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Cutting balloon angioplasty and stent implantation for left pulmonary artery stenosis in a case with Alagille syndrome

Alagille sendromlu bir olguda sol pulmoner arter darlığına kesici balon anjiyoplasti ve stent yerleştirilmesi

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Alagille syndrome is a rare autosomal dominant disorder associated with an impaired development of intrahepatic bile ducts, cardiac, skeletal, eye, kidney disorders, and characteristic facial appearance. Peripheral pulmonary stenosis is the most frequently seen cardiac anomaly in patients with Alagille syndrome. In this article, we report a case who was diagnosed with Alagille syndrome due to the coexistence of neonatal cholestatic jaundice, posterior embryotoxon, characteristical facial appearance, and peripheral pulmonary stenosis. Symptomatic relief was achieved by cutting balloon angioplasty and stent implantation applied when the degree of the left pulmonary stenosis increased at four years of age.

Keywords: Alagille syndrome; cutting balloon angioplasty; peripheral pulmonary artery stenosis; stent implantation.

Alagille sendromu intrahepatik safra kanallarının gelişim bozukluğu, kalp, iskelet, göz, böbrek anormallikleri ve karakteristik yüz görünümü ile ilişkili otozomal dominant geçişli nadir bir hastalıktır. Alagille sendromlu hastalarda en sık görülen kalp anomalisi periferik pulmoner arter darlığıdır. Bu yazıda, yenidoğan döneminde kolestatik sarılık, posterior embriyotakson, karakteristik yüz görünümü ve periferik pulmoner arter darlığı eşlik etmesi nedeniyle Alagille sendromu tanısı konulan bir olgu sunuldu. Dört yaşında sol periferik pulmoner arter darlığının derecesinin artması üzerine yapılan kesici balon anjiyoplasti işlemi ve stent yerleştirme ile semptomatik iyileşme sağlandı.

Anahtar sözcükler: Alagille sendromu; kesici balon anjiyoplasti; periferik pulmoner arter darlığı; stent yerleştirilmesi.

Alagille syndrome (AGS), first described by Alagille et al.[1] in 1969 and by Watson and Miller[2] in 1973, is a multisystemic disorder which is inherited in an autosomal dominant manner. It is characterized by the scarcity of interlobular bile ducts and may be accompanied by the following diagnostic criteria: congenital heart defects (the most common anomaly is peripheral pulmonary artery stenosis), skeletal system abnormalities (the most common anomaly is butterfly vertebrae), ocular abnormalities (especially posterior embryotoxon), and a dysmorphic face (a prominent forehead, deep-set eyes, a small and pointy chin, a saddle nose, and a characteristic triangular facial appearance). The jagged 1 (JAG1) mutation that codes the ligand in the Notch signaling pathway or a deletion in this locus has been noted in the majority of patients with AGS,[3] and based on the presence of liver disease in newborns, it has a prevalence of 1:70,000.[1] Peripheral pulmonary artery stenosis may appear as an isolated defect, or it may accompany Williams, Noonan, or congenital rubella syndromes or AGS, as in our case. Herein, we present the case of a patient with AGS who underwent cutting balloon angioplasty and stent implantation to relieve left pulmonary artery stenosis.

CASE REPORT

The characteristic facial appearance of someone with AGS, including a prominent forehead, deep set eyes, a small and pointy chin, and bilateral posterior embryotoxon, was detected in the physical examination at the time of the patient's admission to the hospital for newborn jaundice. In addition, a cardiovascular examination revealed a 3/6 systolic

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murmur at the upper left sternal border, and an echocardiographic examination determined a pressure gradient of 40 mmHg in the left pulmonary artery. However, no pressure gradient was found in the right pulmonary artery. Because of the neonatal cholestatic jaundice, posterior embryotoxon, characteristic facial appearance, and peripheral pulmonary stenosis, the patient was diagnosed with AGS.

He had been followed up in the pediatric cardiology outpatient clinic periodically up until the age of four when an echocardiographic examination revealed enlargement and hypertrophy of the right ventricle and a pressure gradient of 50 mmHg in the left pulmonary artery. The right ventricular enlargement and hypertrophy were thought to be caused by pulmonary stenosis, so it was decided to perform angiographic visualization of the pulmonary artery and its branches along with balloon angioplasty of the peripheral pulmonary artery. In addition, if necessary, a stent would be implanted following angioplasty.

The procedure was conducted under general anesthesia. Since the hepatic enzyme levels were high, fentanyl (1 μg/kg) and propofol (2 mg/kg) were used during the induction of general anesthesia in which a laryngeal mask was used and 1-2% sevoflurane was given. The pressures were measured via right-sided cardiac catheterization using the right femoral vein. The right ventricle pressure was 54/5 mmHg, the pressure before pulmonary stenosis was 53/25 with a mean of 35 mmHg, and the pressure after stenosis was 16/12 with a mean of 14 mmHg (pressure gradient at the level of stenosis of 37 mmHg). A 23 mm long segment of stenosis with a diameter of 2.1 mm was observed, and the diameter of the normal peripheral pulmonary arterial segment after stenosis measured 3.7 mm.

Stenosis was not decreased after balloon angioplasty procedure was performed using the Tyshak II balloon dilatation catheter (B. Braun Interventional Systems, Inc., Bethlehem, PA, USA). Therefore, the angioplasty procedure was applied to the left pulmonary artery stenosis twice via a cutting balloon. Furthermore, we used a long sheath to prevent the damage that could have been done to the surrounding structures. After the procedure, the stenotic segment had dilated to 2.7 mm in the angiographic examination, and the 24 mm Palmaz® Genesis® balloon-expandable stent [Cordis Europe, Middle East, Africa (EMEA), a division of Johnson & Johnson Medical N.V./S.A, Waterloo, Belgium) was later implanted in the stenotic area using a 7 mm x 25 mm balloon.

After the stenting procedure, the stenotic pulmonary artery segment was dilated to 3.7 mm, and the gradient at this level regressed to 14 mmHg (Figure 1). No complications developed during or after the procedure, and the 18-month echocardiographic examination revealed no significant pressure gradient across the stent.

DISCUSSION

Cardiovascular abnormalities are the diagnostic criteria for AGS, with their presence having been reported in 94% of cases. The most common congenital cardiac defect is the stenosis/hypoplasia of the branch pulmonary artery, which is found in two-thirds of all cases,[1] and tetralogy of Fallot (TOF) is the most commonly reported complex structural anomaly (12%). In addition, atrial septal defect (ASD) and ventricular septal defect (VSD) are among the intracardiac anomalies which may be associated with AGS. Moreover, Emerick et al.,[4] found a correlation between mortality and the presence of cardiac disease

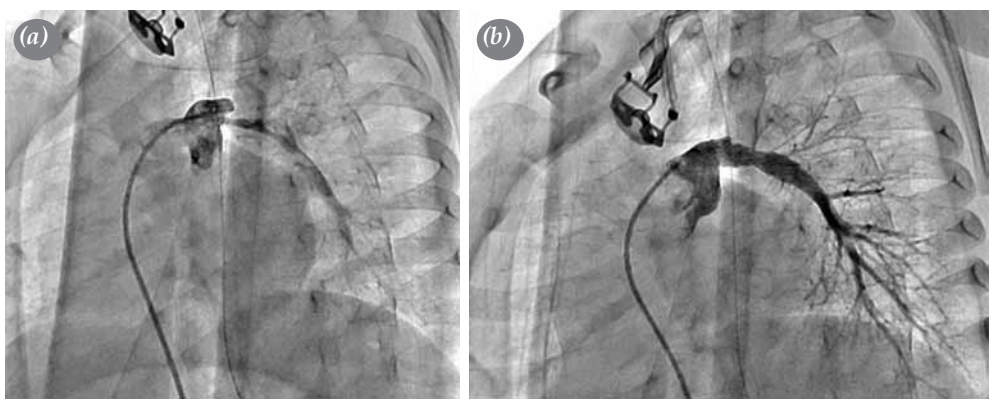

Figure 1. (a) Pulmonary artery angiography before the procedure shows the severe long-segment stenosis. **(b)** Pulmonary angiography shows the significant dilatation of the stenotic segment and the increase of the pulmonary blood flow after the cutting balloon angioplasty and stenting.

in their study that focused on the results of patients with AGS.

Either the JAG1 mutation or a deletion in this locus exists in most patients with AGS; however, no correlation was found between the phenotype of the cardiovascular anomaly and the location of the JAG1 mutation in the study by McElhinney et al.[3] Nevertheless, due to the high incidence of congenital cardiac defect in patients with AGS, a cardiological examination should be performed.[5]

Surgical repair of the peripheral pulmonary artery stenosis is difficult and often unsuccessful. On the other hand, balloon angioplasty, which has been performed since the beginning of the 1980s, is safe and reliable.[6] The indications for balloon dilatation and stent implantation in peripheral pulmonary artery stenosis have been defined in the literature.[6] For our case, the indications for balloon dilatation were peripheral pulmonary artery stenosis with a segmental structure and right ventricular hypertrophy, and stent therapy was indicated by the continuation of relative stenosis after the cutting balloon angioplasty.

Cutting balloon angioplasty is preferred peripheral pulmonary artery stenosis resistant to dilatation with conventional angioplasty. A cutting balloon is a device with three or four microtomes mounted longitudinally on its surface. During the dilatation procedure, the device is guided toward the surgical incision in the media of vessels, which may cause the dilatation of the interincisional tissue. However, the reliability and safety of cutting balloon angioplasty have been verified in experimental animal models.[6]

This type of angioplasty may also have the advantage of creating controlled cuts instead of uncontrolled tears,[6] and it is effective for resistant peripheral pulmonary artery stenosis when conventional balloon angioplasty was unsuccessful.[7,8]

Both balloon angioplasty and stent implantation are safe interventional treatments. However, Baerlocher et al.[9] reported an increase in mortality due to the high balloon-to-vessel ratio after the application of balloon angioplasty, particularly in infants. Even though stents appear to be a safer and more permanent alternative treatment, other additional interventions may be required afterwards. The stent area should also be enlarged surgically in cases in which maximal diameters have been reached.

A successful procedure is defined as achieving a 50% increase in the diameter and a 20% decrease in the ratio of right ventricular systolic pressure to aortic systolic pressure after the procedure.[7] According to this description, our cutting balloon angioplasty procedure was partially successful, but the subsequent stent implantation procedure was a complete success.

Peripheral pulmonary artery stenosis, which is seen in more than half of all AGS cases, may affect the quality of life (QOL) of patients and therefore must be treated. When the difficulty and failure of surgical procedures are taken into consideration, balloon angioplasty and stent implantation are safe and effective alternatives. However, further studies with long-term follow-up are required to confirm the safety of cutting balloon angioplasty.

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