Quadricuspid aortic valve in a patient with Turner syndrome

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A quadricuspid aortic valve is an uncommon congenital anomaly that is often associated with other cardiac disorders. Most reported cases of quadricuspid aortic valves are detected incidentally during necropsy or aortic valve replacement and, therefore, the potential clinical course still remains unclear. A case of a 47-year-old woman with grade III to IV aortic insufficiency and mild left ventricular dilatation with an end-diastolic diameter of 59 mm is presented. During surgery for aortic valve replacement (Ross procedure), a quadricuspid aortic valve was identified. Two years after the successful Ross procedure, a molecular genetic study of this rare anomaly was performed using karyotyping, fluorescence in situ hybridization and polymerase chain reaction. Cytogenetic analysis detected chromosomal aberration 45,X0/46,XX, indicating a low-level X chromosome mosaicism; repeat karyotypes were normal. This is the first reported case of a quadricuspid aortic valve in a woman with Turner syndrome.

Key Words: Cardiovascular malformations; Quadricuspid aortic valve; Turner syndrome

According to recent literature, more than 180 cases of quadricuspid aortic valve (QAV) have been identified so far, most of them discovered incidentally during necropsy or aortic valve replacement (1). The present case of QAV is the first to be reported in a woman with Turner syndrome (TS). The QAV was discovered in a 47-year-old woman who had been admitted to undergo cardiac surgery because of aortic insufficiency grade III to IV. The patient had an unremarkable facial appearance of TS.

TS is caused by haploinsufficiency of the short arm of the X chromosome, and affects approximately one in 2500 female live births (2). Cardiovascular malformations, especially coarctation of the aorta and bicuspid aortic valves, are frequently observed in patients with TS. In addition, aortic root dilatation and hypertension have been recognized as increased risks in women with TS (3). Therefore, cardiovascular abnormalities are one of the main causes of increased mortality in TS, especially during childhood (4). Of patients presenting with TS, 50% have X chromosome monosomy (45,X0) and the other 50% are mosaics, characterized by other X chromosome aberrations. Additionally, abnormalities and mosaicism with Y chromosomes are also present. Our patient most likely has limited mosaicism with a chromosomally normal cell line. Mosaicism is the result of nondisjunction in the first mitotic division of a 46,XX 2ygoe.

CASE PRESENTATION

A 47-year-old woman was admitted to undergo cardiac surgery in September 2003 because of a history of grade III to IV aortic insufficiency. She had left ventricle dilatation and a left ventricular ejection fraction of 45%. Echocardiography showed a malformed aortic valve without calcification and mild left ventricular dilatation with an end-diastolic diameter of 59 mm (5). During a Ross procedure using the subcoronary technique, four aortic valve leaflets type c, based on the Hurwitz and Roberts (6) classification, were identified. Two larger leaflets represented the right and the noncoronary leaflets and two smaller leaflets together represented the left coronary leaflet; all leaflets were thickened. Cytogenetic analysis on lymphocytes using a fluorescence in situ hybridization probe detected chromosomal aberration 45,X0/46,XX mosaicism (Figure 1). However, a normal karyotype was obtained (Figure 2). Four hundred nuclei were scored for signals of the X chromosome-specific probe. In

Figure 1) Fluorescence in situ hybridization probe on interphasic nuclei, showing a cell with one X chromosome (arrow)
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Figure 2) The patient showed a normal karyotype with 2n=46 chromosomes. Female; G-banding

39 of 400 cells, only one signal of the X chromosome-specific probe was detected, and the rest of the cells had two signals, thereby indicating a low-level X chromosome mosaicism. The patient had an unremarkable facial appearance of TS and no other abnormalities were detected. Molecular studies with multiplex for short tandem repeat and X-Y amelogenin polymerase chain reaction detected an X chromosome peak. A second skin tissue biopsy was suggested because of the limited mosaicism seen in the lymphocytes. Informed consent was obtained from the patient.

DISCUSSION

TS is a genetic disorder that affects approximately one in 2500 live female births. Of the patients presenting with TS, 50% have X chromosome monosomy (45,X0), and the other 50% show other X chromosome aberrations such as 45,X0/46,XX, 45,X0/46,X,i(Xq) or 45,X0/46,X,r(Xq). Additionally, abnormalities and mosaicism affecting the Y chromosome (eg, 45,X0/46,XY) may also be present. The phenotype of TS is characterized by short stature, gonadal dysgenesis, webbing of the neck, cubitus valgus and a large spectrum of other disorders (2,7). Females with TS have a highly increased risk of congenital cardiovascular anomalies and most reports conclude that echocardiographic evaluation is essential after the diagnosis of TS. Mazzanti and Cacciari (8) evaluated 594 patients with TS, and reported an 23% incidence of cardiac malformations in this group of patients. The most common lesions of cardiac malformations in TS are coarctation of the aorta and bicuspid aortic valves. In addition, aortic root dilation and hypertension have been recognized as increased risks in women with TS. Therefore, cardiovascular abnormalities are one of the main causes of increased mortality in TS, especially during childhood (2-4). According to recent literature, the present paper is the first report of QAV in a woman with TS. Our patient most likely has limited mosaicism with a chromosomally normal cell line. Mosaicism is the result of nondisjunction in the first mitotic division of a 46,XX zygote. Partsch et al (9) examined growth in 50 females with triple mosaicism, and reported a direct correlation between height standard deviation scores and the proportion of 46,XX cells in peripheral lymphocytes, as well as an indirect correlation between these scores and the proportion of 45,X0 cells.

Greater than 180 cases of QAV have been identified to date, most of which were discovered incidentally during necropsy or aortic valve replacement associated with severe valvular dysfunction (10,11). However, the genetic origin of congenital cardiovascular defects in TS is unknown.

CONCLUSION

We describe the first known case of QAV in a patient with TS. Our patient had a low genetic manifestation, and did not have the typical phenotype of TS. Based on our case and on existing literature, we hypothesize that there is involvement of X-linked factors and cardiac defects in TS. Further research is required.

REFERENCES