Echocardiographic Evaluation of Cardiac Valvular Abnormalities in Adults with Down's Syndrome

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HAMADA, T., GEJYO, F., KOSHINO, Y., MURATA, T., OMORI, M., NISHINO, M., MISAWA, T. and ISAKI, K. *Echocardiographic Evaluation of Cardiac Valvular Abnormalities in Adults with Down's Syndrome*. Tohoku J. Exp. Med., 1998, **185** (1), 31-35 — It is well known that congenital heart abnormalities are common in children with Down's syndrome. However there are few studies on cardiac abnormalities in adults with Down's syndrome. Therefore, we estimated cardiac abnormalities by means of echocardiography in 30 institutionalized Japanese adults with Down's syndrome, but without cardiac symptoms. Two-dimensional echocardiography showed an incidence of 26.7% in mitral valve prolapse and 20% increase of echo brightness in the mitral valve. Doppler echocardiography revealed an incidence of 16.7% in mitral valve regurgitation, and 13.3% in aortic valve regurgitation. Thus, even adults with Down's syndrome who are apparently free of cardiac symptoms may be at risk for valvular disease. ————— Down's syndrome; mitral valve prolapse; mitral regurgitation; Doppler echocardiography
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Down's syndrome is a form of mental retardation due to an aberration of chromosome 21 that is commonly associated with congenital heart disease, diabetes mellitus, and hypothyroidism. Among the heart diseases observed in children with Down's syndrome, the frequency of congenital heart disease is increased (Shaher et al. 1972). However there are few studies on heart disease in adults with Down's syndrome (Goldhaber et al. 1986). There are often kept at home or are institutionalized and medical treatment of asymptomatic adults with

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Down's syndrome is frequently neglected. On a population of asymptomatic, institutionalized adults with Down's syndrome, we used noninvasive echocardiography to evaluate cardiac valvular abnormalities, and regurgitation to try to clarify the actual incidence of heart disease and its clinical significance.

SUBJECTS AND METHODS

We selected 30 Japanese adults, 14 males and 16 females aged 20–49 years (mean age $\pm$ s.d., 33.2 ± 8.8 years) with Down's syndrome but without cardiac symptoms and none had a previous diagnosis of congenital heart disease. They were residents of 8 different institutions in Fukui Prefecture. The diagnosis of Down's syndrome was confirmed by chromosomal examination, in each case. There were 27 cases of 21-trisomy and 3 cases of the mosaic type. We chose 30 age-matched healthy volunteers, 20 males and 10 females aged 21–48 years old (mean age $\pm$ s.d., 30.5 ± 7.7 years), as controls.

Echocardiography was performed with a Toshiba SSH-160A Sonolayergraph (Tokyo) equipped with an ultrasound frequency transducer of 3.5 MHz. We observed morphological changes in various sections by two-dimensional echocardiography.

In an attempt to find any relationships between the serum levels of certain substances and calcification of the mitral annulus, we compared the serum levels of calcium (Ca), phosphorus (P), calcitonin (CLT), and carboxyl-terminal parathyroid hormone (PTH-c) for the Down's syndrome patients with and without mitral annular echo enhancement.

Regurgitation was confirmed using the colored Doppler echocardiography and a 2.5 or 3.5 MHz probe by use of a pulse-repeating frequency of 4 kHz. The flow signal was judged as a clinically significant regurgitation when the maximum area of the regurgitant jet signals was more than 1.0 cm².

Subjects were kept calm during the recording sessions by their caregiver, who reassured the individual. Written consent for participation in this study was obtained from each patients and his guardian.

Differences in proportions between groups were assessed by use of Fisher's exact test. A level of $p < 0.05$ was accepted as statistically significant.

RESULTS

Morphological observation of each section by two-dimensional echocardiography showed that mitral valve prolapse (MVP) was significantly more frequent in the Down's syndrome group (26.7%) than in the control group (3.3%) ($p < 0.05$). In the Down's syndrome group, the incidence of enhancement of echo brightness at the mitral valve and at the aortic valve was 20% ($p < 0.05$) and 3.3%, respectively, but neither enhancement occurred in the control group. The serum levels of Ca, P, CLT and PTH-c were within the ranges of normal, with no differences observed between the Down's syndrome patients with and without mitral annular

TABLE 1. *Two-dimensional and color Doppler echocardiographic findings for Down's syndrome patients and controls*

Parameter	Downs syndrome (<i>n</i> = 30)	Healthy controls (<i>n</i> = 30)
Two-dimensional echocardiography		
Mitral valve prolapse	8 (26.7%)*	1 (3.3%)
Mitral annular echo enhancement	6 (20.0%)*	0 (0%)
Aortic valve echo enhancement	1 (3.3%)	0 (0%)
Color Doppler echocardiography		
Mitral valve regurgitation	5 (16.7%)	0 (0%)
Aortic valve regurgitation	4 (13.3%)	0 (0%)
Tricuspid valve regurgitation	3 (10.0%)	0 (0%)

**p* < 0.05

Fig. 1. Color Doppler echocardiogram showing aortic valve regurgitation from a 20-year-old Down's syndrome patient
 Ao, aorta; LA, left atrium; LV, left ventricle; RV, right ventricle.

echo enhancement. Although Doppler measurements revealed the incidence of mitral valve regurgitation (MR), aortic valve regurgitation (AR), and tricuspid valve regurgitation (TR) in the Down's syndrome group to be 16.7, 13.3 and 10% respectively, differences from the control group were not statistically significant (Table 1 and Fig. 1).

DISCUSSION

In the present study, MVP was found in 26.7% of Down's syndrome patients. It has often been reported that MVP is found in adults with Down's syndrome (Goldhaber et al. 1986). Goldhaber et al. (1986) ascribed its occurrence to a connective tissue disorder that is also involved in the dislocation of the joints observed in Down's syndrome. The enhancement of echo brightness in the mitral valve being confirmed in 20% of Down's syndrome patients. This enhancement is often attributed to calcification, which may be caused or exacerbated (Fulkerson et al. 1979) by the following factors: Aging, especially in elderly female, excessive stress in the mitral valve resulting from an increased pressure in the left ventricle and abnormal valvular movement, abnormal alterative tissue in the valvular ring; and thrombosis due to blood stagnation and coagulation. Because the enhancement of echo brightness is reported with primary hyperparathyroidism and renal failure, (e.g., dialysis patients), hypercalcemia as well as hyperphosphatemia have been considered as possible factors in mitral annular echo enhancement (Roberts and Waller 1981; Forman et al. 1984). The patients with Down's syndrome group in the present study, however, contained no hypertensive patients, and serum levels of Ca, P, CLT, and PTH-c did not differ in groups with and without enhancement of echo brightness in the mitral valve. The enhancement of echo brightness in the mitral valve established in this study failed to satisfy all the diagnostic criteria (Nair et al. 1984) for mitral annular calcification (MAC). These reasons suggest that the echo enhancement seen here may differ from MAC, and perhaps may indicate an abnormality due to an underlying connective tissue disorder.

Doppler echocardiography confirmed that valvular regurgitation (MR, AR and TR) occurred with greater frequency than in the control group, but the increases were slight and corresponding phonocardiograms were silent. Yoshida et al. (1988) pointed out the high prevalence rate (40–60%) of valvular regurgitation in normal subjects. However, valvular regurgitation was not observed in our normal controls. In our study, to avoid clinically insignificant regurgitation, trivial regurgitation of which maximum regurgitant jet area was less than 1.0 cm² were excluded. MVP, enhancement of echo brightness in the mitral valve, MR and AR are scarcely ever reported in children with Down's syndrome, and are assumed to be conditions encountered only in adulthood (Goldhaber et al. 1986). Longitudinal studies are needed to determine whether these characteristics are attributable to accelerated aging or to other factors.

In conclusion, even adults with Down's syndrome who are apparently free of cardiac symptoms may be at risk for valvular disease. Therefore, more careful regular follow-up by echocardiography are needed in adults with Down's syndrome patients.

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