

CASE REPORT

Robotic surgery for atrial septal defect closure in a case of Kabuki syndrome

Kabuki sendromu olan bir olguda atriyal septal defektin robotik cerrahi ile kapatılması

Burak Onan, M.D., Ünal Aydın, M.D., Zeynep Kahraman, M.D.,# İhsan Bakır, M.D.

Department of Cardiovascular Surgery, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Hospital, İstanbul, Turkey

#Department of Anesthesiology, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Hospital, İstanbul, Turkey

Summary– Kabuki syndrome is a rare congenital malformation syndrome characterized by mental retardation, skeletal deformities, auditory dysfunction, cardiac defects, and distinctive facial appearance. Although complex cardiovascular malformations present in early childhood, rarely, atrioventricular septal defects may also present in young adults. Presently described is case of a 22-year-old female with KS who presented with ostium secundum atrial septal defect with deficient rim and idiopathic thrombocytopenic purpura. In this case, minimally invasive robotic surgery was preferred for closure of atrial septal defect.

Özet– Kabuki sendromu mental gerilik, iskelet deformiteleri, işitme bozukluğu, kardiyak defektler ve belirleyici bir yüz görünümü ile kendini gösteren nadir bir doğumsal malformasyon sendromudur. Bu sendromda karmaşık kardiyovasküler malformasyonlar erken çocukluk döneminde görülürken, atriyoventriküler septal defektler nadiren genç erişkinlerde görülebilir. Bu yazıda, atriyal septal defekt ve idiopatik trombositopeni ile değerlendirilen Kabuki sendromu olan 22 yaşındaki olgu sunuldu. Hastada minimal invaziv robotik cerrahi yöntemi tercih edilerek atriyal septal defekt sorunsuz kapatıldı.

Kabuki syndrome (KS) is a multiple congenital malformation syndrome.^[1] It was named KS because of the resemblance of the patient's face to stage makeup used in Kabuki, a traditional Japanese dance-drama theatre. Patients present with distinct facial characteristics, such as depressed nasal tip, prominent ears, skeletal anomalies, cardiac defects, short stature, and mental retardation. Prevalence of KS in Japanese population is estimated at 1 in 32,000.^[1] This syndrome has been underdiagnosed outside of Japan, but limited series and case studies have been reported.^[2,3] Cardiac defects are seen in up to 90% of KS patients, and reported incidence of septal defects is about 32.9%.^[1-3] Although complex forms of cardiovascular anomalies are diagnosed in early infancy period, patients with KS and associated simple cardiac defects, such as atrial septal defect (ASD) may present at more advanced age.

This report describes KS and its major genetic and clinical findings. The authors also present report of a patient with KS who underwent a minimally invasive robotic surgery for ASD closure.

Abbreviations:

ASD	Atrial septal defect
KS	Kabuki syndrome
ITP	Idiopathic thrombocytopenic purpura

CASE REPORT

A 22-year-old female patient with KS and idiopathic thrombocytopenic purpura (ITP) was referred to our hospital for secundum ASD closure. Diagnosis of KS had been made in infancy, but she had no mental or functional limitation related to syndrome during childhood. She was physically active; mentally normal, with recent intelligence quotient test score of 71; and performing daily activities by herself. Genetic analysis revealed 46,XX karyotype without any chro-

Received: February 22, 2016 Accepted: June 08, 2016

Correspondence: Dr. Burak Onan. İstanbul Mehmet Akif Ersoy Göğüs ve Kalp Damar Cerrahisi Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 34303 Küçükçekmece, İstanbul, Turkey.

Tel: +90 212 - 692 20 00 / 4075 e-mail: burakonan@hotmail.com

© 2017 Turkish Society of Cardiology



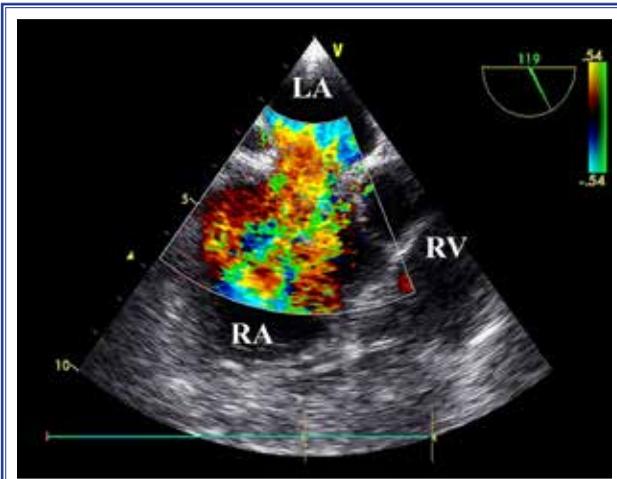


Figure 1. Transesophageal echocardiogram revealed secundum-type atrial septal defect. LA: Left atrium; RA: Right atrium; RV: Right ventricle.

mosomal anomaly. Diagnosis of ITP had been made 6 years earlier following episode of heavy menstrual bleeding complicated by thrombocytopenia. Platelet count was between 60,000 and 80,000/ μL ; hematology department continued follow-up without any medication. Bone marrow examination was consistent with ITP and revealed normal megakaryocytes and other hematopoietic lineages without any fragmented platelets.

On admission, the patient presented with progressive dyspnea on effort. Physical examination showed long palpebral fissures, low-set ears, micrognathia, mildly depressed shoulders, and short stature. Cardiac

examination showed hyperactive precordium on auscultation. Chest roentgenogram displayed increased cardiothoracic ratio and pulmonary vascularity. Biochemical tests yielded platelet count of 196,000/ μL . Prednisolone therapy (80 mg/day per oral) was implemented to increase platelet level before operation. Coagulation tests were normal. Transthoracic echocardiography demonstrated ejection fraction of 62%, secundum ASD of 28x24 mm and dilated right cardiac chambers (Figure 1). Qp/Qs ratio was 1:8. Transesophageal echocardiography confirmed diagnosis of ASD with deficient inferior rim. Magnetic resonance imaging excluded abnormality of cardiac/visceral situs and systemic/pulmonary venous return. Because of the deficiency of the inferior rim of ASD for percutaneous closure, surgical repair was indicated. As a minimally invasive approach, robotic surgery was preferred in order to decrease likelihood of perioperative complications as well as to provide better recovery period.

After induction of general anesthesia, patient was positioned with right chest elevated approximately 30° (Figure 2). Service port was opened through fourth intercostal space on anterior axillary line. Camera port was placed anteriorly through fourth intercostal space. Two additional ports in third and fifth intercostal spaces were used to introduce instruments. Atrial retractor was introduced through fifth intercostal space. Peripheral cardiopulmonary bypass was established via right jugular vein and femoral artery/vein.

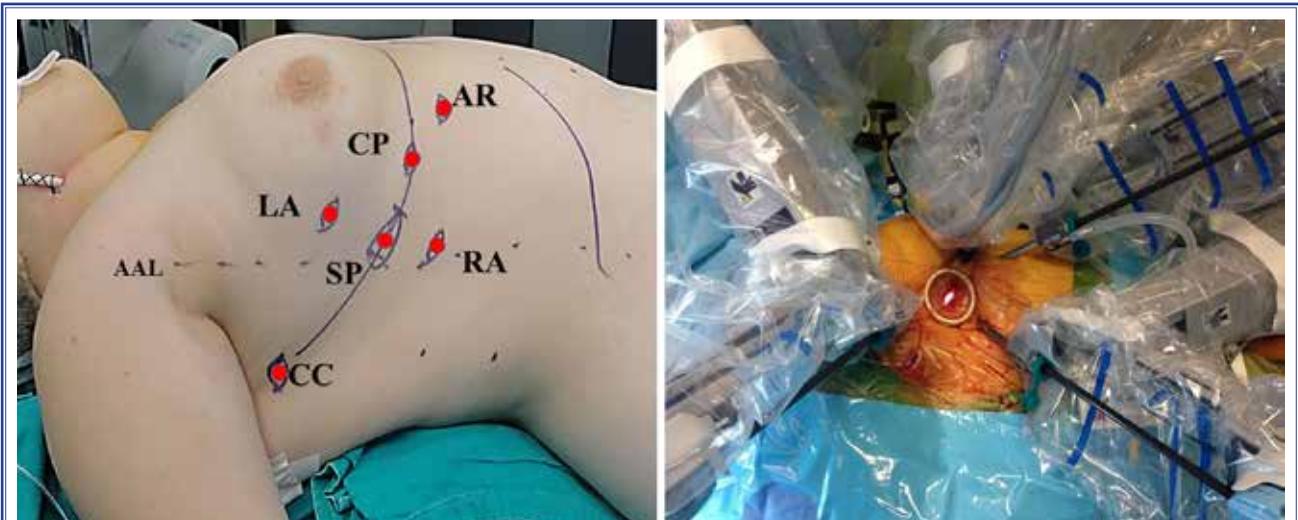


Figure 2. Operative view. AAL: Anterior axillary line; AR: Atrial retractor; CC: Chitwood clamp (Scanlan International Inc., St. Paul, MN, USA), CP: Camera port; LA: Left arm; RA: Right arm; SP: Service port.

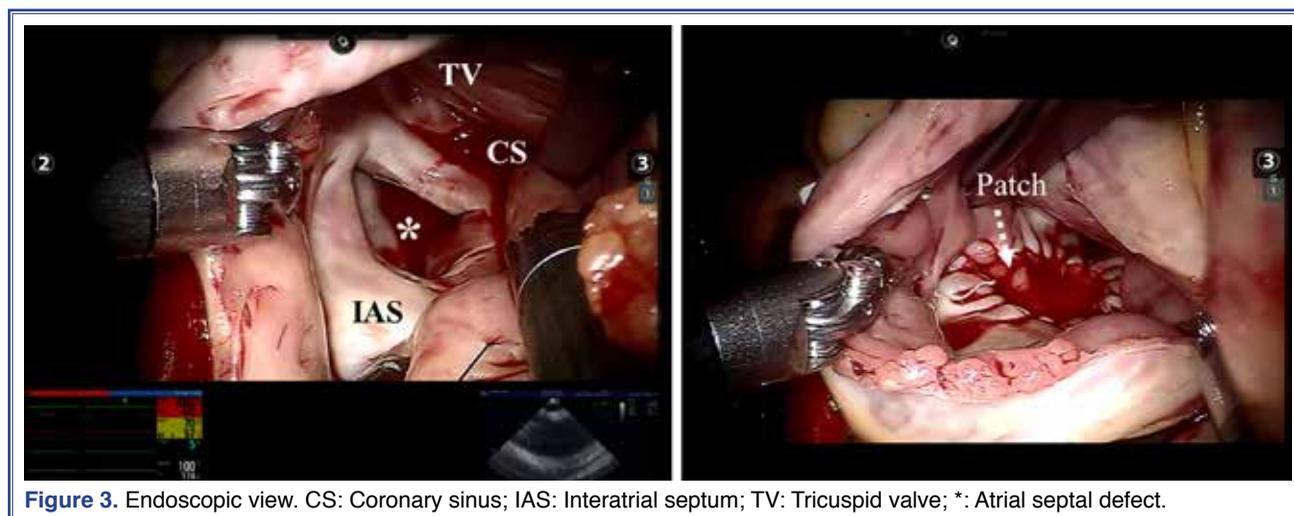


Figure 3. Endoscopic view. CS: Coronary sinus; IAS: Interatrial septum; TV: Tricuspid valve; *: Atrial septal defect.

Transthoracic aortic clamp was introduced through fourth intercostal space on posterior axillary line. At mild hypothermia, cardiac arrest was established with antegrade blood cardioplegia. After right atriotomy, secundum ASD with deficient rim was exposed (Figure 3). This interatrial defect was closed with gluteraldehyde-treated pericardial patch using 4-0 polytetrafluoroethylene suture. Right atriotomy incision was closed and aortic puncture site was sutured. Ventricular pacing wire and chest tubes were positioned, and cardiopulmonary bypass was completed uneventfully. Cardiopulmonary bypass and aortic clamping times were 55 and 30 minutes, respectively.

Patient had an uncomplicated postoperative course and was discharged on postoperative day 3. Platelet count on discharge was $137,000/\mu\text{L}$. Steroid therapy was tapered gradually. Patient was examined 3 months after the operation and was clinically well.

DISCUSSION

Kabuki syndrome is an unusual entity for medical specialists in terms of clinical diagnosis and associated morbidities, such as ITP. This syndrome is frequently diagnosed in early childhood, based on characteristic facial anomalies, mental retardation, congenital heart defects, and skeletal malformations.^[1-3] Typically, patients have broad and depressed nasal bone and tip, large prominent ears, and cleft lip. In differential diagnosis, other syndromes with diagnostic facial characteristics such as Down syndrome, Turner syndrome, or Williams syndrome should be excluded using genetic analysis. Genetic studies have reported several

gene mutations in *KMT2D* and *KDM6A* that lead to large spectrum of KS phenotypes.^[4] These gene mutations are currently diagnostic for KS patients. However, the underlying etiology still remains unknown in some patients.^[1-3] There is no specific laboratory or screen test for KS in prenatal or postnatal period. Characteristic features become pronounced with time and patient growth, and in suspected cases, genetic analysis can determine diagnosis of KS. Life expectancy of KS patients depends upon degree and management of cardiac and other associated anomalies.

Clinically, patients may present with skeletal anomalies such as scoliosis, joint laxity, short stature, short fifth finger, and other anomalies of hip joints, hands, and vertebrae that can be seen radiologically.^[1-3] KS patients may also present with genitourinary anomalies; gastrointestinal anomalies, such as anal atresia; eye disorders, such as ptosis or strabismus; and varying degree of mental growth deficiency, such as mild-to-moderate intellectual disability. Patients can join in social and outdoor activities. They can also perform individual self-care in daily life with education. In severe forms of the disease, motor deficiencies, speech disability, and memory defects may be seen. From 1.6% to 17% of KS patients are diagnosed with hematological disorders, such as ITP, and decreased platelet count may complicate any surgical procedure.^[4] If surgical or percutaneous repair is needed, patients should undergo detailed examination of organ systems to reduce morbidity and mortality.

In the literature, there are limited series on cardiovascular anomalies associated with KS.^[1-3] In these

reports, most common cardiac pathologies include aortic coarctation, ASD, ventricular septal defect, and left-sided obstructive lesions. Major anomalies are frequently diagnosed in early childhood, but patients with simple defects, such as ASD, may present in adulthood. In the first study written on the disorder, which included 62 patients with KS, associated cardiac pathologies were diagnosed in 31% of cases.^[1] In another series with 35 patients, incidence of cardiac anomalies was as high as 58%.^[3] Recently, Yuan^[2] published a review of 76 cases of KS. The author concluded that heart defect is one of the clinical manifestations of KS, as defect was present in 90.6% of patients. Anatomically, left-sided obstruction and septal defect are primary anomalies encountered, accounting for up to 46.1% and 32.9%, respectively.^[2] In reports, incidence of ASD in KS is between 17.1% and 20%.^[2] It is therefore recommended that echocardiographic examination be performed in all patients after clinical diagnosis of KS to exclude associated cardiac anomalies. Diagnosis of ASD that needs surgical repair is rare in adult patients with KS. Treatment options include percutaneous methods as first choice, as well as surgical techniques, if defects are not suitable for percutaneous closure.

Surgical treatment may be selected in cases of large ASD or for those with deficient rim.^[5] This is traditionally performed using sternotomy or thoracotomy incisions. Alternatively, robotic surgery may be performed with negligible operative risk, low morbidity, and early return to daily activities.^[6] Robotic surgery may be performed for primum and secundum-type defects, as well as sinus venous defects associated with partial anomalous venous return of the right lung.^[7] Advantages of robotic ASD closure include less pain, shorter hospital stay, quicker return to daily life activities and work, and decreased transfusion requirements. According to our experience, most patients have uneventful recovery and are discharged within 3 days. Morbidity and mortality rates are similar to those of conventional sternotomy and other minimally invasive approaches.^[6] Disadvantages of robotic surgery include requirement to have robotic endoscopic system, cost, relatively prolonged operative time, and time for learning curve, technical details and pitfalls, and need for surgical experience. Initial cost is a major disadvantage of robotic surgery. However, in a recent study, Morgan et al. concluded that robotic technology did not significantly increase

hospital cost of ASD procedures, despite cost of robotic surgical system.^[8] Although the operative time of robotic operation is relatively longer than conventional surgery, cardiopulmonary bypass and aortic clamping times can be decreased to acceptable levels as experience increases. Bonaros et al. showed that longer cardiopulmonary bypass times had no negative impact on intraoperative and postoperative outcome.^[6] Our experience also confirms that operative time of robotic ASD closure can be comparable to conventional sternotomy and thoracotomy procedure. However, we observe that total procedure time for robotic ASD closure is similar to conventional approaches only after a learning curve has been met.

In the current case, we performed ASD closure using the da Vinci surgical system (Intuitive Surgical, Inc., Sunnyvale, CA, USA) on a patient with KS and associated ITP. According to our literature search, this was the first case of KS and robotic surgery for ASD closure. We preferred robotic approach to decrease postoperative bleeding complications associated with ITP as well as sternotomy incisions. In robotic approach, surgical skin and explorative mediastinal incisions are very small; no major bleeding occurs due to limited surgical incisions. Moreover, we avoided sternotomy-related problems of pain, bleeding, and pulmonary dysfunction. Furthermore, no blood product was also used perioperatively. All of these factors led to quick and favorable recovery period in present patient.

In conclusion, KS is a rare congenital malformation that may present with cardiac anomalies in children and adults. Percutaneous closure is the initial procedure of choice for ASD closure, but in patients who are not suited to percutaneous treatment, robotic surgery may be preferable as an alternative approach, rather than traditional surgery techniques.

Conflict-of-interest issues regarding the authorship or article: None declared.

***Supplementary video file associated with this article can be found in the online version of the journal.**

REFERENCES

1. Niikawa N, Kuroki Y, Kajii T, Matsuura N, Ishikiriyama S, Tonoki H, et al. Kabuki make-up (Niikawa-Kuroki) syndrome: a study of 62 patients. *Am J Med Genet* 1988;31:565–89. [Crossref](#)
2. Yuan SM. Congenital heart defects in Kabuki syndrome. *Car-*

- diol J. 2013;20:121–4. [Crossref](#)
3. Digilio MC, Marino B, Toscano A, Giannotti A, Dallapiccola B. Congenital heart defects in Kabuki syndrome. *Am J Med Genet* 2001;100:269–74. [Crossref](#)
 4. Giordano P, Lassandro G, Sangerardi M, Faienza MF, Valente F, Martire B. Autoimmune haematological disorders in two Italian children with Kabuki syndrome. *Ital J Pediatr* 2014;40:10. [Crossref](#)
 5. Kaya MG, Ozdođru I, Baykan A, Dođan A, Inanç T, Dođdu O, et al. Transcatheter closure of secundum atrial septal defects using the Amplatzer septal occluder in adult patients: our first clinical experiences. *Turk Kardiyol Dern Ars* 2008;36:287–93.
 6. Bonaros N, Schachner T, Oehlinger A, Ruetzler E, Kolbitsch C, Dichtl W, et al. Robotically assisted totally endoscopic atrial septal defect repair: insights from operative times, learning curves, and clinical outcome. *Ann Thorac Surg* 2006;82:687–93. [Crossref](#)
 7. Onan B, Aydin U, Turkvatan A, Bakir I. Robot-Assisted Repair of Right Partial Anomalous Pulmonary Venous Return. *J Card Surg* 2016;31:394–7. [Crossref](#)
 8. Morgan JA, Thornton BA, Peacock JC, Hollingsworth KW, Smith CR, Oz MC, et al. Does robotic technology make minimally invasive cardiac surgery too expensive? A hospital cost analysis of robotic and conventional techniques. *J Card Surg* 2005;20:246–51. [Crossref](#)
-
- Keywords:** Atrial septal defect; Kabuki syndrome; robotic surgery.
- Anahtar sözcükler:** Atriyal septal defekt; Kabuki sendromu; robotik cerrahi.