagnostic criteria for Takayasu arteritis. In J Cardiol. 1996;54(Suppl):S141-7.
12. Ishikawa K, Maetani S. Long-term outcome for 120 Japanese patients with Takayasu's disease – clinical and statistical analyses of related prognosis factors. Circulation. 1994;90(4):1855-60.

13. Fraga A, Mintz G, Valle L, et al. Takayasu's arteritis. Frequency of systemic manifestations (study of 22 patients) and favorable response to maintenance steroid therapy with adrenocorticosteroids (12 patients). Arthritis Rheum. 1972;15(6):617-24.

14. Kieffer E, Pisquois A, Bertal A, et al. Reconstructive surgery of the renal arteries in Takayasu's disease. Ann Vasc Surg. 1990;4(2):156-65.

15. Lande A, Berkmen YM. Aortitis: pathologic, clinical and arteriographic review. Radiol Clin North Am. 1976;14(2):219-40.

16. Tamaki M. Angiocardiography: a contribution to its technical and clinical aspects. Nippon Acta Radiol 1958;18:559.

17. Sano K, Aiba T, Saito I. Angiography in pulseless disease. Radiology. 1970;94(1):69-74.

18. Cho YD, Lee KT. Angiographic characteristics of Takayasu arteritis. Heart Vessels 1992;7(suppl):97-101.

19. Liang P, Tan-Ong M, Hoffman GS. Takayasu's arteritis: vascular interventions and outcomes. J Rheumatol. 2004;31(1):102-6.

20. Sharma BK, Jain S, Bali HK, Jain A, Kumari S. A follow-up study of balloon angioplasty and de-novo stenting in Takayasu arteritis. Int J Cardiol. 2000;75(Suppl 1):S147-52.

21. Gradden C, McWilliams R, Gould D, Williams P, Harris P. Multiple stenting in Takayasu arteritis. J Endovasc Ther. 2002;9(6):936-40.

22. Takahashi JC, Sakai N, Manaka H, et al. Multiple supra-aortic stenting for Takayasu arteritis: extensive revascularization and two-year follow-up. AJNR Am J Neuroradiol. 2002;23(5):790-3.

23. Yadav JS, Wholey NH, Kuntz RE, et al. Protected carotid-artery stenting versus Endarterectomy in high-risk patients. N Eng J Med. 2004;351(15):1493-501.

24. Wholey M, Eles G. Clinical experience in cervical carotid artery stent placement. Carotid Neurovasc Int. 1998;50:301-306.

25. Sundt T, Sandok B, Whisnant J. Carotid endarterectomy. Complications and preoperative assessment of risk. Mayo Clin Proc. 1975;50(6):301-306.

26. Textor SC, Wilcox CS. Renal artery stenosis: A Common, treatable cause of renal failure? Annu Rev Med. 2001;52:421–42.

27. Webster J, Marshall F, Abdalla M, et al. Randomized comparison of percutaneous angioplasty vs continued medical therapy for hypertensive patients with atheromatous renal artery stenosis: Scottish and Newcastle Renal Artery Stenosis Collaborative Group. J Hum Hipertens 1998;12:329-335.

28. Sakaida H, Sakai N, Nagata I, et al. Stenting for the occlusive carotid and subclavian arteries in Takayasu arteritis. No Shinkei Geka. 2001;29(11):1033-41.

29. Lusic I, Maskovic J, Jankovic S, Cambj-Sapunar L, Hozo I. Endoluminal stenting for subclavian artery stenosis in Takayasu's arteritis. Cerebrovasc Dis. 2000;10(1):73-5.

30. Min PK, Park S, Jung JH, et al. Endovascular therapy combined with immunosuppressive treatment for occlusive arterial disease in patients with Takayasu's arteritis. J Endovasc Ther. 2005 Feb;12(1):28-34.