Aorto-Coronary Dissection During Angioplasty in a Patient With Myxedema

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A 67-year-old man with overt hypothyroidism and medically controlled hypertension was admitted for coronary angiography because of exertional angina. His triiodothyronine (T3) and thyroxine (T4) levels had been low for 4 years. Although signs and symptoms of hypothyroidism were apparent, his hypercholesterolemia was mild. Coronary angiography revealed an eccentric stenosis in the distal portion of the right coronary artery and it was decided to perform angioplasty because his angina had continued in spite of medication. The dissection appeared at the lesion site after the first nominal inflation, and a subsequent image disclosed a spiral dissection from the dilated site to the aortic sinus and peripheral coronary artery. Although emergency stenting could not prevent the extension near the origin of the brachiocephalic artery, the false lumen thrombosed and then diminished with conservative therapy. Aorto-coronary dissection is potentially life-threatening and has been recently reported as a complication during cardiac catheterization procedures. Chronic hypothyroid insufficiency may be one of the risk factors for this complication. (*Jpn Circ J* 2000; 64: 316–320)

Key Words: Aortic dissection; Coronary dissection; Hypothyroidism; Percutaneous transluminal coronary angioplasty (PTCA)

Hypothyroid patients are more likely than euthyroid patients to develop coronary artery disease, particularly in combination with dyslipidemia! However, the safety of percutaneous transluminal coronary angioplasty (PTCA) remains to be established especially in overtly hypothyroid patients^{2,3}. On the other hand, it has been recognized that patients with myxedema are prone to aortic dissection, aneurysm and rupture^{4–7}. We report a patient with a long history of overt hypothyroidism, mild hypercholesterolemia and hypertension who had aorto-coronary dissection complicating PTCA.

Case Report

A 67-year-old man was admitted for coronary angiography because of effort angina noticed 1 month earlier. He had been diagnosed as having hypothyroidism 4 years earlier, secondary to Graves' disease that had been treated for approximately 30 years. Although he had been taking a thyroid hormone supplement (levothyroxine sodium, 0.025 mg/day), prescribed at another hospital, his serum triiodothyronine (T3) and thyroxine (T4) levels were lower than the normal lower limit, and his thyroid-stimulating hormone (TSH) level had been high for the previous 4 years (Table 1). He was a heavy smoker and had a 7-year history of medically controlled hypertension. The patient was obese, with a body mass index of 28 kg/m², and had no psychiatric disorders or Marfan features. Physical signs and

symptoms of hypothyroidism, however, were apparent including bradycardia, ankle swelling, hoarseness and dry skin. Hypercholesterolemia was mild. Electrocardiography showed a negative T wave in I, aVL and all precordial leads, and echocardiographic findings were normal except for left ventricular concentric hypertrophy. He was admitted because of the positive findings on stress ²⁰¹Tl-chloride scintigraphy, which showed inferior wall ischemia without a scar. He also complained of angina even though he was taking medication.

Coronary angiography revealed 90% stenosis in the distal portion of the right coronary artery, and thus it was decided to perform PTCA (Fig 1). The right coronary artery was catheterized coaxially by a soft tipped 6Fr 4 right Judkins guiding catheter (SCIMED™, Minneapolis, MN, USA). It was easy to pass across the lesion with a 0.014-inch guidewire (Hi-torque Balance™, ACS, Santa Clara, CA, USA) and a 3.75-mm semi-compliant balloon catheter (Samba Rely™, Bard, Galway, Ireland). After the first inflation of a pressure of 4 atmospheres and a 1.1 balloon/artery ratio, the inflated site dissipated. While we were preparing for bail-out stenting, the patient complained of anterior chest pain. Contrast injection through the guiding catheter revealed dissection of the vessel wall with both antegrade and retrograde spiral extension and dye retention in the right coronary artery and the aortic root (Fig 1). The electrocardiographic changes were nonspecific. Subsequent arteriography showed the spiral contrast flow from the dilated site to the aortic sinus and distal coronary artery. The stenting (3.5-mm Wiktor stent™, Medtronic Inc, Minneapolis, MN, USA), which included sealing the entry port in the distal segment to the ostium, failed to stop progression of the dissection. Every time the contrast medium was injected, the dye retention increased in the false lumen of the Valsalva sinus and the ascending aorta. The procedure was terminated and conservative

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Table 1 Laboratory Data on Admission and the Time Course of Thyroid Hormone Concentration

	On admission					Normal range
	Sep/9/1997	Dec/11/1996	Apr/5/1995	Sep/21/1994	Sep/21/1993	
T3 ($\mu\text{g/dl}$)	2.5	2.8	2.5	2.8	0.3	4.1–12.9
T4 (ng/ml)	0.59	0.43	0.47	0.53	1.7	0.7–2.1
Free T3 (pg/ml)	0.33					1.45–3.4
Free T4 (ng/ml)	0.29					0.71–1.8
TSH ($\mu\text{U/ml}$)	24.94	53.3	124.2	45.0	64.5	0.5–4.6
Anti-thyroglobulin Ab (U/ml)	68.5					<0.3
Anti-peroxidase Ab (U/ml)	169					<0.3
TBII (%)	2.6					–15–+15
Total cholesterol (mg/dl)	229					150–219
Triglyceride (mg/dl)	104					50–149

T3, tri-iodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone; Ab, antibody; TBII, TSH binding inhibitory immunoglobulin.

Fig 1. Right coronary angiography (left anterior oblique view) on admission shows eccentric 90% stenosis in the distal right coronary artery (a). The first inflation of a nominal 4 atmospheres of 1:1 balloon/artery ratio (b). Subsequent contrast injection discloses extensive spiral dissection from the inflated site in both directions. Note the extension of the dissection into the sinus of Valsalva (black arrow) (c). Crescent-shaped dye retention is demonstrated in the Valsalva sinus and the ascending aortic wall (white arrow) after the stenting procedure (d).

Table 2 Case Reports of Aorto-coronary Dissection During Cardiac Catheterization

Case no.	Age, Sex (years)	Diagnosis	Lesion stenosis	Cause	Dissection origin
1	65, F	NCA?	(-)?	Diagnostic	RCA, P
2	48, M	EAP	LAD, M, 100%	Guidewire?	M(?)
3	61, M	EAP	RCA, M, 99%	PTCA guiding	P
4	55, F	AMI	RCA, P, 100%	PTCA guiding	P
5	70, M	EAP?	RCA, P, ≥90%	PTCA guiding	O
6	57, F	EAP?	RCA, P, ≥90%	PTCA guiding	O
7	48, M	NCA?	(-)?	Diagnostic	RCA, O
8	45, F	NCA	(-)	Diagnostic	RCA, P
9	72, F	UAP+OMI	LAD, P, 99%	PTCA guiding	LMCA
10	55, F	AMI	RCA, M, 100%	PTCA guiding?	O
11	48, M	EAP	RCA, P, 90%	PTCA ballooning?	RCA, P
12	62, M	NonQMI	RCA, P&M, ≥90%	PTCA guiding	P
13	70, M	UAP	RCA, M, 100%	Guide wire?	P
14	59, M	AMI	RCA, M, ≥90%	PTCA guiding	just P
15	32, M	UAP	RCA, M, 90%	PTCA guiding?	P
16	67, F	UAP	RCA, O, 100%	PTCA ballooning	O
17	52, M	UAP+OMI	RCA, M, 75%	PTCA guiding	P
18	56, F	NCA?	RCA, P, 50%	Diagnostic	RCA, O
19	64, M	EAP?	RCA, P&M, 75%	PTCA ballooning	P
20	68, M	EAP	LAD, D, 100%	Stent?	LMCA
21	55, M	UAP+OMI	RCA, M, 90%	Guidewire	P
22	67, M	EAP	RCA, D, 90%	PTCA ballooning	D

NCA, normal coronary artery; EAP/UAP, effort/unstable angina pectoris; OMI/AMI, old/acute myocardial infarction; LAD/RCA/LMCA, left ascending/right/left main coronary artery; D/M/O/P, distal/middle/ostial/proximal; El/Em, elective/emergent; CABG, coronary artery bypass grafting; Ao, aorta; AL/JR/IMA, Amplatz left/Judkins right/internal mammary artery catheter; SH, side holes; IABP, intraaortic balloon pumping; CMN, cystic medial necrosis; CTO, chronic total occlusion; AR, aortic regurgitation.

Fig 2. Magnetic resonance imaging 24 h (a) and 24 days (b) after the interventional procedure. The false lumen thrombosed in the ascending aorta on the next day (a), but was diminished before discharge (b).

therapy was selected because of the difficulties with the emergency operation, the patient's stable vital signs, the relief of the chest pain and preserved coronary flow.

The postoperative computed tomography showed dissection from the coronary sinus near the origin of the brachiocephalic artery and a moderate volume of pericardial effusion. The next day, magnetic resonance imaging showed a thrombosed false lumen (Fig 2), although a Q wave myocardial infarction had occurred. The peak creatine kinase level was 919 IU/L 14 h after the event, whereas it was 234 IU/L on admission (normal range, 33–178 IU/L). The patient's pericardial effusion gradually decreased and

the aortic false lumen diminished with no episodes of hypotension or aortic regurgitation (Fig 2). Autoimmune thyroid antibody tests were positive, including those against thyroglobulin and thyroperoxidase, but TSH-binding inhibitory immunoglobulin (TBII) was negative (Table 1). A thyroid echo examination showed remarkable atrophy. Rheumatoid factor, antinuclear antibody and antiphospholipid antibody were negative. The patient was discharged without symptoms, approximately 1 month after the PTCA, after his thyroid hormone level was normalized using levothyroxine 0.1 mg/day.

Treatment	Inhospital result	Comment	Reference no.
Medical	Survival	(-)	11
El CABG	Survival	Unable to cross the lesion	12
Em Ao replacement +CABG	Survival	7FAL3, unable to cross the lesion, severe AR (+)	12
Medical	Death	IABP (+)	13
Medical	Survival	8FAL2, AMI (+)	8
Medical	Survival	8FJR4SH, AMI (+)	8
Medical	Survival	6FJR4, nondominant RCA	8
Medical	Survival	(-)	14
Em Ao replacement +CABG	Survival	(-)	15
Em Ao replacement, CABG (-)	Survival	CMN in autopsy Ao sample	16
Em Stent +CABG	Survival	8FJR4, hemopericardium (+)	17
Em stent	Survival	(-)	9
Em CABG	Survival	Unable to cross the lesion	9
Em Ao replacement, CABG (-)	Survival	6FIMA	18
Em CABG	Death	RCA, P rupture in autopsy sample	18
Em stent	Survival	(-)	10
Medical	Survival	AMI (+)	10
Em Bentall's technique +CABG	Death	CMN in surgical Ao sample, severe AR (+)	10
Em stent	Survival	(-)	10
Em stent	Survival	CTO	19
Em stent	Survival	6FJR4	20
Em stent	Survival	Chronic hypothyroid disease, AMI (+)	Current case

Discussion

Aorto-coronary dissection is presumed to be an extreme type of the relatively common coronary dissection that can occur during PTCA. Recent studies indicate an incidence of 0.008–0.02% for diagnostic catheterization and 0.03–0.07% for interventional procedures^{8–10} In a review of the literature, we found 22 published cases of aorto-coronary dissection, including the present case, as a complication of coronary angiography or angioplasty (Table 2)^{8–20} The mean age of these 22 patients was 58±10 years. Nineteen right coronary arteries (86%) and 8 females (36%) were involved in this complication. Fourteen cases (64%) were reported to have begun as a simple trauma of catheter ostial engagement. Importantly, the dissections were considered to have been exacerbated in all patients by the subsequent contrast injections. The in-hospital mortality was 14% (3 cases).

The present case is unique in that the origin of the dissection was the distal portion of the coronary artery, and it occurred without the aggressive interventional procedures done in the other cases, such as the use of stiffened guidewires, high-pressure and/or repeated ballooning, and vigorous injection of the contrast medium.

The exact mechanism by which coronary dissection, a common complication especially during angioplasty, propagates into the Valsalva sinus is unclear. However, 2 major factors may be related to this complication.^{10,18,21} The first is mechanical trauma caused by the guide catheter, the guiding wire and the balloon inflation, aggravated by subsequent injections. The second is a localized weakened aortic wall due to chest injury, degenerative vascular disease or a collagen vascular disorder such as Marfan's syndrome. In fact, cystic medial necrosis (CMN) has been demonstrated pathologically in 2 patients with aorto-coronary dissection.^{10,16} Thus, in some cases, a medial aortic disorder may be associated with this rare, life-threatening complication.

Although the possibility of coincidental development of aorto-coronary dissection and myxedema cannot be ex-

cluded completely, we suggest that the chronic hypothyroid status and/or the disease itself may be a risk factor for this complication. Hypothyroidism has been reported as a factor associated with aortic dissection, aneurysm and rupture.^{4–7} Leonard et al described 4 hypothyroid patients in their autopsy study of 171 cases of aortic dissection.⁵ That prevalence of 2.3% (gender distribution not shown) was much higher than that in the normal population, especially the male population (male <0.1% and female 1.4%).¹ Kountz et al studied 3 hypothyroid individuals after thyroidectomy complicated by aortic rupture and found that all patients had CMN in varying degrees without significant atherosclerotic change in the walls of their aortae.⁴ Accordingly, the present patient might also have had an inherent disorder, whether it was CMN or not, in his aorta and even in his coronary artery due to myxedema although we did not take a pathological sample.

A marginally significant increased incidence of coronary dissection was reported during PTCA in 48 hypothyroid patients (hypothyroid 50% vs euthyroid 33%; $p=0.06$) in a study on the risks of PTCA in such patients.² However, another study of 13 hypothyroid patients found no significant difference.³ Both were retrospective studies and more than 90% of all the patients investigated were subclinical hypothyroid cases with normal thyroid hormone concentrations and elevated TSH. No prospective study has been reported on overt hypothyroid individuals showing decreased thyroid hormone, elevated TSH, clinical signs and symptoms of hypothyroidism. The safety of coronary angioplasty for clinical hypothyroid patients remains to be established.

Normally a patient with myxedema complicated by angina would be initially treated with medical therapy. If coronary revascularization is necessary, however, due to difficulties in controlling the symptoms, the procedure should be performed carefully. Less aggressive pre-dilatation or direct stenting without forceful injection of the contrast medium or a bypass procedure may be useful in the treatment of such patients.

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