DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness) Syndrome Associated with Myocardial Disease

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SUMMARY

A 30 year old man with DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy and deafness) syndrome associated with myocardial disease is reported. Echocardiographic study revealed a marked symmetric left ventricular hypertrophy. Histology of the endomyocardial biopsy specimen from the right ventricle showed severe glycogen deposition in the myocytes. This case may indicate that DIDMOAD syndrome is a hereditary systemic disease affecting multiple organs, including the myocardium.

Additional Indexing Words:

DIDMOAD syndrome Myocardial disease Glycogen deposition

IN 1938, Wolfram¹⁾ reported four siblings with diabetes mellitus and optic atrophy. This lesion complex often involves diabetes insipidus and deafness, and has recently been designated as DIDMOAD syndrome (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness syndrome).

In this report, a patient with DIDMOAD syndrome associated with myocardial disease, characterized by marked glycogen deposition in the myocytes, is presented.

CASE REPORT

A 30 year old blind man was admitted to our hospital because of dyspnea on exertion. Blindness and deafness first became apparent at age 3 years. At the age of 17 he was diagnosed as having insulin dependent diabetes

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mellitus. His brother is also blind and deaf, and has diabetes mellitus. His parents are first cousins and both of them have diabetes mellitus. Three other relatives also are suffering from diabetes mellitus (Fig. 1).

The patient was completely blind with bilateral optic atrophy observed on fundoscopic examination. An audiograph showed absence of bone conduction. Cardiac murmurs and rales were not audible on auscultation. Slight pitting edema was noted in the lower extremities. Neurological examination was normal. Routine laboratory data were normal except for elevated blood and urine glucose levels. The assay of leukocyte enzymes revealed normal α -glucosidase and α -galactosidase activities. Chest X-ray showed cardiomegaly and pulmonary congestion. Standard electrocardiogram showed evidence of left ventricular hypertrophy. An echocardiographic study showed marked symmetric left ventricular hypertrophy with impaired myocardial contractility. There were many fine bright echoes seen from the

Fig. 1. One patient with DIDMOAD syndrome and 6 patients with diabetes mellitus are noted in the patient's family tree.

Fig. 2. Echocardiograms from the reported patient with DIDMOAD syndrome. There is marked symmetrical hypertrophy of the left ventricular walls and a small pericardial effusion is noted posteriorly. A: Parasternal view; long axis. B: Parasternal view; short axis. C: Apical 4-chamber view.

Fig. 3. A: Histology of endomyocardial biopsy specimen from the right ventricle. Marked hypertrophy and severe vacuolar degeneration of the myocytes are observed (HE 100 $\times$). B: PAS stained specimen shows marked glycogen deposition in the myocytes (PAS 200 $\times$).

inside of a thickened myocardium. Pericardial effusion was noted posteriorly (Fig. 2). Myocardial imaging using ^{201}Tl revealed diffuse hypertrophy of the myocardium and a decreased washout rate. No perfusion defect was detected after ergometer exercise testing. On cardiac catheterization, the pulmonary artery wedge pressure was elevated. Cardiac index determined by the thermodilution method was decreased at 1.8 l/min/m².

Histopathology of endomyocardial biopsy specimens from the right ventricle showed marked hypertrophy and dysarrangement of the myocytes (Fig. 3). Severe vacuolar degeneration of the myocytes was widely observed. PAS stained specimens showed marked glycogen deposition in the myocytes confirmed by the amylase digestion procedure. Ultrastructurally, glycogen granules were seen diffusely in the myocardial cells. Loss of myofilaments and myochondriosis were also observed in the myocytes.

DISCUSSION

DIDMOAD syndrome is thought to be an autosomal recessive hereditary disorder characterized by juvenile onset of insulin dependent diabetes mellitus, bilateral optic atrophy, diabetes insipidus and neurogenic deafness.¹⁾⁻⁴⁾ We are reporting a case with DIDMOAD syndrome who has a severely hypertrophied heart with glycogen deposition in the myocytes. Among the previously reported cases of DIDMOAD syndrome, we were unable to find any with myocardial disease similar to that seen in our case. Carson et al⁴⁾ reported one autopsied case of this syndrome associated with cardiac abnormalities. The heart of his case showed massive right sided hypertrophy, patent foramen ovale, high ventricular septal defect and a thickened pulmonic valve. However, severe left ventricular hypertrophy and increased glycogen deposition as seen in our case were not demonstrated in his case.

From the pathological point of view, the cardiac involvement of our case is similar to that seen in glycogen storage diseases, especially glycogenosis Type II (Pompe's disease).⁵⁾ This disease often induces a myocardial disorder characterized by severe hypertrophy of the heart, lacework appearance of the myocardium and the demonstration of glycogen in the myocytes. However, in the enzyme activity assay of leukocytes, α -glucosidase activity which is decreased in patients with Pompe's disease, was normal in our patient.

Glycogen deposition in the myocytes is sometimes seen in the heart with diabetes mellitus.⁶⁾ It is believed that some unknown metabolic derangement may cause glycogen deposition in some types of diabetes mellitus, but the mechanism is not clear. The association of extreme glycogen deposition in the myocytes with DIDMOAD syndrome that we found in our patient may offer an insight into the mechanism of myocardial glycogen deposition in patients with diabetes mellitus.

The cardiac disorder in DIDMOAD syndrome described here is not well recognized from the clinical and pathological points of view. Although it could not be confirmed that the myocardial disorder in our patient had any relationship to DIDMOAD syndrome, our case suggests that DIDMOAD syndrome is a hereditary systemic disease which affects multiple organs including the myocardium.

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