

# Severe heart disease can cause diabetes mellitus even in younger age:

## Case reports of two Japanese adolescent boys.

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### INTRODUCTION

It is noted that patients with congenital heart disease (CHD) are likely to develop abnormal glucose metabolism and this metabolic deterioration usually occurs after middle age. However, we recently had two patients with CHD, who developed type 2 diabetes mellitus (DM) in their adolescence.

### CASE PRESENTATION

#### Case 1 : Seventeen-year-old boy

##### Perinatal history

He was born at 37w0d of gestation weighting 2628g, with single-ventricle, atrium/ventricular septum defect and pulmonary atresia.

##### Past history

One years old: Glenn shunt  
Two years old: Fontan operation

##### Familial history

Grand father had DM.

##### Complication

hypoxic-ischemic encephalopathy, symptomatic epilepsy, severe mental retardation

##### Present illness

He had been treated by a pediatric cardiologist on our hospital since he was 11 years old. When he was 14 years old, he visited our hospital because of thirst and polyuria that lasted for a week. He was not obese (160.0cm in height, 35.5kg in weight, and 13.87 kg/m<sup>2</sup> in body mass index (BMI) ) at that time.

Laboratory data and glucagon-test proved that he had Type 2 DM. He has been administered Metformin 1500mg daily.

##### Laboratory data

Glu	322	mg/dl	pH	7.338
HbA1c	10.7	%	BE	-2.6
IRI	3.1	μU/ml		
CPR	0.89	ng/ml		
BNP	6.6	pg/ml	Urine analysis	
GADAg	5.0	U/ml	Urine sugar	4+
IA-2Ag	0.4	U/ml	Ketoneuria	±

Glu: blood glucose, IRI: insulin, CPR: C-peptide, BNP: B-type natriuretic peptide

##### Glucagon - test

	0	3	6	10	15	(min)
CPR	1.07	2.46	2.84	3.58	2.54	(ng/ml)

#### Case2 : Sixteen-year-old boy

##### Perinatal history

He was born at 39w2d of gestation weighting 1830g with tricuspid atresia, ventricular septum defect and pulmonary stenosis. He underwent Blalock-Taussing shunt.

##### Past history

He underwent percutaneous transluminal angioplasty (PTA) 6 times.

##### Familial history

Grand-grand-parents had DM.

##### Complication

mental retardation

##### Present illness

When he was 14 years old, it was pointed out that his HbA1c was 7.6% without symptoms. His height, weight and BMI were 142.7cm, 28kg and 14.22 kg/m<sup>2</sup> respectively. He was not obese.

He was diagnosed as Type 2 DM with the laboratory data and oral glucose tolerance test(OGTT).

His glucose metabolic indexes were as follows, indicating slight decrease in insulin secretion.

- HOMA-R=0.97
- Insulinogenic index=0.48
- HOMA-β=28.2%

We have managed him with Metformin and DPP4 inhibitors since then.

##### Laboratory data

HbA1c	7.2	%	Urineanalysis	
BNP	23.5	pg/ml	Urine sugar	-
GADAg	< 5.0	U/ml	Ketoneuria	-

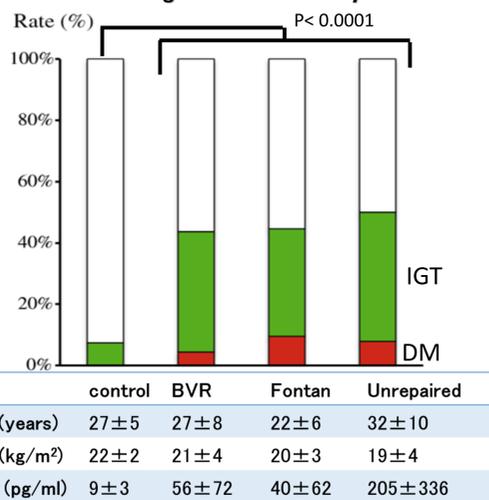
##### OGTT; oral glucose tolerance test

	0	30	60	90	120	(min)
BG	109	183	248	246	244	(mg/dl)
IRI	3.6	39.3	68.3	58.9	33.1	(μU/ml)

### DISCUSSION

There are some reports that the impaired glucose tolerance (IGT) was more frequently observed in adult patients with CHD than without CHD (p<0.0001). Among young patients with CHD, the frequency of IGT was reported to be about 40% and this frequency was equivalent to unrepaired group, although the serum B-type natriuretic peptide (BNP) level was higher in unrepaired group.

#### Evaluation of glucose tolerance by OGTT



IGT: impaired glucose tolerance, BVR: Biventricular

(Ohuchi H, Int J Cardiol. 2014)

In addition, there is a report that the group of patients with cyanotic heart disease have higher risk of developing diabetes than non-cyanotic heart disease.

#### Hazard Ratio of diabetes development in patients with CHD

CHD	Hazard Ratio	95% CI
Cyanotic	2.85	1.77-4.57
Acyanotic	1.35	1.02-1.77

(Nicolas L.Madsen, et al.JAHA.2016)

Case 2 had high BNP levels and hypoxemia so that he had higher risk of DM. On the other hand, in our case 1, the BNP level was in normal range. However he had hypoxemia. It was reported that the risk of developing DM was similar regardless of the degree of heart failure in patients with CHD 1). The risk of developing diabetes cannot be evaluated accurately by the BNP value only. Our 2 cases indicate that cyanotic CHD patients might have higher risk of developing DM even in adolescence and even with fair management of heart failure.

### CONCLUSION

- Patients with congenital heart disease have higher risk of impaired glucose tolerance in childhood and young adulthood.
- Even if they are not obese, it may be needed to evaluate blood glucose level or HbA1c, regularly.

### REFERENCE

- 1) Hideo Ohuchi, et al. Low fasting plasma glucose level predicts morbidity and mortality in symptomatic adults with congenital heart disease, *International Journal of CARDIOLOGY*, June 15(2014)
- 2) Madsen NL, et al. Congenital Heart Disease With and Without Cyanotic Potential and the Long-term Risk of Diabetes Mellitus: A Population-Based Follow-up Study. *J Am Heart Assoc.* Jul 8;5(7)(2016)