Received: 28 May 2021 | Revised: 13 June 2021 | Accepted: 6 July 2021

DOI: 10.1002/ccr3.4626

CASE REPORT

Clinical Case Reports Open Access WILEY

Non-dissecting large thoracic aortic aneurysm leading to chronic aortic insufficiency presenting as acute heart failure

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Abstract

Large, non-dissecting thoracic aortic aneurysms (TAA) up to 13 cm in size are typically found in elderly patients with non-specific respiratory symptoms yet must be detected quickly due to their mortality risk. We present a 31-year-old man with exertional dyspnea secondary to aortic insufficiency from a 9.4 cm TAA.

KEYWORDS

cardiothoracic surgery, cardiovascular disorders, emergency medicine, genetics, vascular surgery

1 | INTRODUCTION

Thoracic aortic aneurysm (TAA) is a vasculopathy seen more commonly in men with an estimated prevalence of 5 per 100,000 that is often asymptomatic and thus found incidentally or post-mortem.[1] When TAAs are discovered in living patients, the average age at the time of diagnosis is 70 years old.[2] Given the condition's variable manifestations and potential for life-threatening consequences if undetected, clinicians must recognize potential signs and symptoms of TAA and understand the natural progression of the disorder. Typically, asymptomatic TAAs are surgically managed when their diameter is greater than 5.5 centimeter (cm) for most patients or 4.0 to 5.0 cm for those with connective tissue diseases such as Marfan, Ehlers-Danlos, Loeys-Dietz, or Turner syndrome.[3] Large TAAs greater than 6 cm in size are rarely encountered in clinical practice yet are a diagnostic imperative due to their yearly death rate of 11.8%.[4] When large TAAs are found in younger patients, clinicians must search for conditions that contribute to early TAA development, yet those patients may worry about the results of genetic testing having a broad impact on their lives. We report a case of a 9.4 cm, non-dissecting TAA in an otherwise young, healthy man who initially presented with signs and symptoms of acute heart failure and was later found to have clinical features suggestive of Marfan syndrome, yet the patient declined genetic testing.

2 | CASE HISTORY/EXAMINATION

A 31-year-old man of Japanese descent presented to his primary care physician in the United States for a five-day

history of new-onset dyspnea on exertion, orthopnea, and non-productive cough. His only significant past medical history was a "heart murmur" incidentally found on routine physical examination one-year prior which was never investigated due to the patient being lost to follow-up. His family history was notable for a sister previously diagnosed with spontaneous pneumothorax who like him was taller than both of their parents, but otherwise, both parents were alive and well with no known cardiac or other medical concerns in aunts, uncles, cousins, or grandparents. The patient had never exhibited any of these symptoms prior to this episode, and his primary care physician's physical examination revealed an audible 2/6 systolic murmur and 2/4 diastolic murmur. An electrocardiogram (ECG) showed normal sinus rhythm, evidence of left atrial enlargement, and left ventricular hypertrophy with strain. The patient was sent to a nearby emergency department where his vital signs were stable. Physical examination was notable for a thin, tall (6"1'/185 cm) man with audible murmur as described above.

3 | DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT

Initially, there was a concern for cardiomyopathy or valvopathy given the diastolic murmur and a relatively acute onset of symptoms. Initial ECG did not reveal any ischemic changes. The patient was at low risk of pulmonary embolism as he did not meet any of Wells' criteria. The patient had normal bilateral breath sounds and no history of trauma, so pneumothorax was deemed unlikely. Testing for cardiac and pulmonary etiologies was pursued.

A chest X-ray showed marked enlargement of his cardiac silhouette, and a transthoracic echocardiogram (TTE) revealed global hypokinesis with a left ventricular ejection fraction (LVEF) of 28%, markedly enlarged left ventricular end-diastolic volume (LVEDV) of 479 ml, trileaflet aortic valve, severe aortic regurgitation, distal ascending aorta 3.2 × 3.0 cm, mild-moderate pulmonary hypertension with right ventricular systolic pressure of 55 mmHg, mild left atrial and right ventricular enlargement, and 9.4 cm ascending aortic aneurysm without dissection at the level of sinus of valsalva (Figure 1A,B). Computed tomography angiogram (CTA) of the chest and abdomen confirmed the aneurysmal dilatation of the ascending aorta from the annulus to the mid/distal ascending aorta, measuring up to 8.7 cm in greatest dimension and severe four-chamber cardiomegaly with asymmetrically enlarged left ventricle (Figure 2). The patient's coronary arteries were noted to be patent, and there was an incidental finding of celiac artery stenosis.

The patient was transferred to a tertiary care center Cardiac Care Unit (CCU) and was evaluated by cardiothoracic surgery. In the CCU, the patient was noted to have Quincke's sign (capillary pulsation) and Corrigan's pulse (also known as water hammer pulse, a forceful bounding pulse with rapid upstroke followed by a collapse). Patient had a repeat TTE which confirmed the TAA, and he underwent testing including for syphilis and HIV, which were negative, and two peripheral blood cultures that showed no growth after 5 days. The patient underwent workup for incidental finding of celiac artery stenosis with lower extremity arterial ultrasound that did not show any evidence of popliteal artery aneurysm.

The patient remained clinically stable until he underwent Bentall procedure, which is an aortic root repair with mechanical aortic valve replacement and reimplantation of coronary arteries. His postoperative course was complicated by cardiogenic shock and atrial fibrillation, but the patient made a full recovery. He was started on amiodarone and digoxin for atrial fibrillation, a beta-blocker, ACE-inhibitor, and aldosterone

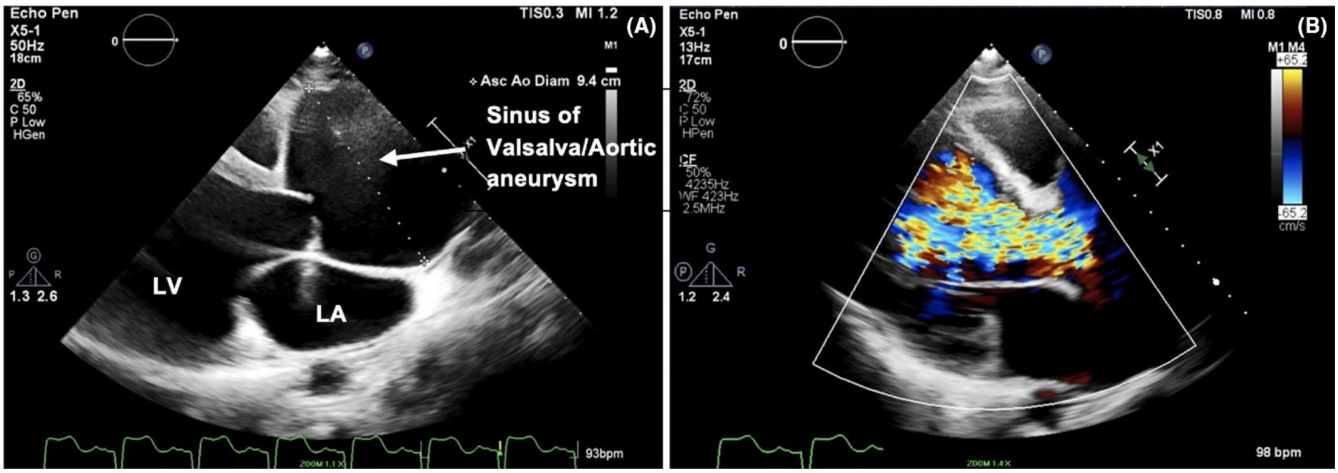

FIGURE 1 Transthoracic echocardiogram showing 9.4 cm ascending aortic aneurysm without dissection at the level of sinus of valsalva (A) and severe aortic regurgitation (B)

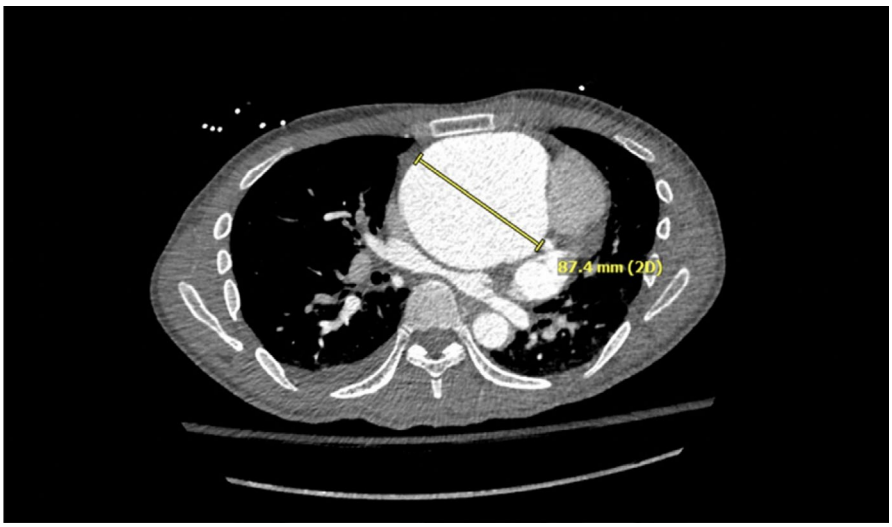

FIGURE 2 Computed tomography angiogram (CTA) of the chest and abdomen

antagonist for heart failure, and life-long warfarin for mechanical aortic valve placement. Pathology of removed aortic valve found myxoid change with no active inflammation or vegetations identified. Pathology from removed aorta showed an elastic vessel with marked medial degeneration, disruption of elastic fibers, and periadventitial fibrosis with mild chronic inflammation (Figure 3). Pathologist recommended investigating inherited etiologies for aortic degenerative changes, and this recommendation was supported by multiple physicians involved in his care. The patient underwent formal genetics consult but declined genetic testing for Marfan syndrome or other connective tissue disorders for the following reasons: I—His wife was pregnant with his first children, and he did not want to distress his wife with news that he may have a genetic disorder, and II—He was concerned that being diagnosed with a genetic disorder would impact his ability to acquire life insurance. His family aside from his wife lived in Japan, so his family was not tested. The patient was discharged 13 days post-operatively in stable condition to home with plan for outpatient cardiac rehabilitation.

4 | OUTCOME AND FOLLOW-UP

At outpatient cardiothoracic surgery clinic three weeks after discharge, ECG showed normal sinus rhythm, so digoxin and amiodarone were discontinued. At heart failure clinic two months after discharge, the patient remained in sinus rhythm and had returned to work without any symptoms. Follow-up TTE at two months post-op showed improved LVEF of 45%. Another TTE performed one-year post-op showed evidence of reverse remodeling with LVEF of 58% (improved from 28% pre-op), LVEDV of 129 ml (improved from 479 ml pre-op), normal right ventricular cavity size (improved from being enlarged pre-op), and normal left atrium size (improved from being enlarged pre-op). The patient's

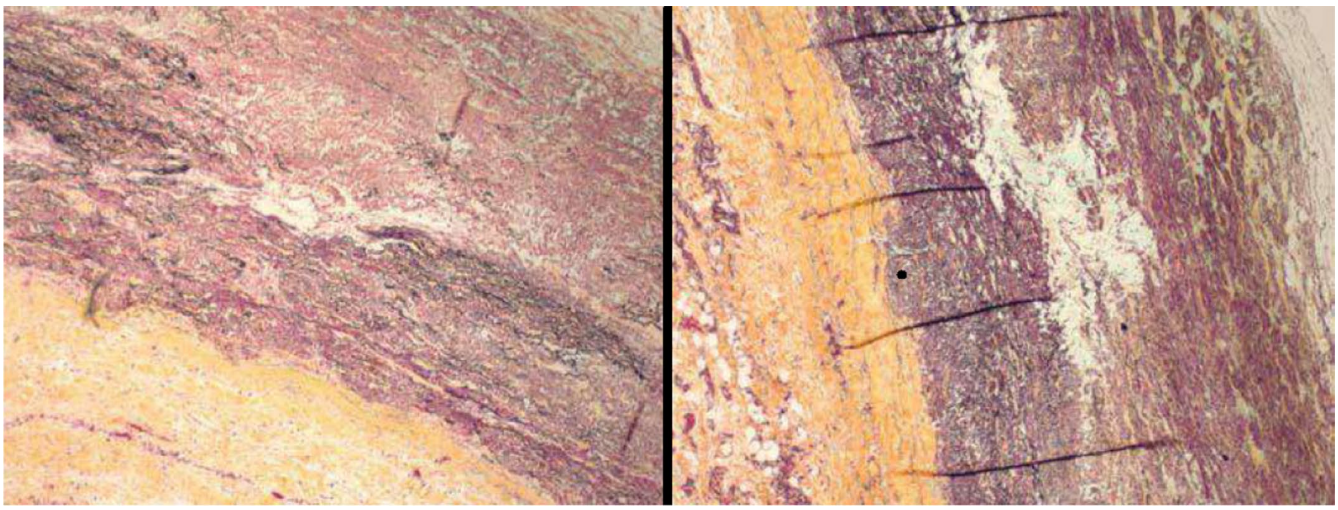

FIGURE 3 Images of the aorta stained with a Movat pentachrome

cardiologist recommended to the patient that his young children undergo genetic testing in the future.

5 | DISCUSSION

In our case, clinically observable manifestations of TAAs included aortic regurgitation and cardiomyopathy. Aortic regurgitation is a common valvulopathy associated with thoracic aortic aneurysms that is generally described as an early diastolic decrescendo murmur.[5] However, there are peripheral signs seen in severe aortic insufficiency including De Musset's sign (systolic head bobbing), Mueller's sign (systolic pulsation of uvula), Quincke's sign (capillary pulsation), and Corrigan's sign (forceful bounding pulse with rapid upstroke followed by a collapse), and the latter two were observed in our case.[6] Although not part of a routine physical examination, clinicians should look for these signs if they have high suspicion for thoracic aortic aneurysm in the setting of non-specific symptoms with new-onset diastolic murmurs. Cardiomyopathy is another manifestation that can be seen with aortic aneurysms when aortic regurgitation is involved. The patient was found to have severe reduction in LVEF, and patients with this finding develop non-specific symptoms including chest pain, shortness of breath, lightheadedness, dizziness, palpitations, and lower extremity swelling. Although ruling out underlying coronary artery disease in patients presenting with acute onset cardiomyopathy is a diagnostic priority, valvular heart disease including aortic regurgitation should be evaluated.

A patient's individual risk factors for developing aneurysm should be considered as part of any evaluation for TAAs. Modifiable risk factors include alcohol, tobacco, or recreational drug use, as well as diet and exercise habits, while non-modifiable factors are age, sex, and family history.[7] Family history of TAA may be suggestive of a few genetic diseases that contribute to aortic aneurysm development including Marfan syndrome, Ehlers-Danlos and Loeys-Dietz syndrome.[5] Bicuspid aortic valve is a common condition that is often associated with ascending aortic dilation and should be excluded in all patients with an enlarged ascending aorta.[5] Our patient, however, had a tricuspid aortic valve.

Based on the current practice guidelines from the American College of Cardiology, asymptomatic sporadic aneurysms warrant surgical repair when at least 5.5 cm in size and between 4.0 and 5.0 cm in those with genetic derived aneurysms or associated aortic valve abnormalities, such as bicuspid valve or severe regurgitation.[3] The threshold for surgical repair is lower if patients have suspected or confirmed connective tissue disease such as Marfan syndrome at >5.0 cm and Loeys-Dietz syndrome at >4.5 cm.[3] The location of the aneurysm (ascending versus descending) also informs surveillance recommendations. Typically, ascending aortic aneurysm of 3.5–4.4 cm is recommended for monitoring by an annual echocardiogram or CT/MR angiography, whereas monitoring of descending aortic aneurysm of 4.0–4.9 cm can be annually screened by CT/MR angiography.[3] The Aortic Institute at Yale-New Haven Hospital takes a more aggressive approach to the management of aortic aneurysms based on their study by Saeyeldin et al that suggested the hinge point at which risk of rupture increases ranges from 5.25 cm to 5.5 cm, which is smaller than the more commonly thought point of 6 cm. Based on this analysis, prophylactic surgical repair is recommended and performed at diameter of at least 5.0 cm with 1% 30-day mortality risk.[8] Additionally, a recently published study from Switzerland used preoperative CT scans to estimate aortic diameter at the time of dissection, and their results suggest that aortic dissection in the ascending aorta occurred at a projected aortic diameter below 4.5 cm in 87.7% of non-Marfan patients, which argues in favor of the threshold for surgical intervention in non-Marfan patients being lowered to less than 4.5 cm if the goal is to treat these patients prophylactically.[9]

Review of 13 previously published case reports (Table 1) of large, non-dissecting thoracic aortic aneurysms of at least 6 cm diameter revealed size range of 6.6 cm to 13 cm as the largest reported in the literature.[10–22] Our review demonstrated the increased incidence in males, who constitute 11 of 13 cases reported. Average age of diagnosis was 64 years old, and average size of TAA was 9.1 cm. The patients endorsed non-specific respiratory symptoms including most commonly dyspnea. Surprisingly, only one patient had diagnosed or suspected connective tissue disease. Our 31-year-old patient was much younger than most of these other examples of large TAAs. One study calculated that an aortic aneurysm at least 6 cm in size is associated with 8 times higher yearly rate of complications including dissection, rupture, and death when compared to that of 3.5–3.9 cm TAAs.[23] Another study found that for aneurysms greater than 6 cm, the combined annual risk of death, rupture, or dissection was 15.6% per year.[4]

An additional consideration once surgical intervention is indicated is the type of procedure that should be performed. Alternatives to the Bentall procedure include the Tirone David procedure, which is a valve-sparing aortic root replacement, and the Ross procedure, which is an aortic valve replacement with the patient's own pulmonary valve as the pulmonary valve is replaced with a pulmonary homograft. In this case, the surgeon opted for the Bentall procedure with mechanical aortic valve after a discussion with the patient regarding how his age and TAA size impacted what surgical options were viable. His young age argued in favor of implanting a mechanical aortic valve rather than using a tissue valve or performing a Ross procedure. Valve-sparing surgery was deemed less feasible due to the severe left ventricular impairment and severely dilated left ventricle that were secondary to his large TAA.

TABLE 1 Large (greater than 6 cm), non-dissecting thoracic aortic aneurysms

Case	Age	Gender	Connective tissue disease diagnosed or suspected	Size (cm)	Symptoms	Reference
1	66	Female	None	6.6	Chest pain, shortness of breath	Boettcher et al[9]
2	44	Male	None	12	Dyspnea on exertion, fatigue	Santagata et al[10]
3	89	Male	None	7.1	Dyspnea on exertion	Gowani et al[11]
4	37	Male	None	9.5	Pleuritic chest pain	Harris et al[12]
5	61	Male	None	8	Not described	Karimov et al[13]
6	82	Female	None	11	Shortness of breath	Chavanon et al[14]
7	56	Male	None	8	Dyspnea on exertion	Pai et al[15]
8	61	Male	None	8.2	Persistent cough	Zanini et al[16]
9	82	Male	None	10.5	Shortness of breath, orthopnea	Bouzas et al[17]
10	75	Male	None	11.6	Not described	Bonilla-Palomas et al[18]
11	40	Male	Marfan	7	Dyspnea on exertion	Sousa et al[19]
12	44	Male	None	13	Shortness of breath	Al-Ebrahim et al[20]
13	62	Male	None	6.6	Asymptomatic	Velasco et al[21]
14	31	Male	Marfan (Suspected)	9.4	Shortness of breath	Our case

Pathology of removed aortic valve found myxoid change, which is defined as replacement of the valve fibrosa with acid mucopolysaccharides and cystic changes, and while this is non-specific, this can be seen in cases of Marfan syndrome.[24] Meanwhile, examination of the removed aorta showed marked medial degeneration, which is commonly seen in Marfan syndrome.[25]

The patient declined testing for Marfan syndrome and other connective tissue diseases on multiple occasions. His stated reasons were related to stigma associated with genetic disorders and the potential impact on his ability to acquire life insurance at a time when his wife was pregnant with his first children. This 31-year-old patient refused genetic testing for reasons that may not have influenced his decision-making if he were closer to the typical age of TAA diagnosis, which illustrates how the age at TAA diagnosis can impact management. This patient with suspected Marfan syndrome missed the window of opportunity for adequate screening and monitoring and presented symptomatically with findings of a massively enlarged ascending aortic aneurysm with severe aortic regurgitation and systolic heart failure. If he had been diagnosed with Marfan syndrome and found to have a TAA, recommendations would have included regular monitoring of aortic size, use of beta-blockers at the time of Marfan diagnosis, and restrictions on physical activity, as the risk of adverse events is lower when such recommendations are followed.[26]

In conclusion, acquiring a detailed history and performing a thorough physical examination can allow for early diagnosis of TAAs. Once a patient is diagnosed with TAA, clinicians should risk-stratify according to size, patient risk factors, and symptoms and provide appropriate recommendations as complications associated with TAAs can be devastating. However, when a large TAA is found in a young patient, the patient's age influences not only the options available for surgical management but also decision-making regarding genetic testing.

ACKNOWLEDGEMENTS

Published with written consent of the patient.

AUTHOR CONTRIBUTIONS

JYB served as a first author, was responsible for initial conception of this work, reviewed all cited literature, wrote initial drafts of each section of the manuscript, and made revisions. CT served as a second author, revised initial drafts for clarity, accuracy, and for inclusion of additional intellectual content, and acquired relevant clinical data. KH served as a third author, revised drafts for clarity, accuracy, and for inclusion of additional intellectual content, and acquired relevant clinical data. MS served as a fourth author, revised drafts of all sections, and contributed to echocardiogram image and video selection. CH served as a final author, made the final diagnosis, was responsible for reviewing cited literature, saw the patient at outpatient follow-up visits, and revised drafts for important intellectual content.

ETHICAL CONSIDERATIONS

Our institutional review board (IRB) does not require that case reports be submitted for IRB approval. The subject of this case report gave written consent to submit this case report for publication.

DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.

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How to cite this article: Bae JY, Teng C, Hussein KI, Steinhardt MJ, Howes C. Non-dissecting large thoracic aortic aneurysm leading to chronic aortic insufficiency presenting as acute heart failure. *Clin Case Rep*. 2021;9:e04626. https://doi.org/10.1002/ccr3.4626