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Diagnosis and treatment of Takayasu arteritis in Turkey: A single center results

Türkiye'de Takayasu arteritinin tanı ve tedavisi: Tek merkez sonuçları

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ABSTRACT

Background: This study aims to evaluate clinical, laboratory, and radiological features as well as the surgical and endovascular procedure outcomes of patients with Takayasu arteritis in our hospital.

Methods: Hospital records of 38 patients who were followed with the diagnosis of Takayasu arteritis between April 2002 and January 2014 were retrospectively evaluated. Records included the clinical history of Takayasu arteritis, comorbid diseases, laboratory and angiographic findings at the time of diagnosis, and mode of treatment.

Results: The female/male ratio was 3.75:1. According to angiographic classification; 11 patients were type 1, three patients were type 2a, three patients were type 2b, four patients were type 3, six patients were type 4, and 11 patients were type 5. Eighteen of 38 patients were administered endovascular or surgical intervention (8 surgeries and 10 endovascular procedures). There was no early mortality.

Conclusion: Demographic and angiographic features of our patients were similar to those of Japan and Mediterranean populations. The long-term follow-up of endovascular procedure success, and the management of restenosis may be among challenges to be faced in the future. Bypass surgery remains the gold standard for achieving long-term patency. Endovascular treatment may provide short-term symptom relief in patients who are not suitable for surgical treatment.

Keywords: Endovascular procedures; surgery; Takayasu arteritis.

ÖZ

Amaç: Bu çalışmada hastanemizdeki Takayasu arteritli hastaların klinik, laboratuvar ve radyolojik özellikleri ile beraber cerrahi ve endovasküler girişim sonuçları incelendi.

Çalışma planı: Nisan 2002 - Ocak 2014 tarihleri arasında Takayasu arteriti tanısı ile takip edilen 38 hastanın hastane kayıtları geriye dönük olarak incelendi. Kayıtlar Takayasu arteritinin klinik öyküsünü, eşlik eden hastalıkları, tanı sırasındaki laboratuvar bulgularını, anjiyografik bulguları ve tedavi şeklini içeriyordu.

Bulgular: Kadın/erkek oranı 3.75:1 idi. Anjiyografik sınıflamaya göre; 11 hasta tip 1, üç hasta tip 2a, üç hasta tip 2b, dört hasta tip 3, altı hasta tip 4 ve 11 hasta tip 5 idi. Otuz sekiz hastanın 18'ine endovasküler veya cerrahi girişim uygulandı (8 cerrahi, 10 endovasküler girişim). Erken mortalite olmadı.

Sonuç: Hastalarımızın demografik ve anjiyografik özellikleri Japonya ve Akdeniz toplumları ile benzerdi. Endovasküler işlemlerin uzun dönem sonuçları ve restenoz yönetimi gelecekte karşılaşılabilecek zorluklardan olabilir. Baypas cerrahisi uzun dönem açıklık elde etmek için altın standart olmaya devam etmektedir. Endovasküler tedavi, cerrahi tedaviye uygun olmayan hastaların semptomlarında kısa süreli rahatlama sağlayabilir.

Anahtar sözcükler: Endovasküler işlemler; cerrahi; Takayasu arteriti.

Takayasu's arteritis (TA) is a chronic, inflammatory disease that primarily affects large vessels such as the aorta and its main branches. The etiology of this disease is still not completely known, but various factors may have an impact on the pathophysology.[1,2]

The most common finding of TA is granulomatous inflammation in the adventitia and medial wall of the involved vessels. In turn, this can lead to stenosis or occlusion in the lesions because of fibrosis followed by vessel dilatation via the deformation of

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elastic structures in the medial wall.[3,4] The clinical presentation and findings are directly related to the affected organ.

Disease activity is the main factor that determines the progression of the lesions, and revascularization of the stenotic or occluded vessels or repair of an aneurysm play important roles in TA. Various interventions have been used to treat this disease, with the success rate depending on which vessel is affected. In addition, aneurysmal dilatation at the suture lines after surgical reconstruction is a serious complication that makes the procedure challenging. In this study, our goal was to evaluate the clinical and radiological features of TA as well as the outcomes of surgical and endovascular interventions of patients with this disease.

PATIENTS AND METHODS

In this retrospective study, we analyzed the clinical and demographic data of 38 patients (30 females and 8 males; mean age 36±2.1 years; range 19 to 51 years) with TA who were followed up at a university hospital in Turkey. Local institutional review board approved the study, and our research conformed to the principles of the Declaration of Helsinki.

Among the patients who visited our department between April 2002 and January 2014, 38 were diagnosed with TA according to the 1990 American College of Rheumatology criteria[5] and out of these, 18 underwent either vascular or endovascular procedures. The patients' mean follow up duration was 3.2±1.8 years. Of the 38 patients, eight had undergone reconstructive surgery while endovascular procedures had been performed on 10 others. We retrospectively reviewed the medical records of all of the patients, including their medical history and presence of comorbid diseases as well as their laboratory, angiographic and echocardiographic findings at the time of the initial diagnosis. After examining the initial total blood count (CBC), erythrocyte sedimentation rate (ESR), high sensitivity-C reactive protein (hs-CRP) levels and creatinine levels, we identified the following comorbid diseases in our patient: hypertension (HT), diabetes mellitus (DM), dyslipidemia, renal dysfunction or azotemia, and congestive heart failure.

The diagnosis of TA was confirmed by magnetic resonance angiography (MRA), computed tomography angiography (CTA), aortography (for patients who had undergone surgical or endovascular procedures), or digital subtraction angiography (DSA). We also evaluated the arteriographic classification according to the system accepted at the International Conference on TA in Tokyo in 1994. The patient classifications are summarized in Figure 1.[6]

All of the procedures were performed by the same vascular or endovascular team involving cardiovascular surgeons and interventional radiologists in the peripheric angiography suite or the operating room, and the indications that were considered for intervention included uncontrolled HT due to renal artery stenosis, severe cerebrovascular disease, severe aortic regurgitation or coarctation, stenotic or occlusive lesions resulting in critical limb ischemia, and aneurysms at the risk of rupture.

During the endovascular procedures, the femoral approach was used as the standard except for patients with a severe caudal angle of renal arteries, aortoiliac occlusion, or lesions in the upper extremity arteries. For these patients, the brachial approach was used.

RESULTS

The symptoms of the patients had started 40 years earlier, and fatigue, malaise, myalgia, arthralgia, palpitations, headaches, weight loss, and fever being present in the majority (57%). Other symptoms such as claudication and pallor in the extremities, decreased extremity pulsations, asymmetric blood pressure in the upper extremities, and arterial HT were also present. The symptomatology is summarized in Table 1.

Full aortography was performed on all of the patients after the inflammatory activity was brought under control, and the results were as follows: 11 were classified with type 1 inflammation, three with type 2a, three with type 2b, four with type 3, six with type 4, and 11 with type 5 (Table 2). The patients were followed up by the rheumatology department. Corticosteroids and immunosuppressives were administered in addition to anti-aggregant agents, and prednisolone was used as the first line of treatment with an initial dose of 1 mg/kg/day (total maximum dose 60 mg/day), which subsequently was gradually decreased. The most frequent immunosuppressive drug used was methotrexate (78%), with the second most common being cyclophosphamide (22%). Corticosteroid therapy was started at 40-60 mg/day and the dose was then reduced based on the disease activity.

Of the eight patients for whom open surgery was performed, three underwent aortic valve and ascending aorta replacement, one had a subclavian carotid bypass, two underwent an aortobifemoral bypass, one had a descending thoracic aorta-to-terminal aorta bypass, and another underwent a

Table 1. Clinical characteristics of the patients with Takayasu arteritis

Clinical feature	Number of patients	%
Constitutional symptoms	32	84.2
Asymmetric blood pressure	20	52.6
Claudication and pallor of the extremity	12	31.5
Decreased extremity pulsations	18	47.3
Arterial hypertension	12	31.5
Bruits	9	23.6
Aortic valvular insufficiency	4	10.5
Cardiomegaly	3	7.8
Aortic aneurism	4	10.5
Dyspnea	3	7.8
Arthritis	2	5.2
Erythema nodosum	1	2.6
Cerebrovascular event	6	15.7
Uveitis	1	2.6
Visual disturbances	3	7.8

subclavian artery-to-brachial artery bypass. Furthermore, four of the 10 patients who underwent an endovascular intervention had carotid balloon angioplasty (Figure 2) and one underwent iliac artery balloon angioplasty (Figure 3). Subclavian artery balloon angioplasty was performed on three more patients (Figure 4), and renal artery balloon angioplasty was carried out on two others (Figure 5). There was no mortality. The mean hospitalization time was 1.2±0.3 days in the endovascular group and 6.9±2.3 days in the surgery group. The patient who underwent the descending thoracic aorta-to-terminal aorta bypass surgery was a 32-year-old female with severe claudication who also had dialysis-dependent

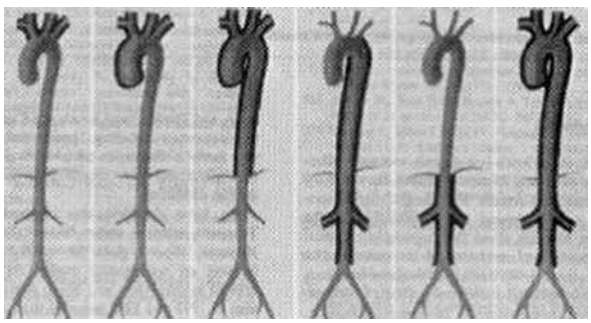

Figure 1. According to this classification. Type 1: Involves branches of aortic arch; Type 2a: Involves ascending aorta, aortic arch and its branches; Type 2b: It is a combination of type 2a plus involvement of thoracic descending aorta; Type 3: Involves thoracic descending aorta, abdominal aorta and/or renal arteries; Type 4: Involves only abdominal aorta and/or renal arteries; Type 5: It is a combination of type 2b plus type 4.

Table 2. Angiographic classification of the patients

	Number of patients	%
Type 1	11	28.9
Type 2	4	10.5
Type 2b	1	2.6
Type 3	2	5.2
Type 4	13	34.2
Type 5	8	21

renal insufficiency waiting for renal transplantation. Thus, she was scheduled for a staged surgery (bypass followed by renal transplantation to obtain an acceptable blood inflow for the new kidney). In the operation, the surgeon performed a left posterolateral thoracotomy incision and a Risberg incision at the left paramedian localization. We used an 8 mm polytetrafluoroethylene (PTFE) graft in the procedure, and the total operation time was 190 minutes. The patient was discharged on the postoperative seventh day without any complications after normal control MRA results (Figure 6). Unfortunately, the patient died during the 14th month of follow-up before undergoing the renal transplantation. There was no late mortality or morbidity in the other surgery cases, and no reintervention was needed. Cardiopulmonary bypass (CPB) and cardioplegia were used in the three patients who underwent ascending aorta and aortic valve replacement, and in the endovascular group, there was also no mortality. One patient did

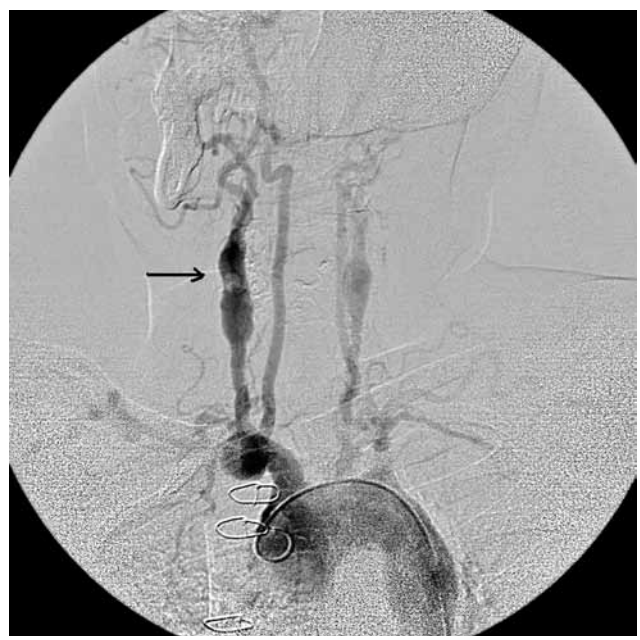

Figure 2. Aneurysm in the carotid artery is shown with arrow.

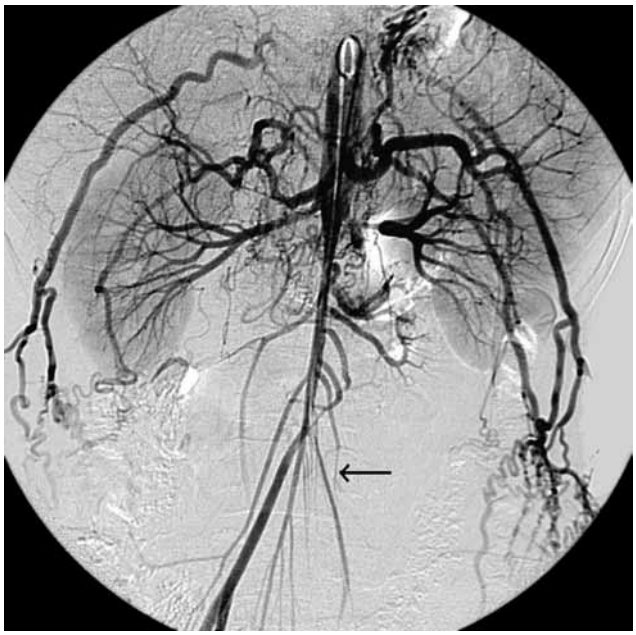

Figure 3. Stenosis in the iliac artery is shown with arrow.

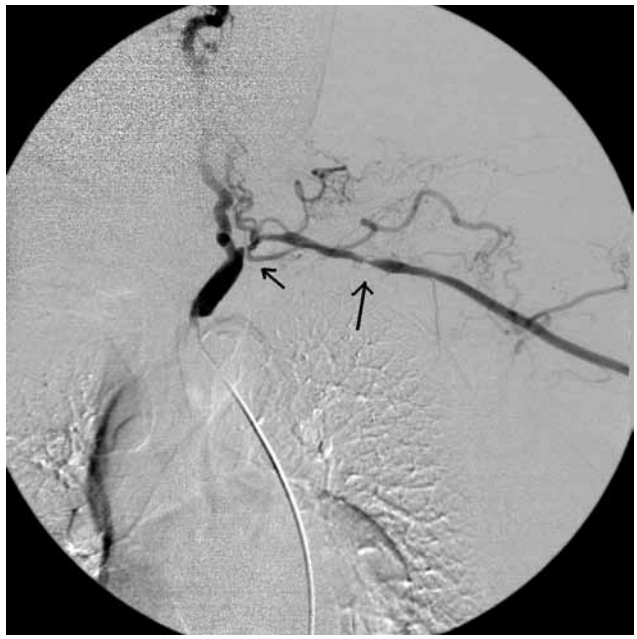

Figure 4. Stenosis in the left subclavian artery is shown with arrow.

have renovascular HT, but after performing balloon angioplasty to the renal artery, the HT resolved. In this case, a cure was defined as the restoration of the blood pressure (BP) to below 140/90 mmHg without the need for anti-HT drugs. This particular patient was followed up for 3.2±1.8 years. Moreover, three reinterventions were required for the five patients who underwent carotid balloon angioplasty, whereas no second interventions were needed in the surgery group. The patients who did not undergo any interventions were followed up with appropriate medical treatment.

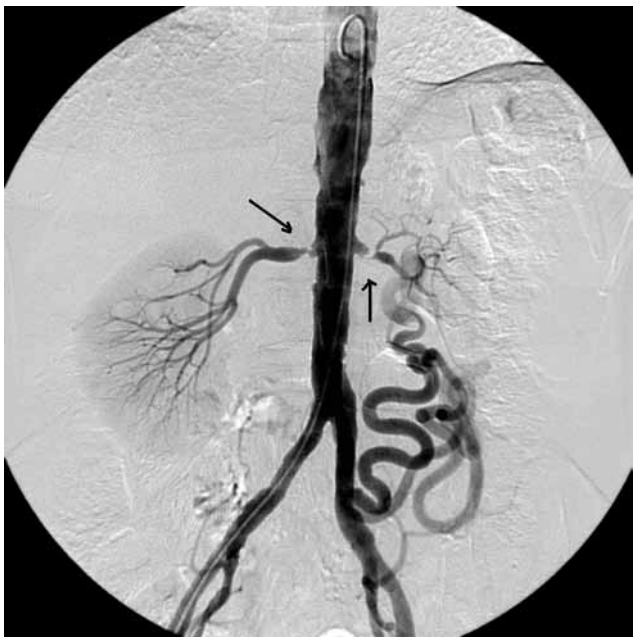

Figure 5. Stenosis in the both renal arteries are shown with arrow.

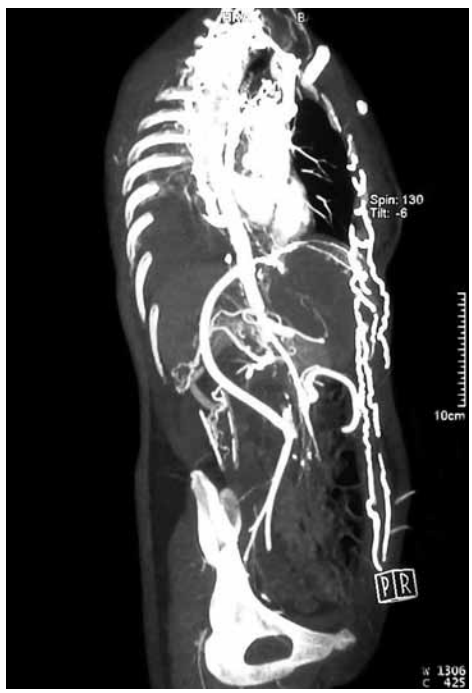

Figure 6. Bypass graft from supracoiliac aorta to iliac artery is shown with arrow.

DISCUSSION

Takayasu's arteritis is a rare condition which features inflammation that affects the aorta and its branches. There seems to be little surgical experience associated with patients with this disease perhaps because it is only present in the late phase when pulses are absent. In that period, the large arteries are affected and either have stenosis or are occluded. However, there are a few studies involving various populations which describe the clinical course, angiography findings, treatments, and clinical outcomes of these treatments.[9,10] Unlike the Japanese population, there may be an under-diagnosis of TA in Turkey since there are only a few series that have originated in this country that have focused on the features of this disease.[1,11,12,18]

Different countries have reported varied incidence and prevalence rates for TA, and the angiographic images in patients with this disease also differ from population to population. In some studies, the abdominal aorta and descending thoracic aorta were affected more often than the arcus aorta,[13,14] but in Japan, the aortic arch and its branches (type 1, 2a and 2b) were the most frequent sites. Type 5 was the most common pattern in Thailand, Brazil, India, and Japan, but this type was seen less often in China and Taiwan.[13,17] In our study, types 1, 4, and 5 were the most frequent angiographic disease patterns, which was similar to the findings of studies from China, South Korea, and Colombia. In addition, our angiographic data was also similar to that found in other studies on TA that have been conducted in Turkey.[1,11,12,18]

The symptomatology of this disease ranges from asymptomatic to very severe, and the clinical presentation usually becomes obvious in the second or third decade of life. In to the symptoms mentioned earlier in this study, the literature also showed a high rate of cerebrovascular accidents in TA patients, and in our series, three patients had a history of previous transient ischemic attacks.

When there is a broad spectrum of disease severity, misdiagnosis or late diagnosis frequently occurs.[19] Therefore, physicians who suspect the presence of TA should perform complete physical and laboratory evaluations using appropriate imaging if further analysis is needed.

Early diagnosis is very important in TA. Late or wrong diagnoses, delayed treatment, or poorly timed endovascular or surgical interventions may lead to unsuccessful outcomes. In past years, conventional angiography was considered to be the best diagnostic modality; however, vascular imaging has evolved, and new techniques are being developed in the field for the non-invasive diagnosis of vascular disease as well as TA. Moreover, because of its invasive nature and need for a contrast load, angiography has some limitations in the early diagnosis of vascular lesions due to changes in the vessel wall. Nonetheless, angiography still should be performed when planning endovascular interventions because contrast CTA along with MRA can show the arterial anatomy, luminal walls, edema, and thickening, which can provide valuable information for an early diagnosis while also preserving the diameter of the lumen. In our patients, we used MRA and CTA as the initial step in our diagnoses, and when intervention was required, we preferred percutaneous digital subtraction radiographic angiography.

Medical treatment options for TA usually include medical therapy with steroids or the combination of immunosuppressive agents and revascularization procedures. The main purpose of medical treatment is to control the active inflammation phase and reduce injuries to the arterial wall. Furthermore, beginning the immunosuppressive treatment at an early stage is vital to prevent the development of vascular complications and aid in the remission phase.

Complications associated with TA usually stem from stenosis and aneurysmal dilatations of the aorta and/or its large branches (i.e., the carotid, subclavian, and renal arteries) and various options, including bypass grafts, renal autotransplantation, and endovascular procedures, have been utilized to treat these lesions. Good results can be obtained by surgery, but this often results in aneurysmal dilatation in the anastomosis lines.[15] When drug therapy fails, surgical reconstruction, especially bypass surgery, has been accepted as the best treatment option for many years. However, when devising a surgical strategy, patients with TA must be evaluated and treated very carefully. First of all, they are not the same as atherosclerotic patients. Although patients with TA are younger that those with atherosclerosis, they may present with multi-organ problems. Hence, a detailed and careful evaluation is mandatory for these patients before undergoing surgical reconstruction. Secondly, it is preferable to avoid surgery during the acute phase of this disease. Surgery generally includes a bypass operation to target vessels which on diagnostic imaging appear to be patent both proximally and distally to the diseased segment of the vessel. The long-term outcomes for TA patients can vary significantly, but this is especially true when surgical intervention is done in the active stage of the disease. Usually, the progressive inflammatory

nature of TA prevents the liberal use of surgical reconstruction, and it is speculated that less than 20% of TA patients actually need surgical intervention. However, studies show surgical procedure rates for these patients range between 12 and 70%.[1-6]

Endovascular approaches may provide a less invasive, cheaper, and safer option for treating vascular lesions in patients with TA.[16] Endovascular interventions have been proven to be successful in the treatment of vascular lesions due to atherosclerosis, but in the early studies, similar results have not been seen in patients with vasculitic diseases, including TA. However, these lesions cannot always be treated by surgical methods; therefore, endovascular interventions certainly have a role in the treatment of lesions in diseased arteries.

The short-term results of some endovascular series have shown the efficacy of these procedures in the treatment of TA as well as other vasculitic disorders, but restenosis and occlusion continue to be major problems after such treatments. In our series, three patients required restenosis while three others needed a second balloon angioplasty procedure.

Conclusions

In this study, we demonstrated that the demographic and angiographic findings of our patients were similar to those from Japan and the Mediterranean region. However, our study was retrospective in nature and only involved a single center; therefore, randomized prospective trials with a larger study group are needed to provide more definitive conclusions. On the other hand, our findings did show that long-term follow-up is needed to determine the success of endovascular procedures and oversee the management of restenosis. Bypass surgery remains the gold standard for long-term patency, but endovascular treatment can provide short-term symptom relief for those for whom surgery is not an option.

Declaration of conflicting interests

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