Fibromuscular Dysplasia Caused Sudden Death due to Acute Myocardial Infarction

— Report of a Case with Involvement of Multiple Arteries Including the Coronary Artery —

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ABSTRACT **We have recently encountered a patient presenting an sudden cardiac death secondary to acute myocardial infarction as a complication of fibromuscular dysplasia (FMD) involving the coronary artery. A 30 years old woman, who had a 6 year history of hyperthyroidism, was carried to our hospital because of sudden cardiac arrest. With no vital signs at arrival, advanced life support make her heart beat and gave a stable hemodynamic condition, which allowed us to make a diagnosis of acute broad anterior myocardial infarction with electrocardiography, echocardiography and serum CK-MB isoenzyme. Her brain activity did not recovered. She died on day 6 of hospitalization. Postmortem examination confirmed a broad anterior wall infarction of a histologic age of several days. Histologic examination also revealed intimal fibrous thickening with an increase of smooth muscle cells and elastic fibers in the right coronary and the anterior descending branch of the left coronary arteries, as well as the vertebral, bronchial, intra-renal and superior mesenteric arteries. Whereas no complete obstruction in the coronary artery was found at autopsy, it seems likely that the intracoronary luminal narrowing induced by fibromuscular hyperplasia might have precipitated a myocardial ischemic insult which caused the sudden cardiac death. Although FMD of the coronary artery has been rare in literature, it is necessary to consider FMD in the differential diagnosis of identifiable causes of sudden death, particularly in the young generation.**

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Key words: Fibromuscular dysplasia, Coronary artery, Acute myocardial infarction, Sudden cardiac death

Fibromuscular dysplasia (FMD) is a nonatherosclerotic and noninflamatory vascular disease of unknown cause, primarily affecting small and medium sized arteries[1]. Clinically significant FMD was first described[2] in 1936 and still occurs most commonly in the renal arteries of young women[3]. Later, it became known that FMD could also affect other arteries such as the carotid[4] or celiac arteries[5]. However, FMD of the coronary artery is still extremely rare[1,6]. We have recently encountered a patient with sudden cardiac death due to acute myocardial infarction, who had wide spread FMD including the coronary arteries.

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Report of a case

A 30 years old woman, a swimming coach, was carried to our hospital because of sudden cardiac arrest.

Seven years before entry, the patient had started to have a hyperthyroidism. Methimazole was effective for controlling the hyperthyroidism at first, however, the patient had a few relapsing episodes with atrial fibrillation. She had never complained of anginal pain.

On the day of admission, patient suddenly fell to the ground from a 2 meter high platform. She was not showing any vital signs, when the ambulance team arrived 6 minutes later. Basic life support was begun and the patient was carried to our emergency room. She still had no vital signs on arrival. Elecrocardiographic monitoring revealed ventricular fibrillation. Advanced life support efforts were started. After direct current cardioversion, the heart began to beat again, and she regained a stable hemodynamic condition. Her blood pressure was 90/50 mmHg, heart rate 140 bpm. However, her consciousness did not recover. The conscious level was 300 on the Japan coma scale (JCS), while the brainstem-auditory evoked potential (BAEP) was within the normal range. Remarkable exophthalmos and goiter were observed. A Grade 2/6, Levine, systolic cardiac murmur was audible at the lower left sternal border. Moist rales were also heard all over the lung. There were no ascites nor edema.

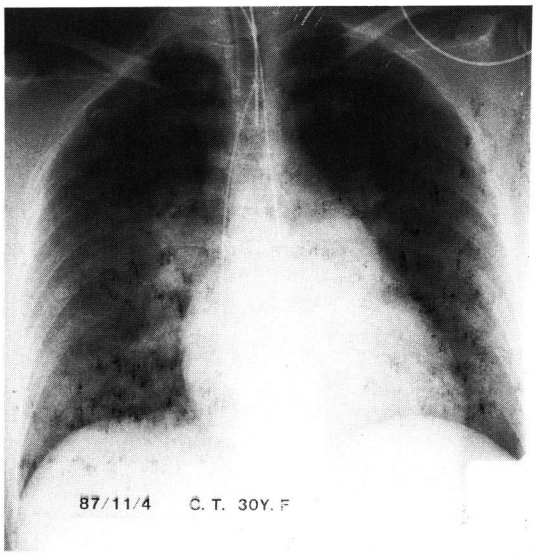

Fig. 1 Chest X-ray film on admission (A-P view).

A chest X-ray film showed bilateral pulmonary congestion and slight cardiomegaly (Fig. 1). In Figure 2a, an electrocardiogram (ECG) five months before the accident had shown an atrial fibrillation and an extreme right axis deviation. Our ECG after recovery from ventricular fibrillation clearly showed the recently developed QS waves with ST segment elevation through V1 to V5 indicating a broad anterior wall myocardial infarction (Fig. 2b). Two-dimensional echo-cardiography revealed akinesis in the wide anterior wall of the left ventricle. There was no high or low density area in the brain CT.

Blood laboratory findings on admission showed severe acidosis, remarkable leucocytosis, and releasing enzymes from the ischemic damaged muscle. Myocardial specific isoenzyme CK-MB gradually increased to the maximum value, 20.9%, 3900 IU/L at 12 hours after the attack, then decreased. Only free thyroxine, T4, was elevated slightly in the thyroid function test.

Four days after the attack, her consciousness was still 300 on the JCS and both the electroencephalography and BAEP had disappeared. She died on day 6 of hospitalization.

Postmorten examination :

There were bilateral bronchial pneumonia and pulmonary congestion. Neither hemorrhage nor softening was found in the brain, although the brain was generally edematous. The thyroid gland was diffusely enlarged, weighing 90 g. Histologic findings revealed the increased height of the epithelium, redundancy of the follicular wall and vacuoles between the colloid and epithelial cells, which were accompanied by interstitial lymphocytic infiltration.

The heart weighed 360 g. There were no macroscopically demonstrable anomalies. Both right and

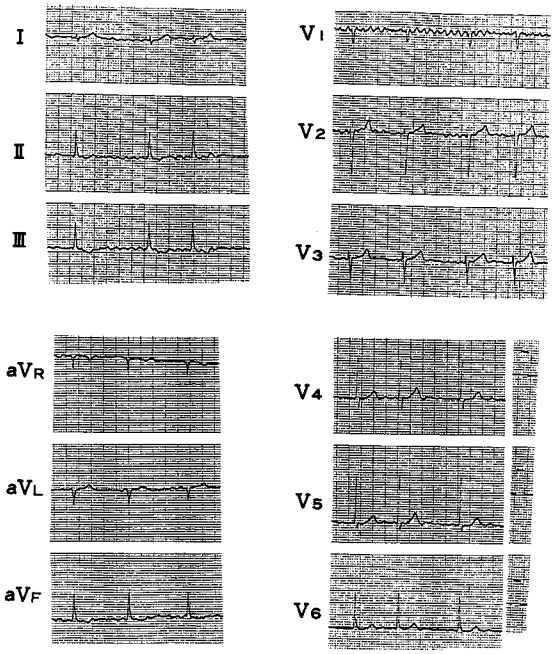

Fig. 2a Electrocardiogram recorded 5 months before the accident showing a right axis deviation and an atrial fibrillation.

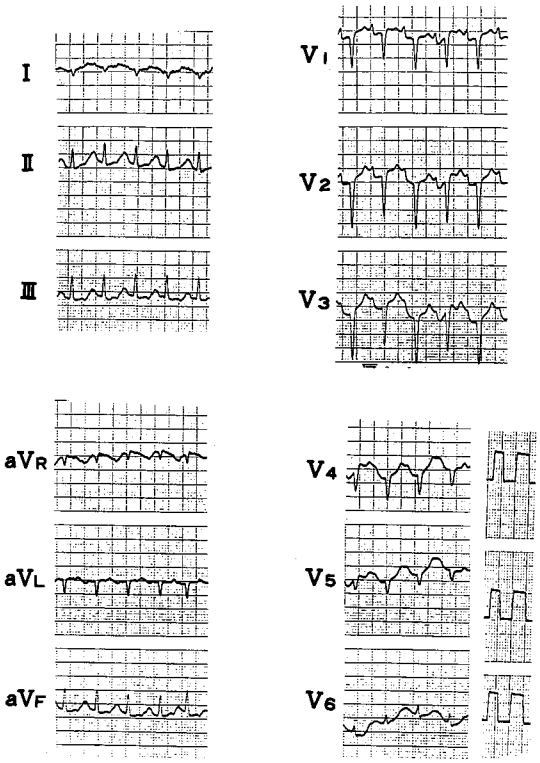

Fig. 2b Electrocardiogram after recovery from ventricular fibrillation on the day of admission clearly showed deep QS waves with ST elevation through V1 to V5 indicating an acute phase of a broad anterior myocardial infarction.

left coronary arteries arose normally from the aorta and were patent without bloody clotting. On gross examination, a broad anterior wall infarction was exhibited. In microscopic examination, Hematoxylin -Eosin staining showed peripheral neutrophil infiltration in the infarcted area. Hematoxylin- Basic-Fuchsin-Picric acid (HBFP) staining[7] indicated a fresh ischemic insult in the broad anterior wall of the left ventricle (Fig. 3a). Masson's trichrome staining did not show massive fibrosis in the infarcted region (Fig. 3b). Those histologic findings indicated the acute phase of a myocardial infarction of an age of several days. Striking changes were found in the cross sectional view of both left anterior descending (Fig. 4a) and right coronary artery (Fig. 4b) 10 mm from bifurcation or origin, the walls of which were severely thickened by intimal hyperplasia, all of which contributed to significant narrowing of their lumens. Similar microscopically fibromuscular alterations were extensive in the vertebral (Fig. 5a), bronchial (Fig. 5b), intra-renal arteries (Fig. 5c) and a superior mesenteric artery. The primary changes were a thickening of the arterial wall by intimal proliferation. Necrotic changes were seen in one meter of the distal end of ileum.

Discussion

The present case was a typical case of sudden cardiac death. Although this patient had a past history of recurrent hyperthyroidism with atrial fibrillation and might have had a hyperactivity of the thyroid gland, the cause of her sudden cardiac death was acute myocardial infarction, which was shown

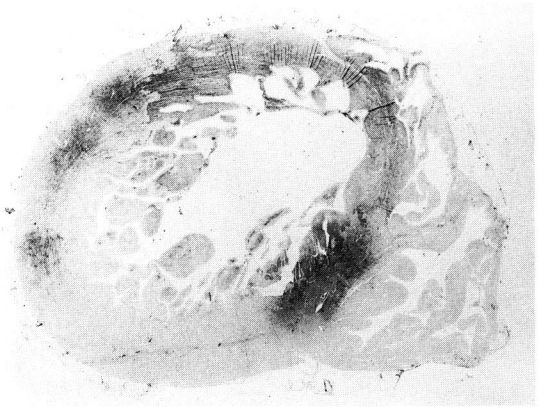

Fig. 3a A positive fuchsin red-color staining indicated a fresh myocardial infarction in the broad anterior wall of left ventricle. (stained with hematoxylin-basic-fuchsin-picric acid. ×1).

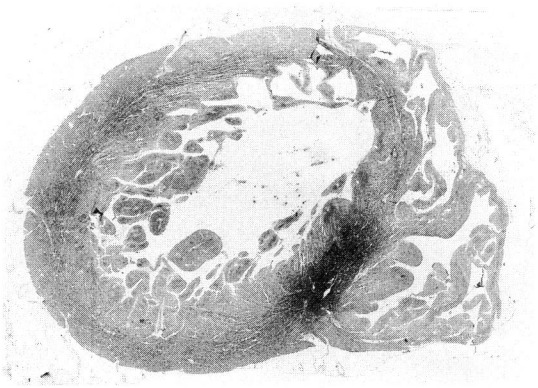

Fig. 3b Fibrosis was not yet predominant in the infarcted area. There was also no obvious fibrotic change indicating an old myocardial infarction. (stained with Masson's trichrome method. ×1).

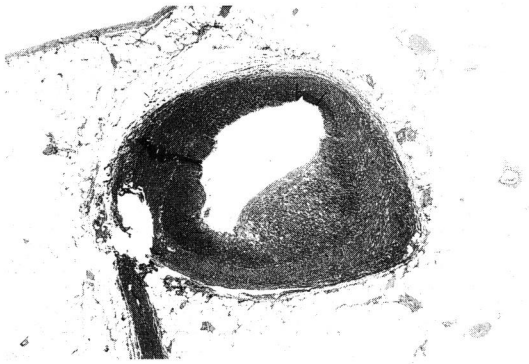

Fig. 4a Cross-sectional photomicrograph of the left anterior descending coronary artery with an intimal fibromuscular hyperplasia. Note the intimal fibrous thickening with an increase of smooth muscle cells and elastic fibers and the absence of degenerative changes. (stained with Elastica van Gieson. ×5).

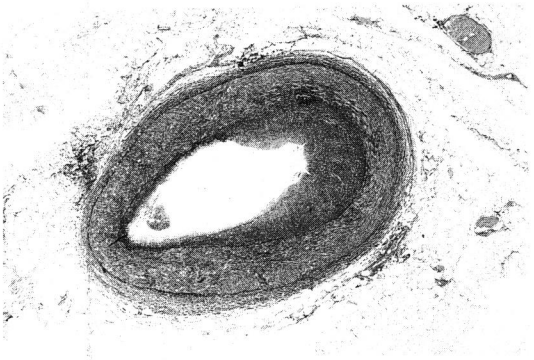

Fig. 4b Cross-sectional photograph of the right coronary artery 10 mm from the origin. (stained with Elastica van Gieson. ×5).

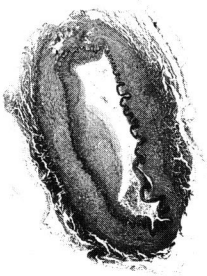

Fig. 5a Vertebral artery. (stained with Elastica van Gieson. ×5).

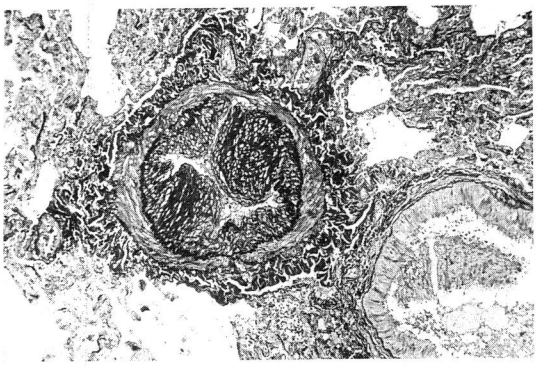

Fig. 5b Bronchial artery. Lumen was almost completely obstructed by the intimal fibrous thickening. (stained with Elastca van Gieson. ×30).

by ECG, two-dimensional echocardiography, myocardial releasing enzymes and the pathologic findings.

In addition to confirming the diagnosis of acute myocardial infarction, the histopathological examination also revealed the characteristic alteration of fibromuscular dysplasia in both the right coronary artery and the left anterior descending coronary artery, as well as in the vertebral, bronchial, renal and superior mesenteric arteries. Whereas no complete obstruction was found in the coronary artery at autopsy, it seems likely that the intracoronary luminal narrowing induced by the fibromuscular intimal hyperplasia might have precipitated a myocardial ischemic insult which caused the sudden cardiac death.

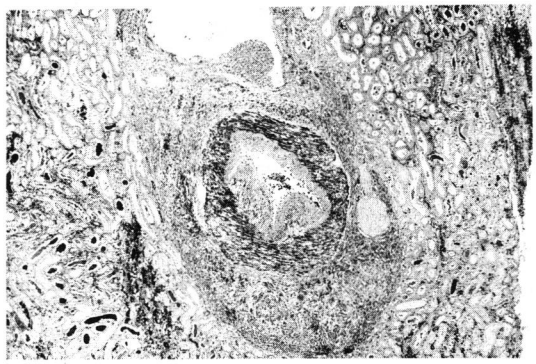

Fig. 5c Intra-renal artery. (stained with Masson's trichome method. ×10).

Although FMD may be found in virtually any small and medium sized arteries, FMD of the coronary arteries has been rare in the literature[1,3,6]. In Table 1, a list of the previous reports in which FMD involved coronary arteries are shown. Recently, from careful examination of their 92 patients with FMD, Lüscher *et al*[3]. reported that two or more different arteries were involved in 28% of their patients, however, FMD involving coronary arteries was seen in only two patients with sudden death. They also suggested that systemic FMD was found in patients without clinical evidence of further arte-

Table 1 *A list of reported cases of fibromuscular dysplasia involving coronary artery*

Authors	Age/Sex	Affected vessel	Type	Outcome
Hill[8]	73/F	coronary artery (LCX)	I+M	rupture of coronary arterial aneurysm
	28/F	coronary artery (LAD)	I	post-operative death (mitral valvuloplasty)
Naka[9]	37/M	multi-v including coronary artery	I	MOF (multiple organ failure)
James[10]	7/M	SA node artery	I+M	VF, sudden death
	64/M	SA node artery	I+M	VF, sudden death
Scully[11]	41/F	coronary arteriovenous fistula	M	successful operation
Lie[6]	24/M	coronary artery (RCA)	M	AMI due to coronary dissection
Arey[12]	9/M	intramyocardial coronary artery	I+M	AMI, sudden death
Bekki[13]	27/F	multi-v including coronary artery (LAD+LCX)	I	AMI
Meredith[5]	13/F	multi-v including gastrointestinal and coronary artery	I	MOF
Dominguez[14]	11wk/F	multi-v including coronary arteries	M	AMI, sudden death
	5wk/F 7wk/F			
present case	30/F	multi-v including coronary artery (LAD+LCX)	I	AMI, sudden death

I: intimal, M: medial proliferation type of FMD, multi-v: multivessels

rial disease, since a considerable number of patients with extrarenal FMD were asymptomatic. Our patient had never complained of an anginal episode. One of the possible explanation is that FMD had proceeded slowly enough to develop collateral circulation. James and Marshall[10] described two patients, both of whom died suddenly, who had multifocal narrowing of the sinus node artery with intimal hyperplasia. Recent reports[12,14] including ours, revealed cases with sudden unexpected death secondary to acute myocardial infarction as a complication of fibromuscular dysplasia involving the major coronary arteries. Thus, FMD must be considered in the differential diagnosis of identifiable causes of sudden death, particularly in the young generation.

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急性心筋梗塞にて突然死したFibromuscular Dysplasiaの1例

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Fibromuscular dysplasia (FMD) は腎動脈のみならず全身の動脈にも起こり得ることが知られているが冠動脈病変例の報告は少ない. 急性心筋梗塞にて突然死したFMDの1例を経験したので報告する. 症例は30歳女性, 水泳指導員. 6年前に甲状腺機能亢進症発症, 抗甲状腺剤治療にて寛解・再然を繰り返していた. 水泳指導中, 突然見張り台から転落したが, その直後すでに心拍・呼吸が停止していたため, ただちに一次救命措置が開始された. 25分後に当院へ緊急搬入された際には心室細動の状態であった. 再三の直流除細動を含む二次救命処置にて心拍は再開し, 昇圧剤投与下に血圧も90/50 mmHgとなったが, 意識は回復せず第6病日に死亡した. この間, 心電図, 断層心エコー図ならびに血清酵素 (CK-MB) 上昇から急性広汎前壁心筋梗塞と診断された. 剖検にて急性広汎前壁心筋梗塞が, さらに組織学的に左・右冠動脈をはじめ, 脳底・気管支・腎及び上腸間膜動脈と広範囲にわたる内膜性FMDが認められた. 若年者における突然死の原因として冠動脈を巻き込んだFMDによる急性心筋梗塞の存在も考慮しておく必要がある.