

Familial Aortic Coarctation: A Rare Cause of Refractory Hypertension in the Elderly

A Case Report

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Abstract: We report the first case of late presentation of familial aortic coarctation, a rare cause of hypertension. Diagnosis of familial aortic coarctation in the elderly is exceptional, given that in the absence of endovascular or surgical repair patients do not usually survive beyond 50 years of age. Our case concerns a 72-year-old woman with hypertension of long evolution, control of which improved markedly after endovascular repair of the coarctation. Her son had undergone surgery for repair of aortic coarctation at the age of 23 years.

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Abbreviations: CTA = computed tomography angiography, HYVET study = hypertension in the Very Elderly Trial, MRA = magnetic resonance angiography, OR = odds ratio.

INTRODUCTION

Aortic coarctation is a rare cause of hypertension, accounting for 0.1% of cases of secondary hypertension.¹ The disease is usually diagnosed and treated in childhood; presentation in adults is rare and usually as refractory hypertension.^{1,2} Diagnosis in the elderly is exceptional, with only 21 cases reported so far.^{1–21} The long-term survival of patients without endovascular or surgical repair of aortic coarctation is rare, and most do not exceed 50 years of age.^{1,2,4,6,8,10,14,19,22–25} However, the indication for

surgery in elderly patients with coarctation of the aorta has been questioned, and there is no agreement about its benefit. In addition, some cases of coarctation of the aorta have been reported to follow a pattern of familial clustering.^{26–28}

We report the case of a 72-year-old woman diagnosed with aortic coarctation after being referred from primary care for the study of refractory hypertension. Of note, the patient's son had undergone repair for aortic coarctation at the age of 23 years. To our knowledge, this is the first case of late presentation of familial aortic coarctation described in the literature.

CASE REPORT

The patient was a 72-year-old woman with a history of hypercholesterolemia, treated with atorvastatin 10 mg per day, and toxic multinodular goiters, treated with Iodine¹³¹ 2 years earlier. She had hypertension detected at 26 years of age, which had been well controlled with hydrochlorothiazide 25 mg per day, atenolol 50 mg per day, and enalapril 20 mg per day until 1 year earlier, when her blood pressure became persistently higher than 160/95 mm Hg, despite the successive addition of amlodipine 5 mg per day, spironolactone 25 mg per day, and doxazosin 4 mg per day. The patient was on a low-sodium diet and reported no consumption of nonsteroidal anti-inflammatory drugs. She had no dyspnea, chest pain, or claudication or lower limb weakness. Her son had undergone repair of aortic coarctation at 23 years of age.

Physical examination showed a blood pressure of 165/98 mm Hg, with no differences between arms. Her body mass index was 28.5 kg/m². Funduscopy showed grade 1 hypertensive retinopathy. Cardiac auscultation revealed a 2/6 aortic systolic ejection murmur. Her femoral pulses were weak and delayed compared to the radial pulses. The lower limb blood pressure was 145/88 mm Hg. There was no clinical evidence of heart failure.

Analytical tests showed blood glucose 98 mg/dL, creatinine 0.8 mg/dL, creatinine clearance 72 mL/min, LDL cholesterol 95 mg/dL, HDL cholesterol 54 mg/dL, negative microalbuminuria, and a normal thyroid profile. Holter blood pressure monitoring showed a mean blood pressure of 158/92 mm Hg, with a nondipper pattern. Chest radiography showed rib punch, slight cardiomegaly, and a posterior mediastinal calcification suggestive of a thoracic aneurysm. The electrocardiogram showed bifascicular block (right bundle branch block with left anterior hemiblock). The transthoracic echocardiogram showed signs of left ventricular concentric hypertrophy predominantly septal (interventricular septum 13 mm), altered diastolic function with a normal ejection fraction, and a trans-coarctation peak systolic gradient of 24 mm Hg.

Thoracoabdominal computed tomography angiography (CTA) confirmed the initial clinical suspicion of aortic

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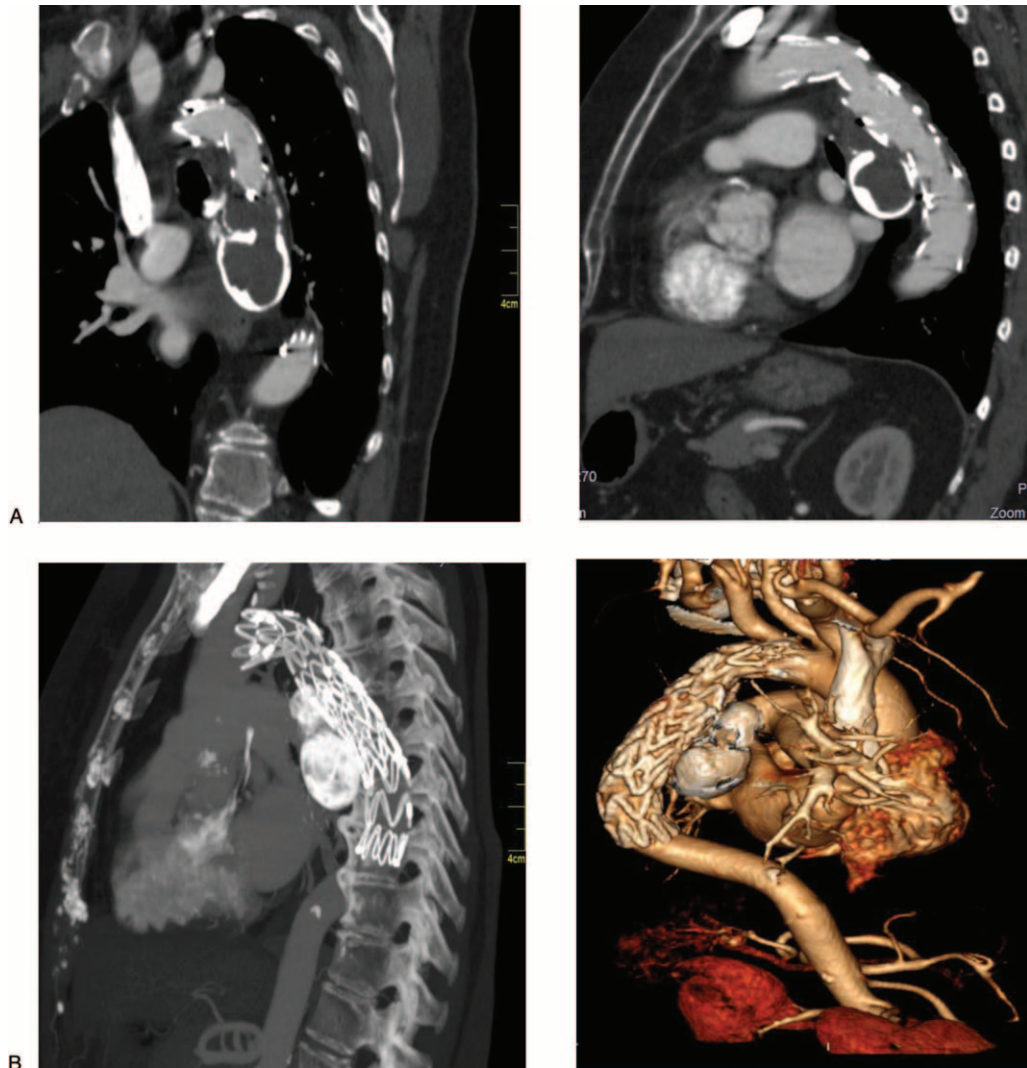


FIGURE 1. Thoracic-abdominal computed tomography angiography (CTA) before (A) and after surgery (B).

coarctation (Figure 1A), distal to the origin of the left subclavian artery, with a partially thrombosed post-stenotic saccular aneurysm of the descending thoracic aorta, measuring 40×36 mm. Magnetic resonance angiography (MRA) of the circle of Willis ruled out the presence of aneurysms and abdominal ultrasound showed no pathological findings.

After matching clinical recommendations about the convenience of an interventional repair with the patient's preferences, balloon angioplasty with placement of a covered stent was undertaken (Figure 1B). The peak-to-peak coarctation gradient fell from 26 to 8 mm Hg after repair.

Following the intervention, the patient's antihypertensive medication could be reduced and her blood pressure has been well controlled (mean: 135/80 mm Hg) with olmesartan 40 mg per day, hydrochlorothiazide 12.5 mg per day, and atenolol 25 mg per day. Three years after the repair the patient remains asymptomatic and with good blood pressure control.

This case report was approved by the Ethics and Research Committees of the Carlos Haya Hospital, and informed consent was obtained from the patient.

DISCUSSION

Aortic coarctation is a rare cause of refractory hypertension in adults, whose long-term survival is very unusual. In the absence of repair, the mean life expectancy of affected patients after diagnosis of this condition is 35 years, with 75% to 90% dying before the age of 50 years.^{1,2,4,6,8,10,11,14,23} This high mortality is due to cardiovascular complications such as heart failure, aortic dissection, or rupture of cerebral aneurysms. The prolonged survival and low clinical expression of some cases occurring in elderly persons could be explained by the development of highly effective compensatory mechanisms, such as the formation of collateral vessels that maintain flow to distal territories and prevent stenosis.^{2,8} The coarctation gradient in our patient was not very high, which could potentially explain the chronic behavior of the aortic coarctation in this case. This case is clearly the consequence of a misdiagnosis when the patient was in her 20s and illustrates the presence of clinical shortcomings with the current guidelines. This therefore emphasizes the need for a careful evaluation of young hypertensive patients in order to exclude secondary causes of hypertension.

Coarctation of the aorta usually occurs sporadically. However, reports exist of a tendency to familial aggregation²⁹ with a multifactorial Mendelian inheritance pattern.^{10,30,31} A few case series have shown involvement in two or more generations, suggesting an autosomal dominant pattern of inheritance with incomplete penetrance and a variable expressivity.^{30,32–34} Although several recent publications have commented on the genetics of aortic coarctation, most concern cases of coarctation combined with other congenital heart or lung disorders are written in the context of a genetic disease.^{32,33,34} In the present case, the aortic coarctation was diagnosed late in life, even though a first-degree relative (son) of the patient developed the same condition in youth, thus demonstrating the high variability in the clinical symptoms of familial cases of aortic coarctation. It is therefore important to consider the potential existence of familial aggregation in order to provide genetic counseling^{10,30,32} and actively search for possible cases of coarctation of the aorta in hypertensive families, even in advanced age. In this case, we did not study the family for any clinical or genetic traits, but we recommended that her son undergo genetic testing.

Our case illustrates how a congenital cardiac malformation such as aortic coarctation can remain undiagnosed until an affected elderly patient presents with just hypertension, and given the clinical signs in this situation it can easily be overlooked in the absence of a complete physical examination.

Table 1 summarizes the characteristics of patients aged over 65 years with aortic coarctation published to date. The table shows cases with available information ($n = 18$), including three patients in whom the aortic coarctation was a surprise finding at autopsy. The mean age was 73 years (range 65–92), with a predominance of males (61.9%). In all cases, the clinical presentation was hypertension that was difficult to control, accompanied by heart failure in four cases (22.2%) and chest pain in six cases (33%). Most of these patients (55.6%) also had a heart murmur on physical examination. In half the cases (50%), there was a mismatch in the blood pressure readings between the upper and lower limbs and between the arterial pulses in the lower limbs. The most commonly used diagnostic test (12 patients) was angiography, while CTA was used in three cases and MRA in one case.

Refractory hypertension is the most common presentation of aortic coarctation in adults, but the mechanism of this refractoriness has not been clearly determined. It has been postulated that coarctation could induce a stimulation of the renin–angiotensin system.³⁵ Unfortunately, we did not determine the aldosterone-to-renin ratio in our patient because the diagnosis of aortic coarctation was evident and we did not consider it clinically appropriate to discontinue antihypertensive drugs for a few weeks, a condition that is required in order to perform a reliable plasma renin assay.

The current guidelines for the management of adults with aortic coarctation recommend intervention when the peak-to-peak coarctation gradient ≥ 20 mm Hg³⁶ or when there is a pressure difference >20 mm Hg between the upper and lower limbs, with upper limb hypertension ($>140/90$ mm Hg in adults), or significant left ventricular hypertrophy.³⁷ As our patient had refractory hypertension and met all the above criteria, we recommended corrective treatment considering her good general clinical state and long life expectancy.

A large retrospective study²⁵ suggests that surgical repair of aortic coarctation in adults is preferable to conservative treatment because surgery was associated with resolution of the hypertension in a high percentage of patients or less need for antihypertensive medication in other cases; the perioperative

mortality and risk for restenosis were low. Mortality associated with surgical repair (end anastomosis with interposition of a patch) is about 1% and the incidence of complications is close to 2%.¹³ Endovascular procedures (angioplasty and/or stent placement) entailed a risk of rupture due to the histological changes in the vascular wall associated with aging, as well as further development of restenosis (25%) and aneurysm (20%).^{12,38}

A meta-analysis based on 22 studies compared the results of surgery with those of endovascular repair in adolescents and adults with aortic coarctation.³⁹ The authors conclude that the cure rate of hypertension was similar with surgical (64%) and endovascular (61%) treatment. Although the risk of restenosis was higher with stenting (OR 6.0) and angioplasty (OR 8.6) than with surgery, the complication rate was lower with stenting than surgery (OR 1.3) and angioplasty (OR 2.4).

The low incidence of aortic coarctation in the elderly explains the lack of controlled studies. There is no consensus about the best treatment option for this age group and the attitude to follow is based on the experience of the few published cases.^{4,13,18} Some authors advocate a conservative approach in cases of coarctation detected at a late age and with little clinical expression,^{2,6,8,10,14,40} given the risk associated with the types of interventions necessary in the elderly and the possible persistence of hypertension after repair, especially in patients aged over 25 years.^{10,14,22–24,38,41,42}

As different types of surgical and interventional treatment are now available, treatment should be individualized according to the characteristics of the patient and the coarctation. Endovascular therapy is currently the treatment of choice for aortic coarctation in older patients with multiple comorbidities due to its lower rate of morbidity and mortality than surgery.² Balloon angioplasty has shown a high success rate with a low rate of complications,⁴³ and stent implantation reduces the incidence of late restenosis.⁴⁴ Covered stents are preferred in patients with aortic wall aneurysm and in older patients in whom the vessel wall is relatively less compliant.⁴⁵ Taking into account the advanced age of our patient and the presence of post-stenotic dilatation of the descending aorta, we considered that implantation of a covered stent was the best choice in this case because of the high risk of dissection or rupture using classic stenting.

Of the 18 cases of aortic coarctation diagnosed pre-mortem in subjects over 65 years of age, half received conservative treatment, and in two cases who underwent coronary revascularization the coarctation was not repaired. The other half underwent repair: in five cases by graft surgery (one patient underwent repair of the coarctation and coronary revascularization in the same procedure) and in four cases by percutaneous endovascular therapy (one angioplasty, one stent, and two angioplasties plus stent). Unfortunately, most reports fail to mention the long-term evolution of the patients, thus precluding conclusions about which therapeutic behavior can be recommended for elderly subjects. Among patients treated conservatively, there is one case of prolonged survival (24 years after diagnosis). In the five cases treated by surgery, there was one death due to surgical complications and one case of prolonged survival (of unspecified duration), while in the remaining three cases only short-term survival (less than 1 year) was mentioned. Among the four patients treated percutaneously, there was one death from aortic rupture after angioplasty, while the remaining three cases survived the procedure but there are no data on long-term evolution.

We consider it essential to individualize treatment based on the patient characteristics (age, comorbidity, life expectancy) and the surgical risk in each case. We must not forget that

TABLE 1. Characteristics and Clinical Course of Patients With Aortic Coarctation Over 65 Years of Age

Author, Year (Reference)	Age/Gender	Clinical Symptoms	Diagnosis	Treatment	Evolution
Liberthson et al, 1979 ³	72 M	HTN	-	Surgery	Perioperative death
Haldane, 1983 ⁴	74 M	HTN, dyspnea, murmur, reduced lower limb pulses	Angiography	Conservative	-
Bartlett, 1985 ⁵	74 M	HTN, dyspnea, murmur, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography	Conservative	Long-term survival (24 years)
Convens et al, 1996 ⁶	72 M	HTN, angina, murmur, reduced lower limb pulses	Angiography	Conservative, coronary revascularization	Survived (2 years)
O'Byrne et al, 1997 ⁷	73 M	HTN	-	Conservative	Survived (2 months)
Patel et al, 1998 ⁸	79 M	HTN, angina, heart failure, murmur, transient ischemic attack	Angiography, MRA, CTA	Surgery (graft)	Long-term survival (not specified)
Sheikhzadeh et al, 1999 ⁹	68 F	HTN, dyspnea, murmur, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography, CTA	Conservative	-
Simon et al, 1974 ¹⁰	80 M	HTN, angina, heart failure, murmur, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography, CTA	Surgery (graft)	Survived (1 year)
Koerselman et al, 2000 ¹¹	67 F	HTN, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography	Percutaneous angioplasty	Survived (1 year)
Petrik et al, 2001 ¹²	68 F	HTN, angina, dyspnea, murmur, increased blood pressure in the upper limbs	Angiography, MRA	Surgery (anastomosis and graft)	Survived (10 months)
Varma et al, 2003 ¹³	65 F	HTN, murmur, increased blood pressure in the upper limbs, reduced lower limb pulses	MRA	Percutaneous angioplasty and stent	Perioperative death (dissection)
Cevik et al, 2004 ¹⁴	80 M	HTN, murmur, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography, MRA	Conservative, coronary revascularization	Survived (1 year)
Toste et al, 2006 ¹⁵	75 F	HTN, heart failure	Angiography, MRA	Stent	Survived (48 hours)
Luliano et al, 2007 ¹	65 F	HTN, angina, increased blood pressure in the upper limbs, reduced lower limb pulses	CTA	Conservative	Survived (18 months)
Hussein et al, 2009 ¹⁶	68 M	HTN, dyspnea, increased blood pressure in the upper limbs, reduced lower limb pulses	Angiography	Percutaneous angioplasty and stent	Survived (week)
Tundidor et al, 2010 ¹⁷	83 F	HTN, increased blood pressure in the upper limbs, reduced lower limb pulses	CTA	Conservative	-
Alvarez et al, 2011 ¹⁸	69 M	HTN, heart failure, reduced lower limb pulses	Angiography, CTA	Coronary revascularization	Survived (3 years)
Tanaka et al, 2012 ¹⁹	74 F	HTN, murmur, increased blood pressure in the upper limbs	CTA	Surgery (anastomosis and graft) and aortic valve replacement	-
				Conservative	-

CTA = computed tomography angiography, F = female, HTN = hypertension, M = male, MRA = magnetic resonance angiography.

adequate control of hypertension reduces cardiovascular morbidity and mortality in the short term and may improve cognitive function, even in very old subjects (Hypertension in the Very Elderly Trial: HYVET study),^{46,47} so we should not discard surgical repair of the coarctation in elderly subjects who have hypertension refractory to medical treatment, provided that the perioperative risk is low and life expectancy is adequate. Endovascular procedures can be an especially attractive alternative in elderly patients because of their safety and marked efficiency (comparable to surgery) for the resolution or improvement of hypertension.

CONCLUSION—CASE CONTRIBUTION

The presentation of aortic coarctation in elderly patients is rare and its therapeutic approach is controversial. We report the first documented case of familial aortic coarctation in an older patient. The coarctation was diagnosed during the study of refractory hypertension. Endovascular repair of the coarctation (angioplasty and stenting) improved blood pressure control, although the patient continued to require antihypertensive therapy.

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