A Rare Case of Syphilitic Aortic Aneurysm in the Era of Modern Antibiotics

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Abstract

Introduction: In this age of medicine, most abdominal aortic aneurysms are of atherosclerotic in origin. Cardiovascular syphilis is a tertiary form of syphilis occurring in 10% of infected patients. It can affect the heart, great vessels and medium-sized arteries. Aortic involvement can present as uncomplicated aortitis, coronary ostial stenosis, aortic regurgitation, and aortic aneurysm. If left untreated, the mortality rate at 1 year can reach 80% due to the high rate of rupture of these aneurysms.

Case: A case of a 65-year old male who came in due to few weeks history of abdominal pain. CT aortogram revealed a fusiform infrarenal aneurysm. Coronary angiogram was done which revealed 3-vessel coronary artery disease. He was tested positive for syphilis and was treated with Penicillin. A dilemma sets in if CABG and open repair of the infrarenal aneurysm is possible. A Thallium scan showed no inducible ischemia, hence, CABG was postponed. An open repair via retroperitoneal approach was done. Histopathologic examination of the aneurysm was consistent with syphilitic aneurysm. He was discharged apparently well until his most recent follow-up.

Conclusion: Tertiary syphilis, though a rare disease in this age of antibiotics, is a re-emerging cause of aneurysm and should be considered in patients with risk factors.

Keywords: Aortic Aneurysm; Syphilis; Tertiary Syphilis; CABG; Coronary Artery Disease

Introduction

In this age of medicine, most abdominal aortic aneurysms are of atherosclerotic in origin. Infectious aneurysms have become less frequent. However, historically, before the era of antibiotics, all recorded aneurysms were considered to be of syphilitic in origin and those of atherosclerotic in origin were considered rare [1].

Tertiary syphilis has become a rare disease since the discovery of Penicillin in the 1920s. However, before its discovery, a considerable percentage at around 5 - 10% of cardiovascular deaths is attributable to tertiary syphilis manifesting as thoracic aortic aneurysm [2]. Despite of the lack of published journals, tertiary syphilis and cardiovascular syphilis with its complications is currently a rare entity [3].

Syphilis has different stages: primary, secondary, latent, and tertiary, and may also occur congenitally. Sir William Osler referred to it as "the great imitator" due to its different clinical presentations.

Cardiovascular syphilis is a tertiary form of syphilis which occurs in 10% of patients. Manifestations usually appears in the 4th - 5th decade of life or 5 - 40 years after the primary infection. Infected individual may be symptomatic or asymptomatic being diagnosed incidentally during a routine chest X-ray or when a fatal aneurysmal rupture happens [4].

It can affect the heart, great vessels and medium-sized arteries. Aortic involvement may present as uncomplicated aortitis, a coronary ostial stenosis, an aortic regurgitation, and aortic aneurysm [5].

Syphilitic aortic aneurysm (SAA) predominantly affects the ascending aorta (50%), followed by the arch of the aorta (30 - 40%) and descending thoracic aorta (5 - 15%). Involvement of the abdominal aorta, in particular infrarenal, is considered very rare [4]. If untreated, the 1 year mortality rate can reach 80% due to the high rate of rupture of these aneurysms [6]. Clinicians need to be aware of still a possibility of encountering cases of SAA. We present a rare case of fusiform aneurysm of infrarenal aorta caused by syphilis.

Case Report

This is a case of a 65-year-old male, who is non-hypertensive, non-diabetic, a 60-pack-year-smoker and previous occasional alcoholic drinker, who has a history of having sex with men. He came in at the Emergency Department due to few weeks history of abdominal pain. A whole abdominal CT scan was done which showed a fusiform 9.17 x 4.19 x 5.2 cm (LxWxAP) dilated infra-renal portion of the aorta extending to the aortic bifurcation with peripheral fat stranding. CT Aortogram was then requested which showed a fusiform aneurysm involving the infrarenal abdominal aorta commencing just after the take-off of the left renal artery extending down just before the bifurcation with a length of 6.8 cm and a maximum cross-sectional diameter of 5.1 x 4.6 cm (APxW) (Figure 1 and 2). He was then admitted for surgical intervention. Pertinent physical examination findings include: BP 160/90 mmHg, CR 92 bpm, RR 18 cpm, no neck vein engorgement, clear breath sounds. Cardiac examination revealed adynamic precordium, point of maximal impulse at the 6th intercostal space left anterior axillary line, no thrills, no heave, S1 and S2 were normal, normal rate, regular rhythm, no murmurs. The lower extremities showed full and equal pulses. Chest x-ray showed vascular crowding on left paracardiac and basal areas with left ventricular prominence, a tortuous, dilated and calcified aorta (Figure 3). 12 lead electrocardiogram showed sinus rhythm, normal axis, left ventricular hypertrophy, intraventricular conduction delay and inferior wall ischemia (Figure 4). 2d-echocardiogram revealed concentric left ventricular hypertrophy and adequate wall motion, contractility and systolic function. Aortic valve sclerosis. Mitral valve sclerosis with mild mitral regurgitation. Trivial tricuspid regurgitation. Normal pulmonary artery pressure with pulmonic regurgitation (Figure 5). The assessment on admission was Atherosclerotic Infrarenal Aortic Aneurysm, to consider Coronary Artery Disease. He was immediately started on Nicardipine drip with a target blood pressure of 110 - 120 mmHg. Atorvastatin, Losartan and Metoprolol were also started. Due to the risky sexual behavior of the patient, a test for syphilis was done which showed positive. The haemogram, blood chemistry and coagulation tests were unremarkable and the viral markers tested negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B and C. ESR and CRP were elevated. In this clinical scenario, a diagnosis of tertiary syphilis with cardiovascular involvement was made and he was treated with penicillin. The size of the aneurysm is a class I indication for surgical treatment and surgery was scheduled as soon as possible. He underwent coronary angiogram for risk stratification and revealed 60 - 70% tubular stenosis at the proximal segment of the left anterior descending artery, 80% discrete proximal stenosis and another 60% discrete mid segment stenosis of the left circumflex artery and 80% mid segment stenosis and luminal irregularities along the segment of the right coronary artery (Figure 6). Owing to the increased risk of peri- and post-operative morbidity, with a EuroScore of 7.7%, a coronary artery by-pass graft was contemplated. However, we were hesitant in doing both the procedures at the same time because of a higher risk for morbidity and mortality. Because of this dilemma, a myocardial perfusion SPECT with Thallium-201 was done which revealed no evident inducible myocardial ischemia. During the course, patient had persistent abdominal pain. A repeat CT aortogram revealed an increase in the size of the aneurysm (Figure 7). He underwent emergency open AAA repair via retroperitoneal approach. The patient was cooled to 28°C and the aortic and common iliac arteries were cross-clamped. Aneurysm was opened and thrombus were removed. A proximal anastomosis between 40 cm Uni-Garft[a] K DV and aorta was done using Prolene 3-0 with reinforcement. The left renal artery was re-anastomosed using saphenous vein graft conduit. Distal anastomosis between graft and external iliacs was done using Prolene 5-0. Weaning was straightforward and haemostasis was uncomplicated. The postoperative course was uneventful and patient was discharged. Histological examination of the aneurysmal wall showed areas of fibrosis, cholesterol clefts, cystic medial necrosis, and frequent areas of patchy smooth muscle cell nuclei loss. There were also areas of congested vascular channels, several lymphoplasmacytic infiltrates, and hemorrhages on the adventitia (Figure 8). On Masson's trichrome stain, it revealed focal areas with moderate intralamellar mucoid extracellular matrix accumulation and several areas of marked increased collagen fibers (Figure 9). A Van Gieson elastic stain showed several areas with severe loss and fragmentation of elastic fibers (Figure 10). A Grocott's Silver stain was also done which was negative for spirochetes (Figure 11). On post-operative follow-up at 1 and 2 months, patient was well and asymptomatic. A repeat CT aortogram showed neither aneurysms nor anastomotic site-related complications (Figure 12).

Discussion

Countless microorganisms may cause infected aortic aneurysms, which can lead to rupture and death. Currently, Staphylococcus aureus and Salmonella species are the major causes of IAA. Before the discovery of penicillin, syphilis was the most common etiology [7]. Syphilis is a sexually transmitted infection that has a chronic phase. It is caused by the bacterium Treponema pallidum. Although claims that this disease is rare, currently, its incidence is increasing since 2001 mainly because of wrong sexual practices. In the US, primary and secondary syphilis increased by 19.0% to about 7.5 cases per 100,000 population during the year 2014 - 2015. This was the highest rate

Figure 1: CT Aortogram showing a fusiform aneurysm involving the infrarenal abdominal aorta commencing just after the take-off of the left renal artery extending down just before the bifurcation with a length of 6.8 cm and a maximum cross-sectional diameter of 5.1 x 4.6 cm (APxW).
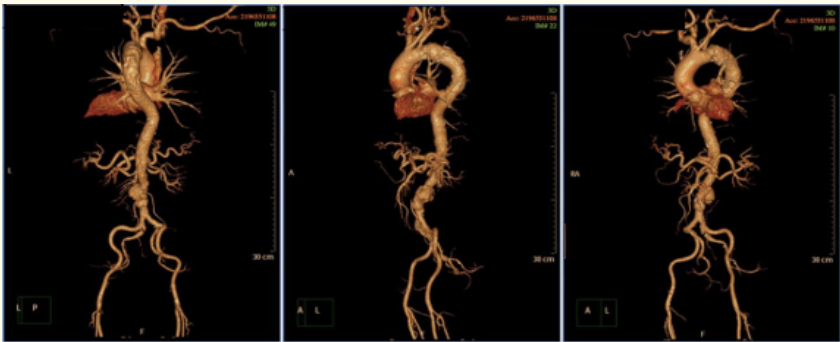

Figure 2: 3 dimensional reconstruction of the aorta showing a fusiform aneurysm involving the infrarenal abdominal aorta commencing just after the take-off of the left renal artery extending down just before the bifurcation.

Figure 3: Chest x-ray of a 65 year old male showing vascular crowding on left paracardiac and basal areas with left ventricular prominence, a tortuous, dilated and calcified aorta.
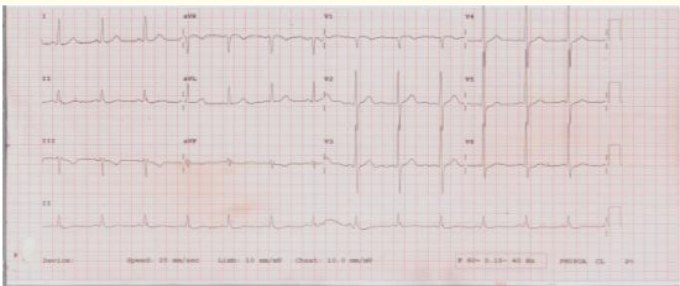

Figure 4: 12 lead electrocardiogram showing Sinus rhythm, Normal axis, Left ventricular hypertrophy, Intraventricular conduction delay and Inferior wall ischemia.
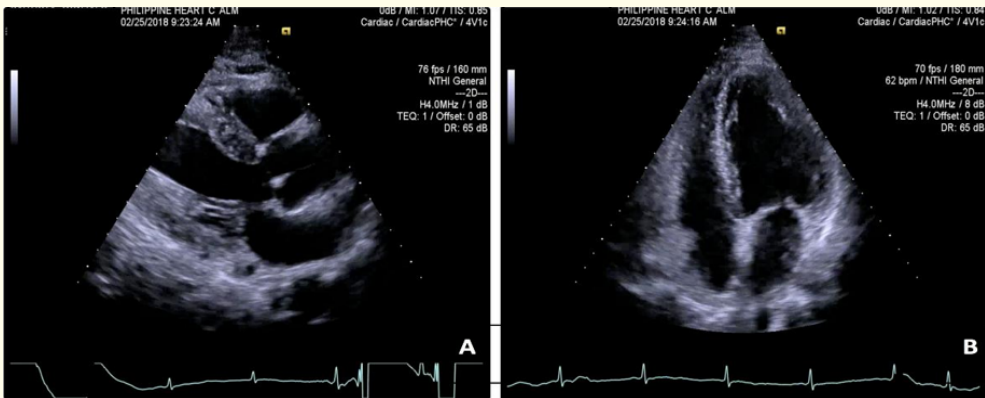
Figure 5: Two dimensional echocardiogram (A. PLAX view. B. A4C view) showing concentric left ventricular hypertrophy and adequate wall motion, contractility and systolic function. Aortic valve sclerosis. Mitral valve sclerosis with mild mitral regurgitatiuon. Trivial tricuspid regurgitation. Normal pulmonary artery pressure with pulmonic regurgitation.
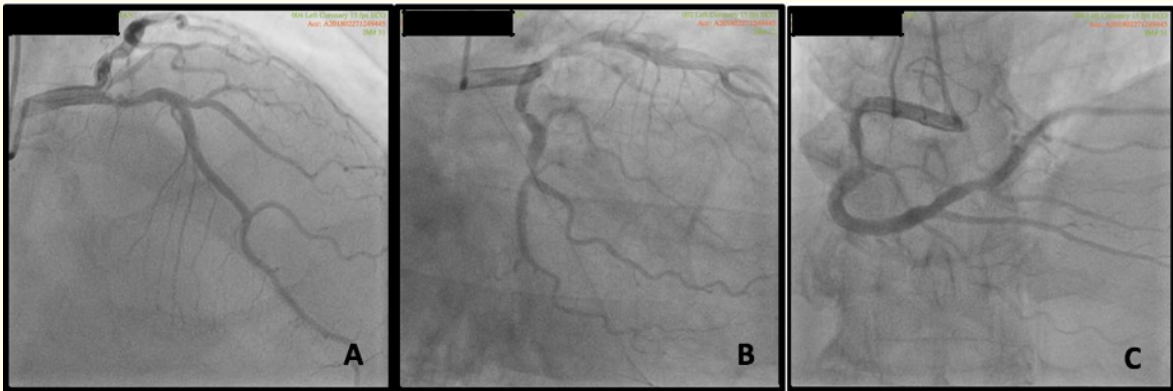

Figure 6: Coronary angiogram showing (A) 60-70% tubular stenosis at the proximal segment of the left anterior descending artery, (B) 80% discrete proximal stenosis and another 60% discrete mid segment stenosis of the left circumflex artery and (C) 80% mid segment stenosis and luminal irregularities along the segment of the right coronary artery.
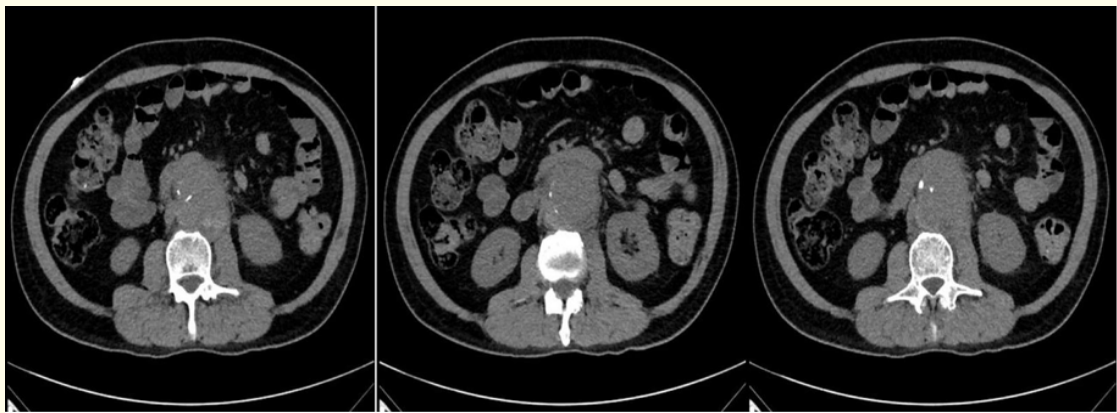

Figure 7: 12 lead electrocardiogram showing Sinus rhythm, Normal axis, Left ventricular hypertrophy, Intraventricular conduction delay and Inferior wall ischemia.
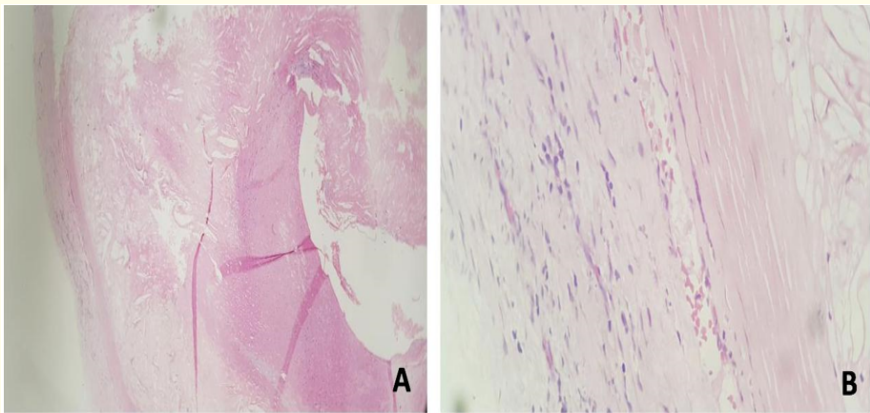
Figure 8: Microscopic examination of the aneurysmal wall showing (A) areas of fibrosis, cholesterol clefts, cystic medial necrosis, and (B) frequent areas of patchy smooth muscle cell nuclei loss. There were also areas of congested vascular channels, several lymphoplasmacytic infiltrates, and hemorrhages on the adventitia.
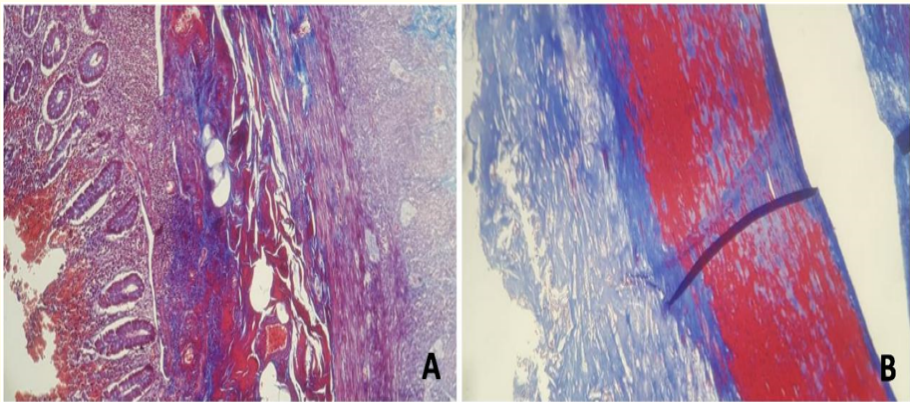

Figure 9: Microscopic examination of control (A) and the aneurysmal wall on Masson's trichrome stain showing focal areas with moderate intralamellar mucoid extracellular matrix accumulation and several areas of marked increased collagen fibers (B).
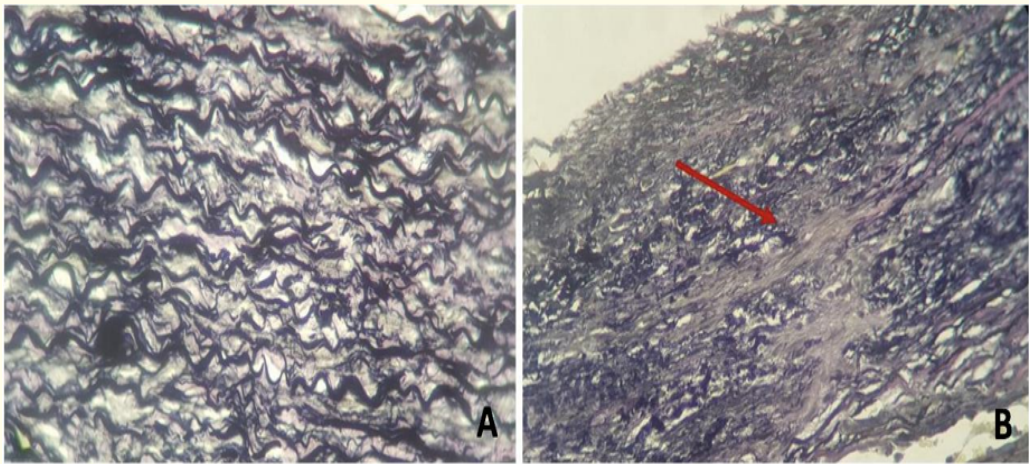

Figure 10: Microscopic examination of control (A) and the aneurysmal wall on Van Gieson elastic stain showing several areas with severe loss and fragmentation of elastic fibers (B).

Figure 11: Microscopic examination the aneurysmal wall on Grocott's Silver stain showing negative for spirochetes.
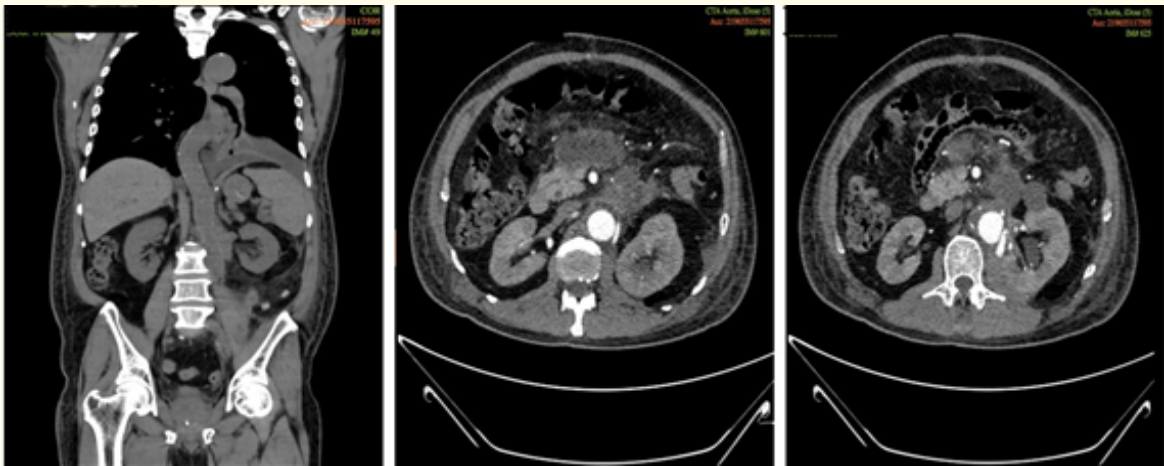

Figure 12: CT aortogram post-AAA repair showing that the previously noted infrarenal pseudo-aneurysm/aneurysm no longer seen. No IV contrast leak in the region of aortic surgery. The aortic anatomosis site is patent with no contrast extravasation at the time of examination. The rest of the aorta is atherosclerotic. The left internal iliac artery is occluded from its proximal segment. The inferior mesenteric artery is not visualized.

reported since 1994 [8]. Clinical manifestations of syphilis are seen in 3 phases. Painless chancre is pathognomonic during the primary phase. About a quarter of these patients will progress to secondary phase which is manifested by non-specific systemic symptoms including fever, rash, malaise, and diffuse lymphadenopathy. If left untreated, it will develop to tertiary phase in about 3 - 15 years, which may affect the central nervous system, cardiovascular system, and the skin (gummatous syphilis).

During the primary or initial secondary phase of syphilis, screening tests become negative even after a few months of antibiotic therapy. While patients with more advanced disease stage will have positive serologic markers for months or years or forever [9].

Screening individuals can be performed using non-specific, non-treponemal anti-cardiolipin serological test (e.g. rapid plasma reagin [RPR] or Venereal Disease Research Laboratory [VDRL]) with subsequent confirmation of positive results by a specific treponemal test (e.g. *Treponema pallidum* particle agglutination [TP-PA] or the fluorescent treponemal antibody-absorption test [FTA-ABS]). However, there is an increasing trend towards use of treponemal-specific enzyme immunoassays (EIA) and chemiluminescence immunoassays (CIA) for initial syphilis screening, followed by a non-treponemal test (RPR/VDRL) on specimens with positive results [10]. The most recent EIA/CIAs appears to be more sensitive (95 - 99%) and specific (98 - 99%) than prior generations of these assays [11]. In our case, although admitting past history of risky sexual behaviour, the patient had no recollection of any primary lesions or symptoms related to secondary syphilis. He tested positive for syphilis and was treated with penicillin.

Most of the syphilitic aneurysms are saccular and located at the level of the thoracic aorta, especially the ascending aorta. The bacterium has predilection in this area because of its rich lymphatic supply. Lesions below the diaphragm are rare and only 10% of SAA involve the abdominal aorta and renal arteries. It is presumed that the abdominal aorta is not often involved in syphilis because of the lack of vasa vasorum and the lymphatics at this level [12]. Abdominal atherosclerotic aneurysms usually occur below the renal arteries [13].

According to Lakhwani., *et al*. SAA were unique because of the smooth surface, thin-walled and ruptures easily if handled carelessly especially during procedures [14]. Morphologically, fusiform was more common than saccular in infrarenal AAAs. In their study, syphilitic infrarenal AAA constituted 18.5% of the total AAA and only one had associated supradiaphragmatic arch aneurysm which was discovered after an emergency repair of the ruptured infrarenal AAA. Prognosis of syphilitic infrarenal AAA is way better than the other types of infections with 80% surviving surgery. Fusiform aneurysms were more common in the syphilitic infrarenal AAA than the saccular variety accounting for 90% of the cases [14].

Though syphilis is rare as compared in the past, its potential to become a source of aneurysmal disease remains significant. Rates of syphilis fell sharply since it was first reported in 1941. There was a 90% fall in the incidence of primary and secondary syphilis in the 1990s and a nadir of 5979 cases in 2000. However, from 2001 to 2008, the cases of primary and secondary syphilis more than doubled, with most of the new cases came from men who have sex with men [15]. These data, however, does not reflect the true number of cases, since milder manifestation of the disease do not alarm patient to seek medical consult. Accordingly, the rise in early syphilis increases the risk of resurgence in late disease in years to come.

Definitive diagnosis of syphilitic aneurysm may be difficult because of the long asymptomatic period from primary infection to development of aneurysm and the inability to grow *Treponema pallidu*m on standard culture media. Patients may be diagnosed clinically when they are positive serologically with syphilis and the characteristic vascular pattern of involvement. Aortitis typically spares the sinuses of Valsalva with involvement of the ascending aorta, the aortic arch and the descending aorta [16].

It is estimated that 70% of patients with syphilitic aortitis has concomitant atherosclerosis which sometimes masks the typical intimal syphilitic manifestations [17]. Estes in his study suggested using this criteria in identifying the cause of aneurysm. (1) The aneurysm is atherosclerotic if there are other atherosclerotic lesions or aortic calcification. (2) The aneurysm is syphilitic if serology is positive and clinical data are convincing for syphilis. (3) The aneurysm is mixed if the two conditions co-exist [18].

Present guidelines recommend screening for coronary artery disease in patients with risk factors as part of pre-operative evaluation. Our patient, though asymptomatic, has risk factors for coronary artery disease such as gender, age, a 60-pack-year smoker and a 10-year ASCVD risk of 41.1%. Coronary angiogram was done which showed 3 vessel disease.

In approximately two-thirds of patients with AAA will have angiographic evidence of coronary artery disease of which one-third are asymptomatic [19]. In a study by Heggtveit, 7 of the 23 patient with syphilitic aneurysm or 30% has significant coronary artery disease. Concomitant hypertension and atherosclerosis may hide the presence of syphilitic aortitis or may confuse the physician of its possibility [20]. AAA repair procedures are strong trigger for acute ischemic events because of its long operative duration, the need for aortic clamping and the physiologic stress to the patient due to the fluid shifts and blood loss. Due to these reasons, AAA open repair has an associated risk of > 5% for perioperative cardiovascular complications such as death, myocardial infarction and stroke [21]. With these reasons, pre-operative risk stratification before the repair and is mandatory and depends on patients risk factors [22].

Our patient has a EuroScore of 7.7% and a revised cardiac risk index of 11% or is high risk for surgery. The dilemma sets in if AAA, CABG or AAA + CABG will be done to our patient. To help guide with the decision, a myocardial perfusion SPECT with Thallium was done which showed no inducible ischemia. Having a presence of coronary artery disease on coronary angiogram but with no inducible ischemia on non-invasive testing, we implied that the patient had a balanced ischemia.

Evaluation of ischemic heart disease can be carried out using intravascular ultrasound (IVUS), fractional flow reserve (FFR) measurement or nuclear imaging with single-photon emission computed tomography with radioisotopes such as Thallium (SPECT-TL) and technetium-99m. SPECT has become the method of choice for the non-invasive evaluation of ischemic heart disease. This method identifies ischemic territories and assesses myocardial viability [23]. SPECT has a reported sensitivity of 85 - 90% but may be affected by different factors including lesion characteristics and exercise test performance [24]. Detection of ischemic areas using nuclear imaging is based on the principle that significant differences in myocardial perfusion in different cardiac regions are identified as reversible defects when

exposed to stress [25]. Global reduction in the uptake of radiotracer can be demonstrated by its quantification. Assessment of Thallium is based on the principle of relative differences between myocardial territories. Hence, a uniformly distributed ischemia in all the myocardial territories can be interpreted as normal and may lead to false negative results [26]. In our case, the associated SPECT-TL indicated homogeneous perfusion of the heart both at stress and rest phases without significant differences relative to the washout or redistribution phases, and was interpreted as normal.

Whittemore *et.al.* has demonstrated that in patients with clinically evident coronary artery disease, an increase in pulmonary capillary wedge pressure was associated with ischemic ECG changes [27]. Bush., *et al.* has reported no increased operative mortality with little depression of cardiac function during aortic cross-clamping in patients with CAD undergoing AAA repair. It was attributed to appropriate volume loading pre-operatively which allowed optimal performance of the left ventricle [28].

Our present guidelines did not specifically mentioned which should be carried out first. A risk stratification was only recommended. Several studies with conflicting results were published. Some recommends to do revascularization due to the increased possibility of myocardial infarction peri-operatively. Some studies recommend to do aneurysm repair because of the increased risk of rupture while waiting for 2 weeks post by-pass. In our patient, he underwent an emergency open repair of the aneurysm because of the increasing size of the aneurysm with anticipation of doing a coronary revascularization if something happens peri-operatively.

Histological examination of the aneurysmal wall of our patient showed areas of fibrosis, cholesterol clefts, cystic medial necrosis, and frequent areas of patchy smooth muscle cell nuclei loss. There were also areas of congested vascular channels, several lymphoplasmacytic infiltrates, and hemorrhages on the adventitia. On Masson's trichrome stain, it revealed focal areas with moderate intralamellar mucoid extracellular matrix accumulation and several areas of marked increased collagen fibers. A Van Gieson elastic stain showed several areas with severe loss and fragmentation of elastic fibers. In a study by Heggtveit, all cases of syphilitic aneurysm showed chronic mesaortitis with patchy destruction of musculo-elastic medial tissue replaced by vascularized connective tissue. Endarteritis obliterans of vasa vasorum with perivascular plasma-cell and lymphocytic "cuffing," adventitial fibrosis, and intimal atherosclerosis were present in all cases [20]. In a study by Roberts., et al. of 34 patients with syphilitic aneurysm, there was involvement of the 3 layers of the aorta. There was thickening of the adventitia mainly replaced by fibrous tissue. The vasa vasorum were also narrowed and thickened surrounded by aggregates of plasma cells and lymphocytes. On elastic stains, there is focal, but extensive, loss of the medial elastic fibers and replacement by fibrous tissue. The medial smooth muscle cells were also replaced by fibrous tissue. The intima was thickened by a typical atherosclerotic plaque. All these resulted in a thickened aortic wall, adventitia and intima. The media however was not thickened [29]. The histologic examination of our patient, showing necrosis, fibrosis, lymphoplasmacytic infiltration, loss of elastic fibers and increase in collagen fibers, strongly support the diagnosis of syphilitic aneurysm

The definitive diagnosis of syphilitic aortitis is difficult to establish clinically. Blood serologic tests may be negative or positive with a low titer. A history of a primary syphilitic infection helps in making the diagnosis.

Conclusion

We presented a case of fusiform infrarenal aortic aneurysm in a 65-year-old male diagnosed with tertiary syphilis and 3-vessel coronary artery disease which showed balanced ischemia on nuclear imaging, who underwent successful open aneurysm repair via retroperitoneal approach.

Given the high prevalence of coronary artery disease in patients with syphilitic aneurysm, coronary angiogram to screen patients for coronary artery disease should be done to those who have risk factors. Given the rare nature of infrarenal syphilitic aortic aneurysm, there are no published guidelines regarding the indications, time, and choice of treatment of these aneurysms.

It is difficult to accurately predict patients who will be at highest risk for a peri-operative complication during AAA repair. Analysis of cardiac risk factors in patients undergoing AAA repair showed that even patients with low computed risk will experience cardiac complications [30].

Although many articles fail to provide useful information, such as a detailed history and the presence of risk factors, we must note that most patients had no predisposing factors and denied a primary infection. Cardiovascular syphilis is still present nowadays and it is important not to forget the "great imitator" in the event of its characteristic symptoms.

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