Coronary Tortuosity

CASE REPORT

Coronary Tortuosity: A Clue to the Diagnosis of Fibromuscular Dysplasia?

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BACKGROUND
Fibromuscular dysplasia (FMD) is a systemic, nonatherosclerotic, noninflammatory vasculopathy that is often overlooked by clinicians. Clinical clues could help in selecting patients for further evaluation for the presence of FMD. Recently, it was observed that tortuosity of the coronary arteries is often present in patients with FMD-related abnormalities of the coronary artery. Therefore, we wondered if the presence of coronary tortuosity might provide a clinical clue to the diagnosis of extracoronary FMD.

CASES
We describe 5 cases of FMD in whom diagnostic studies for FMD were initiated because of the presence of coronary tortuosity. FMD was found in all 5 patients in the renal and/or cervical arteries.

CONCLUSIONS
Our 5 cases suggest that exertional chest pain in the presence of coronary tortuosity may be helpful in selecting patients for further evaluation for the presence of FMD. Further research should focus on the prevalence of FMD among patients with coronary tortuosity and whether the presence of additional clinical clues (such as the presence of hypertension at young age or pulsatile tinnitus) next to coronary tortuosity can predict the risk for FMD in individual patients.

Keywords: blood pressure; carotid artery; coronary tortuosity; fibromuscular dysplasia; hypertension; renal circulation.

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Fibromuscular dysplasia (FMD) is a systemic, nonatherosclerotic, noninflammatory vasculopathy that leads to stenosis, aneurysm, kinking, or dissection of several medium-sized arteries.[1,2] It is still considered a rare disease that is only occasionally diagnosed in cardiovascular outpatient clinics. However, several studies demonstrate that FMD is not so rare: prevalences up to 4.4% have been reported in healthy subjects (potential kidney donors),[3–6] with even higher numbers among patients with hypertension.[6,7] This suggests that many patients who have FMD remain unrecognized and cannot be offered treatment for a potentially curable cause of hypertension.[8] In addition, they will continue to suffer from unexplained complaints such as headache and pulsatile tinnitus.[9] Therefore, improvement of diagnostic strategies is needed.

Over the last years it has become clear that coronary abnormalities may also be related to FMD,[10] most often presenting as a spontaneous coronary artery dissection (SCAD). Interestingly, the coronary arteries from patients with FMD-related coronary artery disease (e.g., stenosis, dissection, dilatation etc.) are almost always very tortuous.[11] This suggests that coronary tortuosity (defined as the presence of ≥3 consecutive curvatures with a ≥45° change in vessel direction measured at end-diastole)[12] is linked to FMD as well. Therefore, we wondered if the presence of coronary tortuosity might provide a clinical clue to the diagnosis of extracoronary FMD and if this could help to improve our strategy to find more undiagnosed FMD patients. In this paper, we present 5 recent cases from our outpatient clinic in whom the presence of coronary tortuosity eventually led to the diagnosis of FMD.

"Patient 1" is a 64-year-old woman, who was diagnosed with hypertension at the age of 29. Previously, she underwent several diagnostic studies (including duplex ultrasound of the renal arteries) in 2 other hospitals to rule out secondary causes of hypertension, all without abnormalities. Her blood pressure was well regulated with 2 antihypertensive drugs. However, she was referred to our Emergency Department several times because of a blood pressure up to 230 mm Hg accompanied by severe headache. At those moments, but also when lying on a thick pillow, she noticed a pulsatile tinnitus in her left ear. Furthermore, she had frequent episodes of exertional chest pain for which she underwent a coronary angiography 2 years earlier. The coronary angiography showed no stenosis, but did demonstrate tortuosity of the coronary arteries (Figure 1a). Therefore, we suspected FMD. A digital subtraction angiography indeed revealed multifocal FMD of the right renal artery (Figure 1b) and "kinking" of the left carotid artery (presumably causing the pulsatile tinnitus, Figure 1c). Balloon angioplasty of the renal artery was performed. Five months later, her blood pressure was stable at 131/84 mm Hg [20 minutes unattended automated

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office blood pressure measurement (AOBPM)], without the use of antihypertensive drugs.

"Patient 2" is a 76-year-old woman who was referred by her general practitioner because of high blood pressure (155/80 mm Hg, AOBPM) despite the use of 5 antihypertensive drugs. She was diagnosed with hypertension at the age of 17. Her medical history also included type 2 diabetes mellitus, surgery for melanoma at the age of 46, and preeclampsia during her first pregnancy. In the past, she underwent a coronary angiography because of exertional chest pain, showing coronary tortuosity but no significant stenosis. One year ago, she was diagnosed with non-ST-elevated myocardial infarction (high-sensitivity troponine T level up to 154 ng/l) in another hospital, but coronary angiography again revealed no other abnormalities than coronary tortuosity (Figure 2a). Based on this observation and her medical history, FMD was suspected. Therefore, we performed renal angiography, which indeed confirmed our suspicion of FMD (Figure 2b). Balloon angioplasty was performed and after 3 months blood pressure had decreased to 111/55 mm Hg (AOBPM) with "only" 3 antihypertensive drugs.

"Patient 3" is a 62-year-old female who was known with high blood pressure (up to 190 mm Hg systolic) since her 20s. One year ago, a coronary angiography was performed because of exertional chest pain. This showed coronary tortuosity, but no significant stenosis (Figure 3a). Given these findings as well as the presence of a pulsatile tinnitus in both ears, FMD was suspected. Computed tomography-angiography revealed kinking of her right carotid artery and coiling of her left carotid artery (Figure 3b) and suggested a string-of-beads of the right renal artery (Figure 3c). As her blood pressure was well controlled (124/71 mm Hg on AOBPM, using bisoprolol 10 mg and isosorbidemononitrate 25 mg once daily) both abnormalities were managed conservatively.

"Patient 4" is a 51-year-old female who was referred from another hospital because of high blood (182/104 mm Hg, AOBPM) despite the use of 6 antihypertensive drugs. Three months before referral, she had a lacunar transient ischemic attack. She was diagnosed with hypertension when she was 22 years old and was recurrently admitted to the hospital because of hypertensive emergencies with systolic blood pressure above 230 mm Hg. A coronary angiography was performed 3 years ago because of exertional chest pain. Although this showed no significant stenosis, coronary tortuosity was observed (Figure 4a). Although renal angiography 10 years earlier in the referring hospital was reported as normal, we still suspected FMD. Therefore, we again performed renal angiography. This indeed showed a typical string-of-beads in the right renal artery (Figure 4b),

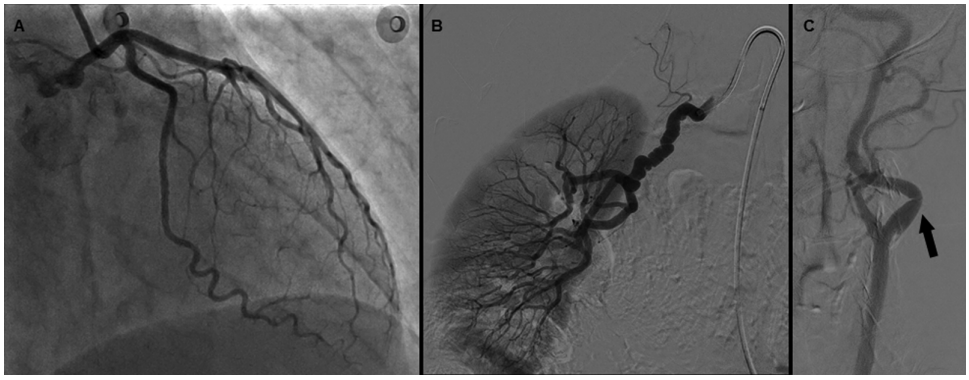

Figure 1. Patient 1: Coronary angiography showing coronary tortuosity in distal part of the circumflex branch of the left coronary artery (**a**), and selective digital subtraction angiographies showing multifocal FMD of the right renal artery (with a typical "string-of-beads" appearance, **b**), and kinking of the left the left internal carotid artery (**c**, arrow). Abbreviation: FMD, Fibromuscular dysplasia.

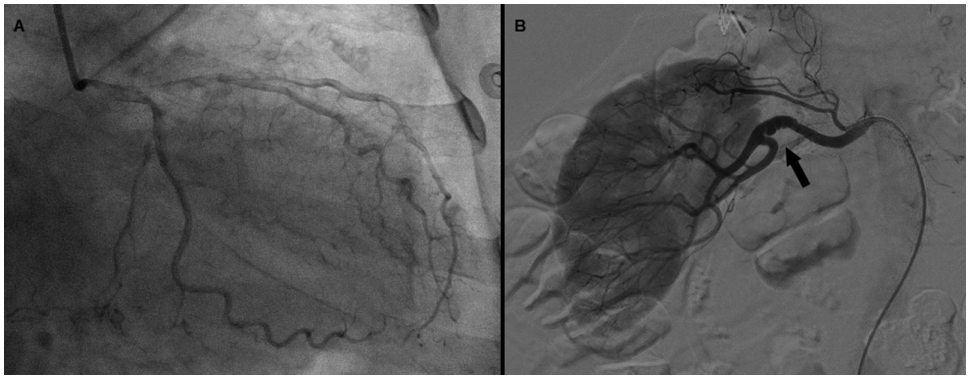

Figure 2. Patient 2: Coronary angiography showing coronary tortuosity in the left anterior descending artery and the circumflex branch of the left coronary artery (**a**) and selective digital subtraction angiography showing multifocal FMD of the right renal artery (**b**, arrow). Abbreviation: FMD, Fibromuscular dysplasia.

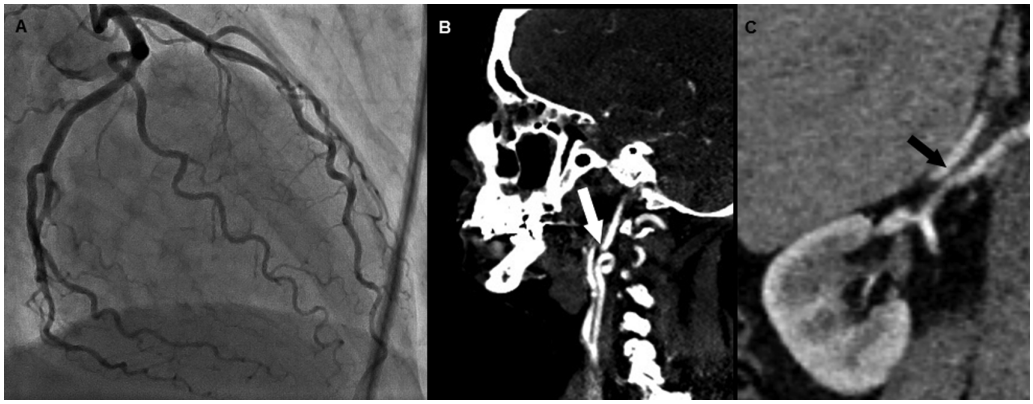

Figure 3. Patient 3: Coronary angiography of the left coronary artery showing coronary tortuosity (**a**). Computed tomography (CT) scan showing coiling of the left carotid artery (**b**, arrow; sagittal imaging plane) and a string-of-beads of the right renal artery (**c**, arrow; coronal imaging plane).

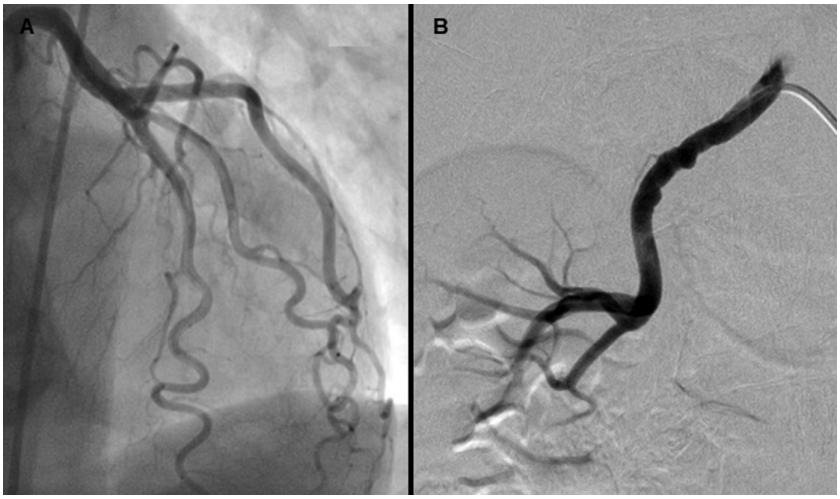

Figure 4. Patient 4: Coronary angiography showing coronary tortuosity in the left anterior descending artery and the circumflex branch of the left coronary artery (**a**) and selective digital subtraction angiography showing multifocal FMD of the right renal artery (**b**). Abbreviation: FMD, Fibromuscular dysplasia.

for which she underwent balloon angioplasty. Two months after the procedure her blood pressure had decreased to 152/88 mm Hg (AOBPM), using 5 antihypertensive drugs.

"Patient 5" is a 48-year-old man who was known with recurrent chest pain for 16 years. Initially, coronary artery disease was suspected, but a coronary angiography was reported to be normal. Later on, the chest pain was attributed to gastro-oesophageal reflux disease, but neither proton-pump inhibitor therapy, nor gastric fundoplication had any effect on his chest pain. Two years ago, he was diagnosed with hypertension, for which he was recently referred to our outpatient clinic. Although his blood pressure was well controlled on 24-hour ambulatory blood pressure measurements (111/80 mm Hg using losartan 50 mg twice daily), he reported episodes of hypertension up to 160/110 mm Hg on home blood pressure measurements. These episodes were accompanied by headache and pulsatile tinnitus in the left ear. As re-evaluation of the coronary angiogram revealed coronary tortuosity (Figure 5a), we suspected FMD. Renal angiography was normal (not shown), but angiography of the carotid arteries showed focal FMD of the left internal carotid artery (Figure 5b) as well as tortuosity of the right internal carotid artery (also known as an "S-curve",[13] Figure 5c). Both abnormalities were managed conservatively.

DISCUSSION

We describe 5 cases of FMD in whom the diagnostic studies for FMD were initiated because of exertional chest pain in the presence of coronary tortuosity. Although for a long-time FMD was considered a disease of only the renal and cervicocephalic arteries, lesions have been described in several other arteries.[1,14] More recently, it was shown that FMD is associated with SCADs: among patients with SCAD, 50–86% of the patients turned out to have FMD in another, extracoronary artery.[12,15–17] Another abnormality associated with SCAD is coronary tortuosity, which is found in 78% of the patients with SCAD and is more severe in patients who also have extracoronary FMD.[12] Interestingly, it is more often observed in females and patients with hypertension,[18] both typical features of FMD. A recent case-series of patients with both coronary and extracoronary FMD reported that

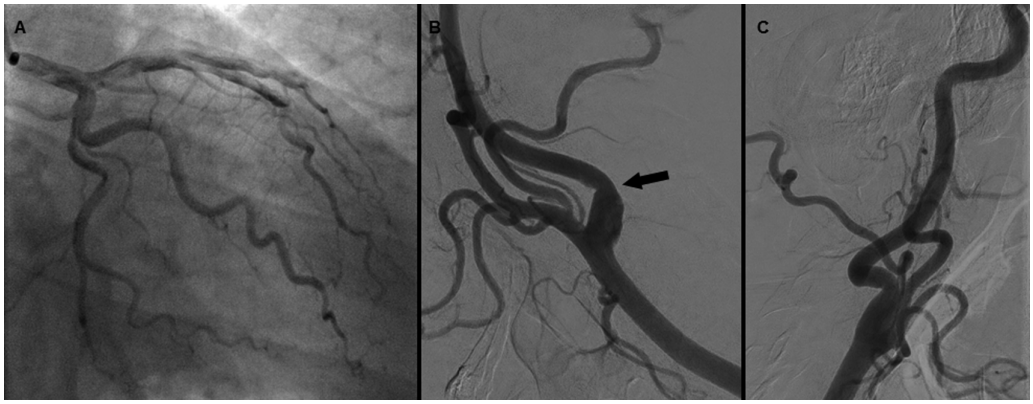

Figure 5. Patient 5: Coronary angiography showing coronary tortuosity in the left anterior descending artery and the circumflex branches of the left coronary artery (**a**) and selective digital subtraction angiographies showing focal FMD of the left internal carotid artery (**b**; arrow), and an "S"-curve (tortuosity) of the right internal carotid artery (**c**). Abbreviation: FMD, Fibromuscular dysplasia.

all 32 patients had coronary tortuosity to some extent.[11] This suggests that coronary tortuosity is linked to FMD as well. Although further data on the association between FMD and coronary tortuosity are lacking thus far, we hypothesize that coronary tortuosity is an early manifestations of coronary FMD, with SCAD or FMD-related coronary artery stenosis at a later stage.

Our 5 cases suggest that the presence of coronary tortuosity may be helpful (next to other clues such as young-onset hypertension and pulsatile tinnitus) in selecting patients for further evaluation for the presence of FMD. As previously mentioned, FMD is presumably often overlooked by clinicians, as there is a large difference between the relatively high prevalence that is observed in screening studies[3–7] and the very low number of patients diagnosed with FMD in "real-life" outpatient clinics. In our cases, the diagnostic studies to FMD presumably would not have been performed without the clue of coronary tortuosity, leaving these patients undiagnosed. The importance of making the diagnosis of FMD was obvious in patients 1, 2, and 4: Balloon angioplasty led to a decrease in blood pressure and/or a reduction in the number of antihypertensive drugs required. Moreover, and perhaps even more importantly, the patients were grateful for knowing the cause of their otherwise unexplained symptoms, decades after their onset: pulsatile tinnitus could be explained by the abnormalities in the carotid artery and in all 5 cases it is likely that the chest pain is linked to coronary tortuosity due to reductions in blood flow and pressure.[19,20] Thus far, no data exist on the diagnostic value of coronary tortuosity in diagnosing FMD. Admittedly, a small series as ours cannot provide the final demonstration of the association of coronary tortuosity with extracoronary FMD. Nevertheless, in all 5 patients that we evaluated because of coronary tortuosity we indeed found FMD, suggesting that coronary tortuosity may be a valuable clue. Further research should focus on the prevalence of FMD among patients with coronary tortuosity and *vice versa* and whether the presence of additional clinical clues (such as the presence of hypertension at young age or pulsatile tinnitus) next to coronary tortuosity can predict the risk for FMD in individual patients.

DISCLOSURE

The authors declared no conflict of interest.

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