Pulmonary hypertension (PH) is defined as the mean pulmonary artery (PA) pressure above \( \geq 25 \text{ mmHg} \) as measured with right heart catheterization. PA hypertension (PAH) is a group of diseases which demonstrate similar clinical, and pathological characteristics based on different etiologies (idiopathic, Eisenmenger syndrome, connective tissue diseases). Early diagnosis, and initiation of appropriate specific therapy have critical values in that if untreated PAH leads to right heart failure, and death.[1]

Takayasu arteritis causes vasculitis of major vessels, and mostly involves aorta, and its branches frequently associated with PA involvement. It is seen most often in young women. In this case, we planned to discuss a patient who developed PAH with isolated PA involvement, and stent restenosis.

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A 53-year-old female patient consulted to the cardiology outpatient clinic with fatigue, and shortness of breath. Her complaints persisted for nearly three years, but aggravated within the last month.

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The patient consulted to another center 3 years ago with similar complaints, and during her transthoracic echocardiographic examinations systolic PA pressure of 90 mm Hg was detected. Then etiological factors of PAH were investigated while her immunological markers, and lower extremity venous Doppler ultrasonographic findings were within normal limits. Ventilation perfusion scan detected multiple perfusion defects in both lungs. Department of Chest Diseases evaluated the patient, and in the light of the findings of clinical, laboratory, and computed tomography (CT) of the chest any evidence of pulmonary thromboembolism was not detected.

**Figure 1.** (A) Stent in the left pulmonary artery (B) Angiographic image of the left pulmonary artery. (C) Diffuse in-stent stenosis of the pulmonary artery is seen. (D) Stent in the right pulmonary artery. (E) Angiographic appearance of the right pulmonary artery, and post-stent stenosis. (F) Arrow indicates a stenotic segment distal to the stent in the right pulmonary artery. (G) Angiographic appearance of the distal stenosis of the right pulmonary artery.
With the aid of cardiac catheterization pulmonary capillary wedge pressure (PCWP) (7 mm Hg), PAP (90/40/58 mmHg), right ventricular (RV) pressure (90/80/10 mmHg), right atrial (RA) pressure (10 mm Hg), left ventricular (LV) pressure (120/0/5 mmHg), and aortic pressure (120/70 mm Hg) were measured. Pulmonary angiography detected severe stenosis in the proximal segments of right, and left PA which necessitated bare metal implantation into both vessels. During control, PA pressure regressed down to 60 mm Hg, and the patient was discharged, and follow-up visits were planned.

The patient presented to our center because of fatigue, shortness of breath, and swelling in various regions of the body, and on her physical examination, arterial blood pressure of 130/70 mm Hg, pulse rate of 80 bpm, and jugular venous distension were detected Her cardiac examination findings were as follows: regular heart sounds, 3/6 early ejection murmur best heard over pulmonary area, normal pulmonary sounds, liver palpable 3 cm below the costal arch, and +/+ pretibial edema. Sedimentation rate was 50 mm/h, and C-reactive protein level 32 mg/L. Other hematologic, and biochemical values were within normal limits. Autoimmune markers of connective tissue diseases were not detected. On ECG of the patient RV hypertrophy, and right axis deviation was observed. On her anteroposterior chest X-ray stent implanted in the PA, and increased cardiothoracic ratio were seen. Transthoracic cardiography revealed normal LV functions, and heart valves. Systolic PAP calculated in consideration of paradoxical septum mobility, hypertrophic RV, 3+ tricuspid insufficiency was 120 mm Hg. The widest diameter of the main PA was measured as 38 mm. Brain-natriuretic (BNP) level was 2240 pg/ml. Six-minute walk test distance was 100 meter. Magnetic resonance imaging of the heart detected diffuse thickening of the interventricular septum, and paradoxical mobility, pulmonary root diameter of 39 mm, and systolic PAP was measured as 39 mm at the level of the pulmonary root. In both lungs, mosaic attenuation, and stent material, and circular hypointensity on the periphery in consistent with in-stent intimal thickening were observed. Then the patient underwent pulmonary perfusion scanning which detected heterogeneous distribution of radioactivity in both lungs, and diffuse perfusion defects more prominent in the upper lobes. The patient underwent right heart catheterization. PA pressure (110/46; median 89) was measured at the level of main PA, while it was 106/45 mm Hg; (median 86 mm Hg) at the proximal segment of PA. The blood pressure at the distal segment of the stent was detected as 48/25 mm Hg; median 34 mmHg). A difference of 58 mm Hg was observed between proximal, and distal parts of the stent.

PA pressure of the left main pulmonary artery was 103/47 mmHg (median, 84 mm Hg), at the distal part of the stent it was 57/28 (median 47) mmHg, and systolic blood pressure gradient was detected as 46 mmHg. Detection of pressure gradient (47 mmHg) distal to the PA stenosis was attributed to diffuse arteriolar involvement. On pulmonary angiograms diffuse 60 % in-stent restenosis was detected in the stent inserted into the left lower lobe. In the right PA 60 % stenosis was detected in the stent extending from the middle, and the lower lobes at the level of PA root into the lower lobe. An 80 % ostial stenosis was detected of a stented major artery. Branches of PA supplying the upper lobes of both lungs were occluded. (Figures 1a-f). Left heart catheterization did not reveal any pathology in the aorta, and its branches, evaluation of renal arteries was unremarkable. On coronary angiograms coronary arteries were normal in configuration. With these present findings the patient was evaluated by the departments of cardiology, cardiovascular surgery, and rheumatology. The presence of a vasculitis coursing with serious pulmonary involvement was presumed. Besides, the patient was also evaluated as for the indication of pulmonary endarterectomy. However because of the presence of diffuse involvement, and detection of stent restenosis, interventional treatment was planned for PA vasculitis. Steroid therapy was initiated, and since the patient had symptoms of the right heart failure, we were very careful not to induce volume overload while escalating steroid doses. The patient weighed 50 kg. Under methylprednisolone therapy (16 mg/d) acute phase reactants regressed to normal levels. Then we decided that the disease activation was suppressed, and it was time for initiating interventional therapy for PA pathology. During control echocardiographic examination systolic blood pressure was measured as 150 mmHg, and her BNP level regressed to 880 pg/ml. During PA control angiography, blood pressures distal (44/4/26 mmHg), and proximal (113/5/52 mmHg) to the left inferior PA stent were also measured. Left PA in-stent stenosis created a systolic blood pressure gradient which was higher than that observed two months ago. Blood pressures distal (41/6/20 mmHg), and proximal (97/4/39 mmHg) to the stent in the right inferior PA were also measured. Following repeated dilations, blood pressures distal (77/2/29 mmHg), and proximal (90/3/34 mmHg) to the left PA stent were also measured. Following balloon dilation, pressure gradient in the left PA regressed to 13 mm Hg, however pressure gradient between BP measurements of the sites distal to the stent rised from 44 mmHg up to 77 mmHg. We thought that the increase of the pressure gradient was due to rise of the blood flow after after elimination of the stenosis. Then right PA was evaluated. Severe, and significant ostial stenosis (80%) of artery within the stent did not change relative to the previous...
evaluation. However, this artery which came out from within stent struts was not intervened, because of serious risk of mortality from probable procedural complication(s). For in-stent stenosis repetitive dilations were performed. Blood pressures distal (41/6/20 mmHg), and proximal (41/6/20 mm Hg) to the PA stent were also determined. Since significant stenosis distal to the stent was not intervened, pressure gradient did not change. At the termination of the procedure, main PA blood pressure was measured as 93/45/61 mmHg. Any complication was not observed after the procedure. The patient was closely monitored as for the development of acute pulmonary edema. Transthoracic echocardiography performed 24 hours after the procedure, and systolic blood pressure was measured as 95 mm Hg. In addition to steroid therapy the patient was started on azathioprine therapy. The patient without any additional complaints was discharged, and called for follow-up visits.

**DISCUSSION**

Development of PAH secondary to isolated PA stenosis is a rarely observed entity. In the adults, it can develop secondary to systemic inflammatory diseases, and vasculitis as Behçet’s disease, Takayasu disease, giant cell (temporal ) arteritis. Pulmonary involvement is frequently observed in vasculitis of major vessels (Takayasu arteritis, giant cell arteritis, naitneutrophilic cytoplasmic antibody “ANCA” related vasculitis, Wegener granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome). In giant-cell arteritis frequently polimyalgica rheumatica, and extracranial involvement accompany the entity, and sedimentation rate increases markedly. In Behçet’s disease recurrent oral, and genital aphthous lesions, and uveitis are diagnostic criteria, and skin lesions are seen in 80 % of the patients. As vascular involvement, venous lesions are more frequently seen than arterial lesions. Arterial involvement emerges as aneurysmatic formation rather than thrombosis. However Takayasu arteritis is known as a pulseless disease, and it most frequently involves aorta, and its branches. In Takayasu arteritis diffuse arterial dilation, and thrombus formation are more frequently observed than giant-cell arteritis. In most of the patients, pulse amplitudes of the right, and left arms differ related to the subclavain artery stenosis. In patients with pulmonary involvement, usually PH is present, and most frequently coughing, dyspnea, and chest pain are observed. The incidence of PA involvement in patients with Takayasu arteritis can be 10-50%, however isolated PA involvement is very rarely seen as demonstrated by published relevant case reports.

Increase in vascular wall thickness, PA stenosis, and complete occlusion as assessed with pulmonary angiography, persistently higher levels of acute phase reactants, and absence of any other concomitant disease which might explain these high levels are findings consistent with PA vasculitis. We have concluded that the most probable diagnosis was Takayasu arteritis progressing with isolated PA involvement. Since we didn’t perform histological examinations other causes of PA stenosis could not be ruled out completely.

In Takayasu arteritis, isolated cases of PAH secondary to PA stenosis are very rarely seen. PA stenosis induces significant increases in RV pressure, and thus it is frequently confused with idiopathic PAH, and chronic thromboembolic PH. In these patients measurement of PH can yield mistakenly supranormal values during right heart catheterization because of the risk of overlapping PCWP with stenotic peripheral PA,. Consequently, etiology of PH may be misevaluated. During examination, higher pressures at the site proximal to the stenotic segment, and decrease in PA pressure after passage of the catheter beyond the stenotic segment should suggest the presence of peripheral PA stenosis.

In Takayasu arteritis, right lung is more frequently affected than the left lung, and lobar vascular structures are more often involved than segmental, and subsegmental vessels. Since in cases with PA stenosis, surgical approach is challenging, frequently balloon angioplasty or stenting is applied. Stenting of proximal PA is performed in adults or older children. Although long-term outcomes of stent implantation for PA stenosis in children are quiet good, in adults excluding case reports, information about long-term results is lacking. In some published case reports maintenance of pulmonary blood flow has been achieved using surgical approach. Complications such as graft occlusion, and aneurysmatic formations at the anastomotic site can be observed. Acute pulmonary edema can be confronted during early post-stenting period. Indeed sudden increase in perfusion of the pulmonary bed also increases distal PA pressure. Consequently because of adaptation of the pulmonary blood flow to these new circumstances distal PA pressure rises. To prevent development of higher distal PA pressure, in patients whose both lungs are involved, simultaneous interventions on both lungs are recommended.

In cases with proximal PA involvement secondary to Takayasu arteritis surgery can be an appropriate treatment modality. In patients with multiple stenosis percutaneous intervention can be applied. Stent restenosis after percutaneous procedure confronts us as an important problem. Spacek et al. suggested application of drug-eluting stent might be an appropriate approach. However Li et
al.\textsuperscript{[26]} observed restenosis after application of rapamycin-eluting stent in a patient with an isolated PA stenosis secondary to Takayasu arteritis, and in the presence of vasculitis they proposed that cellular activations different from atherosclerotic process can induce restenosis. Saadoun et al.\textsuperscript{[27]} reported the risk of restenosis in renal artery as 31% in patients with Takayasu arteritis who had undergone intravascular interventional treatment during postprocedural 5 years of follow-up. Because of complicated progression of the disease, interventional treatments should be planned for eligible patients. However, Şentürk et al.\textsuperscript{[28]} decided that a patient who developed PAH secondary to an isolated PA stenosis due to Takayasu arteritis was in chronic phase of the disease, and followed the patient with bosentan drug therapy which is preferred PAH treatment, considering the patient would not benefit from interventional, and medical immunosuppressive therapy. In patients with diffuse involvement of PA system because of Takayasu arteritis who are not suitable for surgical or interventional approach or those who can not respond to medical treatment inadequately, PAH specific treatment can be an alternative. However, sufficient scientific data are not available on this subject apart from case reports.

In cases progressing with pulmonary arteritis, timing of interventional treatment conveys crucial importance. Risk of restenosis increases if stenting is performed during active stages of the disease.\textsuperscript{[29,30]} In our case we intended to control disease activation before interventional treatment was applied. However, in our patient clinical right heart failure started to develop which prevented implementation of highest doses of corticosteroid treatment because of its salt, and fluid retention effects.

Selection of balloons, and stents with appropriate diameter to be used during the procedure should be performed, and especially in rigid, and chronic lesions higher balloon pressures should be maintained. After the procedure, monitorization of the patients has a critical importance. Indeed, vasculitis of all major vessels demonstrate chronic, and progressive course. Besides, for the prevention of the development of restenosis, and new lesions, corticosteroids, and immunosuppressive treatment are required.\textsuperscript{[29,30]}

Pulmonary arteritis can emerge during the course of Takayasu arteritis, and it can be overlooked in some cases because of different symptoms or its diagnosis can be delayed.

Since pulmonary arteritis induces PAH’ it is a life-threatening complication, and its detection before development of pathological changes related to chronic fibrosis will increase response rates to medical, surgical, and interventional treatment modalities.

\textbf{Conflict of interest: None declared}

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Anahtar sözcüklер: Anjiyoplasti, balon, koroner; pulmoner arteriyel hipertansiyon; stentler; Takayasu arteriti.

Key words: Angioplasty, balloon, coronary; pulmonary arterial hypertension; stents; Takayasu arteritis.