

CLINICAL VIGNETTE

Resistant Hypertension and Spontaneous Carotid Dissection in a Young Woman: Hypertension Rounds

Joseph T. Chang, MD¹ and Pritha P. Gupta, MD, PhD²

¹Department of Internal Medicine, Riverside Community Hospital/UC Riverside School of Medicine

²Department of Cardiology, David Geffen School of Medicine at UCLA

Introduction

We present a case of resistant hypertension leading to the diagnosis of spontaneous coronary artery dissection. Patients with resistant hypertension are at increased risk of end organ damage, especially cardiovascular events. This case demonstrates the workup, causes, and consequences of resistant hypertension.

Case Presentation

A 37-year-old Caucasian woman with a history of pre-eclampsia, hypothyroidism, and basal cell carcinoma status post resection presented for pre-operative examination prior to dermatology surgery and was found to be hypertensive to 190/120 mmHg. Although she was asymptomatic on initial examination, she presented to the emergency department two days later with headache, photophobia, tinnitus, nausea, and vomiting. Her blood pressure was 190/120 and computed tomography scan of the head and lumbar puncture did not reveal any abnormality. Blood pressure was treated with IV labetalol and she was discharged to follow up with her primary care physician. She remained hypertensive on 3-day regimen of labetalol, telmisartan and hydrochlorothiazide and was referred to cardiology for hypertension.

Given her young age and sudden onset hypertensive urgency, fibromuscular dysplasia (FMD) was high on the differential. Extensive endocrine workup, including urine and plasma metanephrines, was negative. Magnetic resonance angiography (MRA) of the renal arteries did not reveal renal artery stenosis or evidence of a pheochromocytoma. Ongoing headaches prompted intracranial and cervical artery imaging. MRI/MRA of the neck revealed a right-sided internal carotid dissection without evidence of flow-limiting stenosis, and MRI/MRA of the brain showed no infarct.

Blood pressure is now controlled with labetalol, hydrochlorothiazide, and hydralazine. She continues to have left-sided occipital headaches and tinnitus. The symptoms have been persistent even when she is normotensive. For possible FMD, she was started on aspirin.

Discussion

With the current more stringent ACC/AHA criteria for stage 1 hypertension, the estimated prevalence of hypertension increased from 32% overall to 46% in the United States. Similarly, the prevalence of resistant hypertension would be expected to increase from 13% to 17%.¹

Resistant hypertension is defined as hypertension that remains above goal despite the use of 3 anti-hypertensive medications, including a diuretic. Recognizing and treating it appropriately is important, as these patients are at higher risk of adverse outcomes, such as heart failure, end stage renal disease, stroke, and all-cause mortality.² Moreover, patients with resistant hypertension are more likely to have secondary hypertension. One study of renal denervation found 50.4% of prospective subjects with resistant hypertension had some form of secondary hypertension.³ Therefore, secondary hypertension should always be considered in patients with resistant hypertension. Table 1 reviews the common causes of secondary hypertension.

Specific evaluation should be driven by clinical presentation, including symptoms, demographics, and prevalence. In our case, fibromuscular dysplasia was strongly suspected in the setting of a young woman with resistant hypertension and migraine headaches. Fibromuscular dysplasia is a rare, non-atherosclerotic, and non-inflammatory vascular disease characterized by abnormal cellular proliferation in small or medium sized arteries. It presents mostly in females (94.7%) at an average age of 47.⁴ Presentation depends on the vascular territory involved. It can cause hypertension in the renovascular arteries, headache or tinnitus in the cerebrovascular arteries, and dissection or aneurysm in any artery.^{4,5} The persistence of our patient's headache after the control of blood pressure suggests that it was a result of the dissection rather than hypertension.

In the absence of vasculitis or other connective tissue disease, the carotid artery dissection could have been secondary to FMD or hypertension. FMD is the most common vascular disorder associated with spontaneous cervical artery dissection (sCAD), present in 15% - 39.5% of cases.^{6,7} Control studies have also shown that hypertension is also a significant risk factor for dissection.⁸ Per AHA guidelines, the diagnosis of FMD requires

CT angiography or MR angiography to visualize focal or multifocal areas of stenosis. The presence of dissection alone is not sufficient to establish a diagnosis. Therefore, our patient's ICA dissection would not meet criteria to be classified as FMD. Nevertheless, this case highlights the importance of CTA or MRA of the brain in patients with severe headache and hypertension or suspected FMD, as either can present with vascular abnormalities. In addition, if FMD is confirmed, then

CT angiogram of the chest, abdomen, and pelvis would also be indicated.

sCAD recurs at a rate of about 11.9% within 10 years.⁹ Case series have shown that the majority of recurrent sCAD, about 80%, occur in patients with FMD. While there are no trials comparing medical therapies, antiplatelet therapy is recommended by medical experts. In addition, it is important to optimize other risk factors for sCAD, such as hypertension.

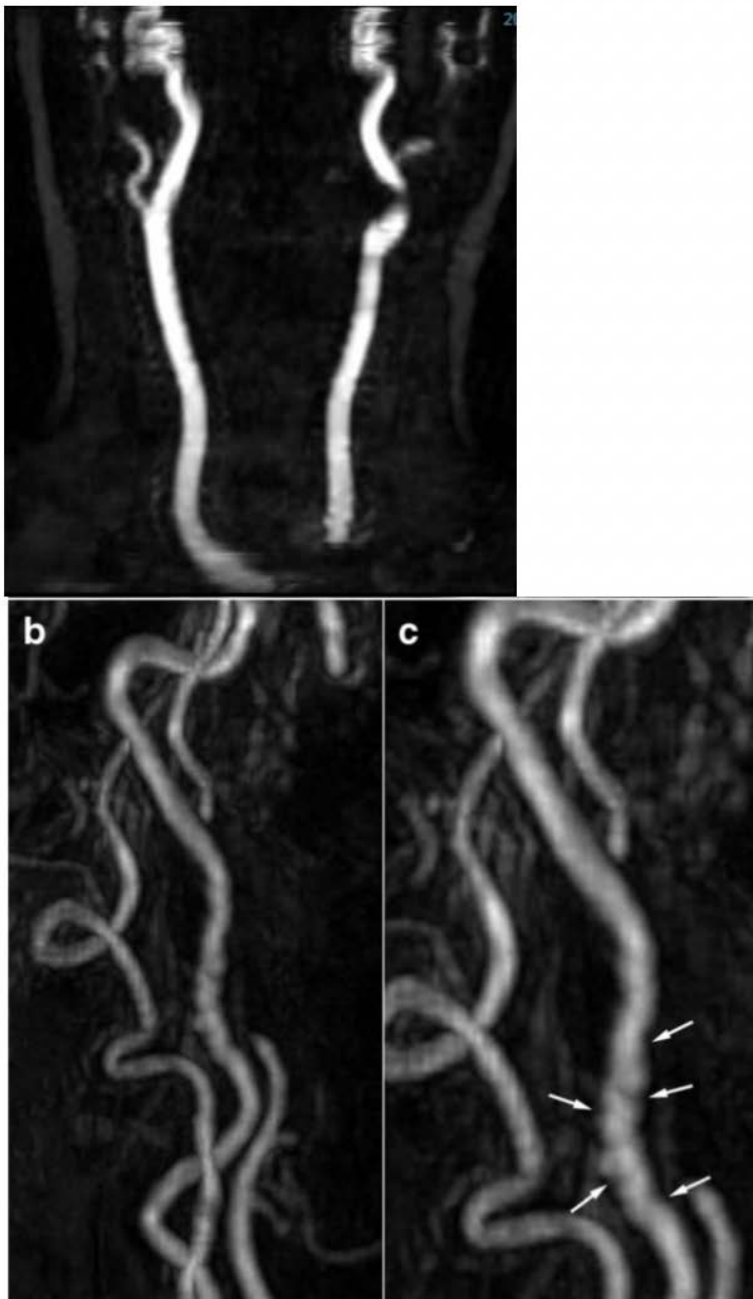


Figure 1: **A.** Radiologic findings in our patient showed right sided cervical carotid dissection. **B.** and **C.** Radiologic findings in a 68-year-old female patient who suffered from an inferior myocardial infarct secondary to spontaneous dissection of the right coronary artery. Three-dimensional gadolinium-enhanced MRA reconstructions in the same patient showing the typical string-of-beads aspect (*white arrows*) of the internal carotid artery, highly suggestive of FMD. Panel b and c comes from Figure 5 of Varennes et al.¹¹

Secondary cause	Prevalence (a)	Prevalence (b)	History	Screening	Clinical Findings	Laboratory Findings
Obstructive Sleep Apnea	>5-15%	>30%	Snoring, daytime sleepiness, morning headaches, irritability	Screening Questionnaire, polysomnography	↑neck circumference; obesity; peripheral edema	Not specific
Renal Parenchymal Disease	1.6-8.0%	2-10%	Loss of good BP-control; diabetes; smoking; generalized atherosclerosis; previous renal failure; nocturia	Creatinine, ultrasound of the kidney	peripheral edema; pallor; loss of muscle mass	↑Creatinine; proteinuria; ↓Ca ²⁺ , ↑K ⁺ , ↑PO ₄
Renal Artery Stenosis	1.0-8.0%	2.5-20%	Generalized atherosclerosis; diabetes; smoking; generalized atherosclerosis; previous renal failure; nocturia	Duplex, or CT, or MRI, or angiography (drive-by)	Abdominal Bruits; peripheral vascular disease	Secondary aldosteronism; ARR ↑; ↓K ⁺ ; ↓Na ⁺
Primary Aldosteronism	1.4-10%	6-23%	Fatigue; constipation; polyuria; polydipsia	Aldosterone-renin ratio (ARR)	Muscle weakness	↓K ⁺ ; ARR↑
Thyroid Disease	1-2%	1-3%	Hyperthyroidism: palpitations, weight loss, anxiety, heat intolerance; Hypothyroidism: weight gain, fatigue, obstipation	TSH	Hyperthyroidism: tachycardia, a fib, accentuated heart sounds; exophthalmos; Hypothyroidism: bradycardia, muscle weakness, myxedema	Hyperthyroidism: TSH↓; fT ₄ and/or fT ₃ ↑; Hypothyroidism: TSH↑; fT ₄ ↓; cholesterol ↑
Cushing's Syndrome	0.5%	<1.0%	Weight gain; impotence; fatigue; psychological changes; polydipsia and polyuria	24h urinary cortisol; dexamethasone testing	Obesity, hirsutism, skin atrophy, striae rubrae, muscle weakness, osteopenia	24h urinary cortisol ↑; Glucose ↑; Cholesterol ↑; K ↓
Pheochromocytoma	0.2-0.5%	<1%	Headache; palpitations; flushing; anxiety	Plasma-metanephrines; 24h urinary catecholamine	The 5 'P's': paroxysmal hypertension; pounding headache; perspiration; palpitations; pallor	metanephrines ↑
Coarctation of the aorta	<1%	<1%	Headache; nose bleeding; leg weakness or claudication.*	Cardiac ultrasound	Different BP (≥20/10 mmHg) between upper-lower extremities and/or between right-left arm; ↓and delayed femoral pulsations; interscapular ejection murmur; rib notching on chest Rx	Not specific

Table 1. Reprinted with permission* from Rimoldi et al¹⁰.

BP, blood pressure; Ca²⁺, calcium; K⁺, potassium; PO₄, phosphate; CT, computer tomography; ARR, aldosterone–renin ratio; Na⁺, sodium; AF, atrial fibrillation; TSH, thyroid-stimulating hormone; fT₄, free thyroxine; fT₃, free triiodothyronine.

^aPrevalence in hypertensive patients.

^bPrevalence in patients with resistant hypertension.

*Kaplan's, Clinical hypertension, Tenth Edition, 2010, Lippincott Williams & Wilkins, p. 363.

Conflicts of Interest: The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

REFERENCES

1. **Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr.** 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018 Jun;71(6):e13-e115. doi: 10.1161/HYP.000000000000065. Epub 2017 Nov 13. Erratum in: *Hypertension*. 2018 Jun;71(6):e140-e144. PMID: 29133356.
2. **Muntner P, Davis BR, Cushman WC, Bangalore S, Calhoun DA, Pressel SL, Black HR, Kostis JB, Probstfield JL, Whelton PK, Rahman M; ALLHAT Collaborative Research Group.** Treatment-resistant hypertension and the incidence of cardiovascular disease and end-stage renal disease: results from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Hypertension*. 2014 Nov;64(5):1012-21. doi: 10.1161/HYPERTENSIONAHA.114.03850. Epub 2014 Aug 4. PMID: 25259745.
3. **Azizi M, Pereira H, Hamdidouche I, Gosse P, Monge M, Bobrie G, Delsart P, Mounier-Véhier C, Courand PY, Lantelme P, Denolle T, Dourmap-Collas C, Girerd X, Michel Halimi J, Zannad F, Ormezzano O, Vaisse B, Herpin D, Ribstein J, Chamontin B, Mourad JJ, Ferrari E, Plouin PF, Jullien V, Sapoval M, Chatellier G; DENERHTN Investigators.** Adherence to Antihypertensive Treatment and the Blood Pressure-Lowering Effects of Renal Denervation in the Renal Denervation for Hypertension (DENERHTN) Trial. *Circulation*. 2016 Sep 20;134(12):847-57. doi: 10.1161/CIRCULATIONAHA.116.022922. Epub 2016 Aug 30. PMID: 27576780.
4. **Gornik HL, Persu A, Adlam D, Aparicio LS, Azizi M, Boulanger M, Bruno RM, de Leeuw P, Fendrikova-Mahlay N, Froehlich J, Ganesh SK, Gray BH, Jamison C, Januszewicz A, Jeunemaitre X, Kadian-Dodov D, Kim ES, Kovacic JC, Mace P, Morganti A, Sharma A, Southerland AM, Touzé E, van der Niepen P, Wang J, Weinberg I, Wilson S, Olin JW, Plouin PF.** First International Consensus on the diagnosis and management of fibromuscular dysplasia. *Vasc Med*. 2019 Apr;24(2):164-189. doi: 10.1177/1358863X18821816. Epub 2019 Jan 16. Erratum in: *Vasc Med*. 2019 Oct;24(5):475. PMID: 30648921.
5. **Olin JW, Froehlich J, Gu X, Bacharach JM, Eagle K, Gray BH, Jaff MR, Kim ES, Mace P, Matsumoto AH, McBane RD, Kline-Rogers E, White CJ, Gornik HL.** The United States Registry for Fibromuscular Dysplasia: results in the first 447 patients. *Circulation*. 2012 Jun 26;125(25):3182-90. doi: 10.1161/CIRCULATIONAHA.112.091223. Epub 2012 May 21. PMID: 22615343.
6. **Schievink WI.** Spontaneous dissection of the carotid and vertebral arteries. *N Engl J Med*. 2001 Mar 22;344(12):898-906. doi: 10.1056/NEJM200103223441206. PMID: 11259724.
7. **Talarowska P, Dobrowolski P, Klisiewicz A, Kostera-Pruszczyk A, Czlonkowska A, Kurkowska-Jastrzębska I, Gąsecki D, Warchol-Celińska E, Światłowski Ł, Florczak E, Januszewicz M, Michalowska I, Józwick-Plebanek K, Szczudlik P, Błażejewska-Hyżorek B, Protasiewicz M, Odrowąż-Pięniążek P, Tekieli Ł, Michel-Rowicka K, Hanus K, Widecka K, Sołtysiak M, Tykarski A, Stryczyński Ł, Szczerbo-Trojanowska M, Hoffman P, Prejbisz A, Januszewicz A.** High incidence and clinical characteristics of fibromuscular dysplasia in patients with spontaneous cervical artery dissection: The ARCADIA-POL study. *Vasc Med*. 2019 Apr;24(2):112-119. doi: 10.1177/1358863X18811596. Epub 2019 Feb 10. PMID: 30739593.
8. **Debette S, Metso TM, Pezzini A, Engelter ST, Leys D, Lyrer P, Metso AJ, Brandt T, Kloss M, Lichy C, Hausser I, Touzé E, Markus HS, Abboud S, Caso V, Bersano A, Grau A, Altintas A, Amouyel P, Tatlisumak T, Dallongeville J, Grond-Ginsbach C; CADISP-group.** CADISP-genetics: an International project searching for genetic risk factors of cervical artery dissections. *Int J Stroke*. 2009 Jun;4(3):224-30. doi: 10.1111/j.1747-4949.2009.00281.x. PMID: 19659826.
9. **Olin JW, Gornik HL, Bacharach JM, Biller J, Fine LJ, Gray BH, Gray WA, Gupta R, Hamburg NM, Katzen BT, Lookstein RA, Lumsden AB, Newburger JW, Rundek T, Sperati CJ, Stanley JC; American Heart Association Council on Peripheral Vascular Disease; American Heart Association Council on Clinical Cardiology; American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; American Heart Association Council on Cardiovascular Disease in the Young; American Heart Association Council on Cardiovascular Radiology and Intervention; American Heart Association Council on Epidemiology and Prevention; American Heart Association Council on Functional Genomics and Translational Biology; American Heart Association Council for High Blood Pressure Research; American Heart Association Council on the Kidney in Cardiovascular Disease; American Heart Association Stroke Council.** Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association.

Circulation. 2014 Mar 4;129(9):1048-78. doi: 10.1161/01.cir.0000442577.96802.8c. Epub 2014 Feb 18. PMID: 24548843.

10. **Rimoldi SF, Scherrer U, Messerli FH.** Secondary arterial hypertension: When, who, and how to screen? *Eur Heart J*. 2014;35:1245-54.
11. **Varenes L, Tahon F, Kastler A, Grand S, Thony F, Baguet JP, Detante O, Touzé E, Krainik A.** Fibromuscular dysplasia: what the radiologist should know: a pictorial review. *Insights Imaging*. 2015; 6:295-307.