CASE REPORT

REVISED Case Report: Multiple atherosclerotic plaques at its extreme in synchrony [version 3; peer review: 2 approved]

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Abstract

Peripheral artery (PAD) disease in association with renal artery stenosis is an important association which predicts the severity of the disease. An increase in the number of vessels affected by peripheral artery disease increases the chances of renal artery stenosis. In our case, the patient had primarily presented with anginal chest pain with complaints of claudication which on further investigation was diagnosed to be a triple vessel coronary artery disease along with bilateral subclavian and bilateral renal stenosis. On detailed history taking, risk factors like hypertension and chronic smoking was found to be present in our case which predisposed to peripheral artery disease secondary to atherosclerosis which was diagnosed on further investigations.

Although the association of renal artery stenosis is not very rare in cases of severe peripheral vascular diseases, the presence of a triple vessel coronary artery disease in synchrony is what makes it unique.

Take away lesson from this case report is importance of early diagnosis of dyslipidemia causing atherosclerosis and its complications. Multiple atherosclerotic lesions in synchrony i.e, bilateral renal artery stenosis with bilateral subclavian artery stenosis with coronary artery triple vessel atherosclerotic disease like in our case and its severity should create awareness among health care individuals and early treatment measures including lifestyle

Open Peer Review

Approval Status ✓ ✓

	1	2
version 3 (revision) 24 Jan 2024		✓ view
version 2 (revision) 27 Dec 2023		? view
version 1 23 Jun 2023	✓ view	✗ view

1. **Vishakha Jain**, All India Institute of Medical Sciences (AIIMS), Bibinagar, Hyderabad, India
2. **Daniel Sykora**, Mayo Clinic School of Graduate Medical Education, Scottsdale, USA

Any reports and responses or comments on the article can be found at the end of the article.

modifications should be considered to avoid such drastic events.

Keywords
atherosclerosis, subclavian artery stenosis, renal artery stenosis, coronary angiography, dyslipidemia, triple vessel disease, peripheral vascular disease,

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Author roles: Toshniwal S: Conceptualization, Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing; **Sahai I**: Data Curation, Writing – Review & Editing; **Ghosh B**: Data Curation, Writing – Review & Editing; **Chaturvedi A**: Data Curation, Resources, Supervision; **Agrawal G**: Conceptualization, Data Curation, Investigation, Supervision, Visualization; **Acharya S**: Conceptualization, Supervision, Visualization; **Kumar S**: Conceptualization, Supervision, Visualization; **Khadse S**: Conceptualization, Data Curation, Investigation, Supervision, Visualization; **Khurana K**: Data Curation

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REVISED **Amendments from Version 2**

Discussion has been revised as per reviewer instructions. Sentences have been revised accordingly.

Any further responses from the reviewers can be found at the end of the article

Introduction

Atherosclerosis is a progressive systemic inflammatory disease causing stenotic lesions in the walls of arteries due to the formation of fibrofatty plaque which further predisposes to myocardial infarctions, cerebrovascular events and even disabling peripheral artery diseases.[1] There is an increased prevalence of renal artery stenosis in patients with peripheral vascular disease in 60 years and above age group due to atherosclerosis and also due to the presence of various cardiovascular risk factors.[2] Peripheral artery disease (PAD), secondary to atherosclerosis is currently the leading cause of morbidity and mortality in the Western world and its risk factors include age, smoking, hyperlipidemia, and hypertension.[3] The outcome of Peripheral artery disease (PAD) patients is substantially determined by the extent of atherosclerotic comorbidities.[4,5] Renal artery involvement in peripheral artery disease depicts the increased severity of the disease and hence while investigating for peripheral artery disease, renal arteries should be looked for stenotic lesions.[2] In a study performed by Aboyans V. *et al,*[2] 681 patients who had got their Digital Subtraction Angiography (DSA) done for peripheral artery disease, 14% were found to be prevalent to renal artery stenosis. The association of coronary artery disease in synchrony due to atherosclerosis is rare and not many cases have been reported with multiple atherosclerotic lesions at multiple sites in synchrony like in this case.

In this case, we present a 60-year-old man who presented with anginal-type chest pain and was diagnosed with a triple vessel coronary artery disease who on further evaluation for his claudication of upper limbs was found to have severe peripheral artery disease with bilateral subclavian stenosis and bilateral renal artery stenosis.

Case presentation

A 60-year-old Asian male laborer by occupation, a known hypertensive for 20 years on regular antihypertensive medications which was uncontrolled and refractory in nature and a chronic smoker since 45 years with no significant family history. He presented to the hospital with anginal-type chest pain since 2 days which was progressive in nature and radiating to both arms and back with sweating and palpitations associated with breathlessness at rest (NYHA III) with orthopnea and paroxysmal nocturnal dyspnea. The patient also complained of pain in both arms on minimal exertion and while lifting weights since more than a year which was suggestive of claudication with complains of blackish discolouration of arms distally with no similar complains in the lower limbs.

On general examination, cold pulseless upper extremities with cyanosed distal upper limbs were noted. Axillary, brachial and radial pulses were non-palpable on examination suggestive of acute bilateral upper limb ischemia which was subsequently detected via doppler assessment. Other peripheral pulses of temporal, facial, carotid, femoral, popliteal, posterior tibial and dorsalis pedis arteries were palpable and the pulse rate was found to be 80/minute. Both heart sounds were heard with apex beat felt at 5th intercostal space just lateral to midclavicular line with no murmurs, bilateral air entry was heard with basal crepts bilaterally on respiratory examination. The abdomen was soft and non-tender with no organomegaly, no visible veins, normal peristaltic sounds, no arterial bruit or any abnormal enlargement or a pulsatile mass. The patient was conscious and oriented to time, place and person with no neurological deficits.

An electrocardiogram was done and was suggestive of ST segment depressions in anterior leads (V1-V6) with T wave inversions in leads II, III and avF suggesting acute myocardial ischemia. Cardiac biomarkers were sent and were found to be raised i.e.; CKMB: 50 IU/L (3-16 IU/L) and tropI: 24 ng/ml (0-13 ng/ml) with a rising trend on serial biomarker investigation leading to the diagnosis of non ST segment elevation myocardial infarction (NSTEMI). 2d echocardiogram was suggestive of reduced ejection fraction (35%) with global hypokinesia leading to the diagnosis of heart failure with reduced ejection fraction. A loading dose of dual antiplatelet and statins (tab aspirin 300 mg, tab clopidogrel 300 mg and tab atorvastatin 80 mg) was given to the patient prior to coronary angiography.

Coronary angiography was done and a triple vessel coronary artery disease was diagnosed as shown in Figure 1. A subclavian puncture was taken to look for a subclavian artery considering the claudication symptoms of the patient and peripheral vascular disease was diagnosed with bilateral subclavian artery stenosis as shown in Figure 2. Considering the severity of claudication pain in our case, bilateral renal and femoral arteries were also checked via aortic flush and bilateral renal artery ostial stenosis was seen, as shown in Figure 3, while the femoral arteries appeared normal bilaterally.

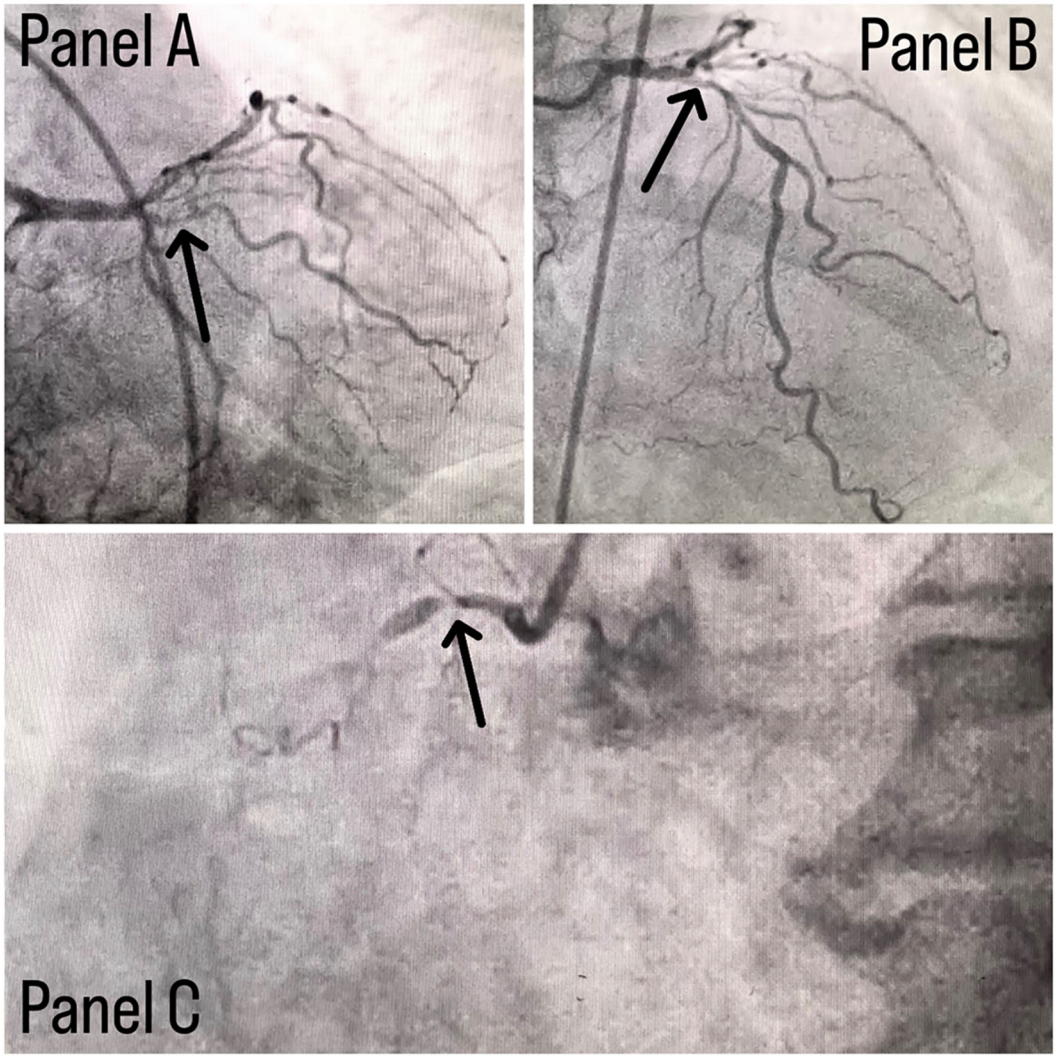

Figure 1. Panel A shows stenosis in proximal LCX with a black arrow, panel B shows stenotic lesion in proximal LAD with a black arrow and panel C shows 100% stenosed RCA with a black arrow.

On further blood investigations, raised homocysteine levels (75 mcmol/L with normal range of <15 mcmol/L), C - reactive protein (CRP) (6 mg/dL with normal range of <0.3 mg/dL) raised total cholesterol (400 mg/dl with normal range of <170 mg/dl) with Low density lipoprotein (LDL) (140 mg/dl with normal range of <100 ng/dl) with raised triglycerides levels (754 mg/dl with normal range of <200 mg/dl) were observed. On renal function test, raised serum creatinine (8.6 mg/dl) with a reduced estimated glomerular filtration rate (GFR) of 40ml/min/1.72sq.metre which was suggestive of stage III chronic kidney disease. cANCA and pANCA with dsDNA and ANA antibodies along with lipoprotein(a) were also evaluated to rule out vasculitis and inherited atherosclerotic risk factors which were found to be negative. The ankle-brachial index (ABI) for upper limbs was 0.4 and lower limb ABI was 0.7 (normal range of 0.9-1.4) which was suggestive of peripheral vascular disease. A CT Aortogram was also done and was not suggestive of aortoarteritis.

A final diagnosis of atherosclerotic triple vessel coronary artery disease with severe peripheral artery disease with bilateral renal artery stenosis was made. The patient was advised coronary artery bypass grafting and was referred to cardiovascular thoracic surgery department for further management with dual antiplatelets and statins (tablet aspirin 75 mg one tablet once daily, tab clopidogrel 75 mg one tablet once daily and tab rosuvastatin 20 mg one tablet once daily at night to be continued), beta blockers (tab metoprolol succinate 25 mg one tablet twice daily to continue) and other supportive treatment with a goal target blood pressure of 120/80 mm of hg and target low density lipid of less than

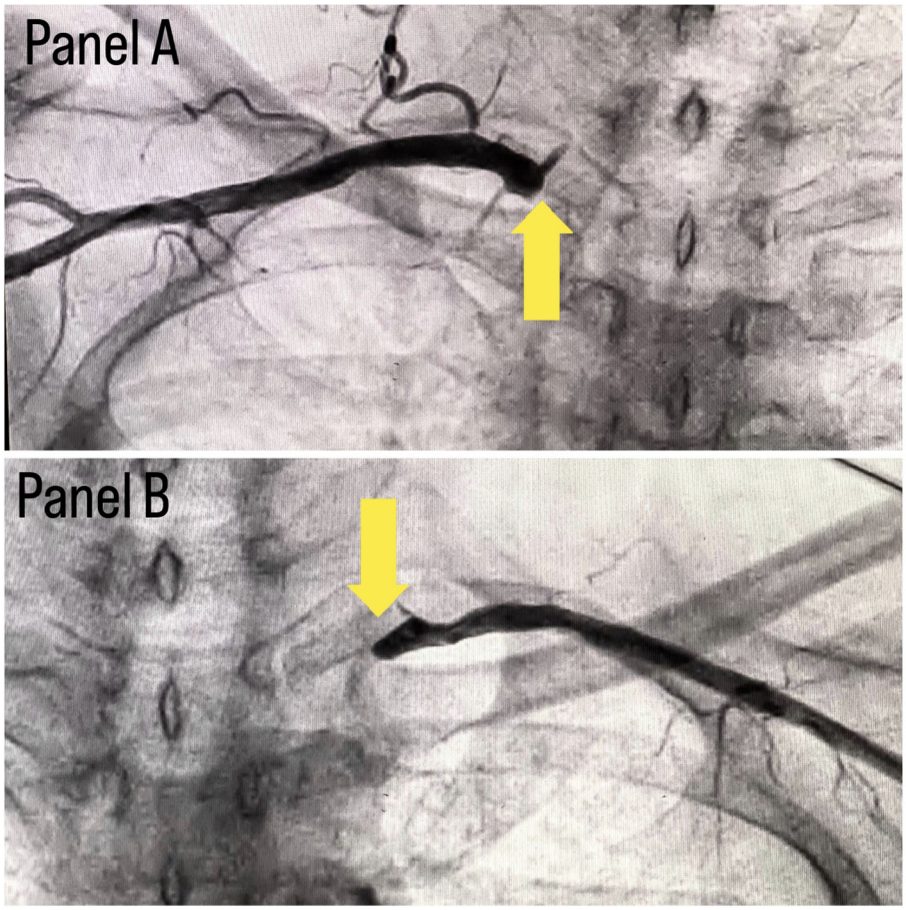

Figure 2. **Panel A shows right subclavian stenosis and panel B shows left subclavian stenosis.**

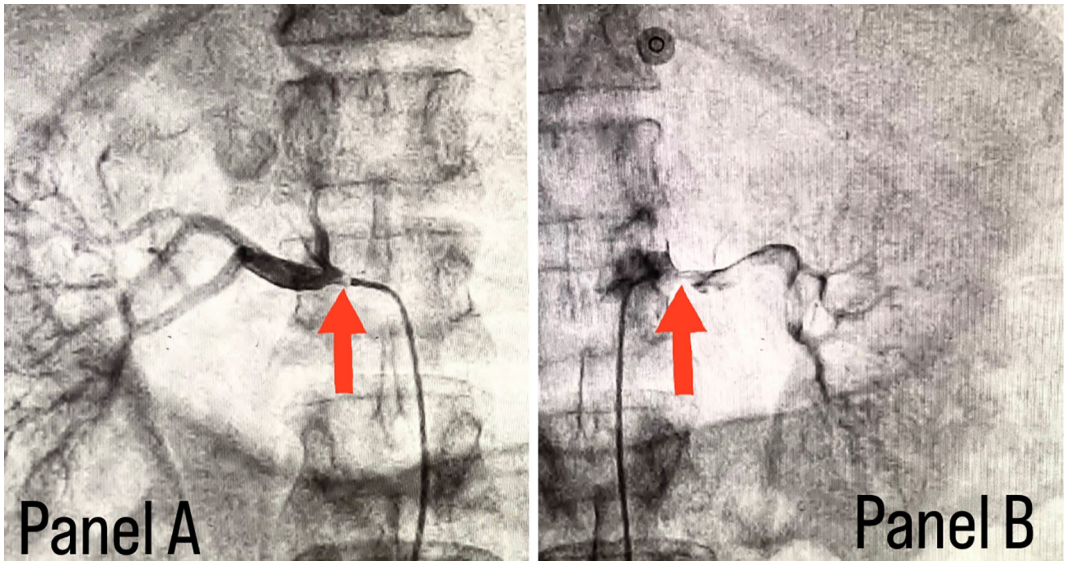

Figure 3. **Panel A shows right renal ostial stenosis and panel B shows left renal ostial stenosis marked with red arrows.**

70 mg/dl. Further endovascular intervention for bilateral subclavian artery and renal artery stenosis was considered and advised to the patient but was not willing for the same and the patient failed to follow up.

Discussion

Atherosclerosis and coronary artery disease are responsible for a significant number of global fatalities, primarily attributed to myocardial infarction and congestive heart failure.[6] Atherosclerosis evolves due to repetitive damage to the inner lining of blood vessels and the buildup of lipids over time.[6] Renal artery stenosis (RAS) frequently occurs as a complication of atherosclerosis and is often connected to chronic heart failure.[7] RAS in individuals suffering from CHF may encompass certain clinical features like high blood pressure, deterioration of CHF symptoms, sudden pulmonary oedema, and declining kidney function.[7] Renovascular disease often lacks noticeable symptoms, but it can manifest as hypertension, gradual impairment of kidney function, and a significant increase in serum creatinine levels. Other potential clinical presentations may include atheroembolic disease, proteinuria, sudden pulmonary oedema, and chronic heart failure (CHF).[8] Peripheral arterial disease, which arises from insufficient blood flow, typically affects the entire cardiovascular system rather than solely the lower extremity blood vessels. Patients displaying symptoms of peripheral arterial disease should undergo an evaluation to assess their risk of atherosclerosis.[9] In its milder form, peripheral arterial disease may only cause intermittent claudication, characterized by pain in the lower extremities during physical exertion that subsides at rest. However, when ischemia becomes chronic, critical, or acute, it significantly heightens the risk of gangrene, tissue death, amputation, and premature death.[9]

In individuals with peripheral vascular disease, renal artery stenosis is frequently observed and is associated with a high mortality rate. Nevertheless, it remains uncertain whether incidentally discovered renal artery stenosis is a risk factor for mortality.[10]

Different methods, both invasive and non-invasive, can be employed to study atherosclerotic plaques. These methods include intracoronary optical coherence tomography, intravascular ultrasonography, ultrasonography, CCTA, and magnetic resonance imaging. Patients with peripheral arterial atherosclerosis affecting two to three regions, has a significant rate of prevalence for cardiovascular risk and coronary artery disease (CAD).[11]

Coronary angiography, which remains the gold standard for identifying coronary stenosis, may be required. In recent years, there has been a revived interest in developing new technologies, leading to the expansion of the clinical use of coronary computed tomography angiography (CCTA).[12] CCTA, when combined with fractional flow reserve measurement (FFR), offers valuable details for patients having intermediate stenosis.[12] This FFR is a measurement that compares the total amount of blood flow in a tapered vessel to the maximum flow threshold in an ordinary vessel.

While non-invasive imaging techniques like brightness-mode USG and magnetic resonance imaging of the heart are utilized to assess early indications of atherosclerosis, they do not offer a comprehensive assessment of the arteries.[13] Traditional coronary angiography and imaging for myocardial perfusion also have limitations when it comes to depicting atherosclerosis, particularly in their early phases or if the condition is well-established but still did not yet compromise the stability of the arterial lumen through positive remodelling. Prophylactic and progressive management via implementing lipid lowering regimen is essential to control and manage these conditions.

Conclusion

Peripheral vascular disease and renal artery stenosis had been found to be associated with one another in more cases than reported. Peripheral vascular disease individually as well as in conjunction with renal artery stenosis present a high risk of death due to cardiovascular disease. Therefore, further emphasis must be given to detailed investigation of all cases of peripheral vascular diseases and renal artery disease for any other associated abnormalities to provide prompt treatment so as to reduce mortality and morbidity in such patients. Early diagnosis of dyslipidemia and the literature depicting the severity of such dyslipidemic conditions causing multiple atherosclerotic lesions in synchrony should create awareness among health care individuals and early treatment measures including lifestyle modifications should be considered to avoid such drastic events. There were very few published studies regarding atherosclerotic triple vessel coronary artery disease with severe peripheral artery disease with bilateral renal artery stenosis in the literature research done for this particular case report. Thus, the identification and publication of such unique reports are equally important to add to the knowledge of medical professionals.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

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PubMed Abstract | Publisher Full Text

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Open Peer Review

Current Peer Review Status: ✔ ✔

Version 3

Reviewer Report 15 February 2024

https://doi.org/10.5256/f1000research.161756.r240439

✔ **Daniel Sykora**
Mayo Clinic School of Graduate Medical Education, Scottsdale, USA

The authors have addressed the outstanding concerns satisfactorily.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: inflammatory cardiomyopathy, cardiac sarcoidosis, peripheral artery disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 19 January 2024

https://doi.org/10.5256/f1000research.160282.r233751

? **Daniel Sykora**
[1] Mayo Clinic School of Graduate Medical Education, Scottsdale, USA
[2] Mayo Clinic School of Graduate Medical Education, Scottsdale, USA

Thank you to the authors for revising their manuscript. Major noted changes in the case presentation include greater specificity in the history and physical exam, notably now denoting how acute limb ischemia was ruled out which is a key factor in this patient's management. The

authors now sufficiently detail the evidence used to diagnose NSTEMI, as well as present transthoracic echocardiogram data to show the patient has new HFrEF due to ischemic cardiomyopathy. The timeline of events is more clear with sequential description of NSTEMI treatment. The conclusion of the case, in respect to management of the CAD as well as recommendations for management of the other arterial stenoses is now sufficiently clarified. The grammar is now globally improved throughout the text.

Regarding the discussion, the first paragraph now more appropriately focuses on the systemic manifestations of atherosclerosis.

There are two more statements in the discussion which warrant revision:

"In our study, we discovered that patients with peripheral arterial atherosclerosis affecting two to three regions of atherosclerosis, along with coronary stenosis exceeding 50 per cent and high to very high scores of cardiovascular risk, had a significant rate of coronary artery disease (CAD)." -- this sentence cites a 2013 study (Cohen et al.,(2013))[Ref-1]and refers to it as "our study", however there are no common authors between this case report and the cited study in JACC Cardiovascular Imaging. If there are no shared authors, I recommend removing the implication that the cited study was performed by the authors.

"We discovered that patients exhibiting plaque vulnerability had significantly elevated levels of LDL-C and total cholesterol." -- it is unclear if this sentence is intended to indicate the authors' reflections on the implications of this current manuscript, or if it is referencing another study by the authors. If the situation is the former, I would recommend removal or rewording of this statement as this case report only reports on a single patient. If the case is the latter, the authors should cite the study they are referring to in this sentence.

References

1. Cohen GI, Aboufakher R, Bess R, Frank J, et al.: Relationship between carotid disease on ultrasound and coronary disease on CT angiography.*JACC Cardiovasc Imaging*. 2013; **6** (11): 1160-7
PubMed Abstract | Publisher Full Text

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: inflammatory cardiomyopathy, cardiac sarcoidosis, peripheral artery disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 24 Jan 2024

Saket Toshniwal

Respected sir,

Thank you for reviewing my article.
The discussion has been revised as instructed. Kindly review.

Thank you.

Competing Interests: No competing interests were disclosed.

Version 1

Reviewer Report 15 December 2023

https://doi.org/10.5256/f1000research.148532.r227820

Daniel Sykora
[1] Mayo Clinic School of Graduate Medical Education, Scottsdale, USA
[2] Mayo Clinic School of Graduate Medical Education, Scottsdale, USA

Toshniwal et al. present a case of a 60-year-old male with hypertension and nicotine use evaluated for angina and upper extremity claudication. Initial evaluation is concerning for cardiac and upper extremity ischemia, and objective evaluation with laboratory and electrocardiography raises concern for NSTEMI. Upon undergoing angiography, he is found to have multivessel coronary artery disease, bilateral subclavian and renal artery stenoses. Ankle brachial index studies also revealed PAD with poorly compressible arteries in the lower extremities. Given the severity of his CAD, the patient is referred for bypass grafting and started on medical management with dual antiplatelet therapy, statin, ACE inhibitor, and beta blocker.

The strengths of this case report include a highly detailed presentation of a patient with multifocal atherosclerosis. The case is interesting and uncommon presentation of multivessel CAD, bilateral upper extremity arterial disease, and bilateral renal artery stenosis. The authors also include high quality angiogram images that add value to the case. This case is an important reminder to all clinicians that atherosclerosis often involves multiple arterial territories.

The weaknesses of the case report include significant omitted details regarding the history, physical examination, and objective findings. The timeline of the patient's management is also unclear. The final outcome of the case (outcome of CABG, decisions regarding intervention for his other stenoses) are omitted. Most importantly, much of the discussion appears unrelated to the case report and focuses on CCTA and FFR and implies that this text is a study, instead of a case report. Due to these concerns, the case presentation and discussion both require crucial substantial revisions, and all the above should be addressed to make this case scientifically sound. The text would also benefit from extensive grammatical and stylistic editing.

Introduction:

1. The authors use the terms "peripheral artery disease" and "peripheral vascular disease"

intermittently in the text. While these terms are often used interchangeably, the authors should use one term only for clarity.

2. The summary statement of the case at the end of the introduction fails to mention the bilateral subclavian artery stenosis, which is an important finding in the setting of upper extremity claudication.

Case presentation:

1. The past medical history of the patient is described but baseline medications are not mentioned. It would be valuable to know if the patient was taking antihypertensive medications at baseline and the degree of control of hypertension, as treatment refractory hypertension is a common manifestation of renal artery stenosis, which is later diagnosed in this patient.
2. The acuity of the chest pain is not mentioned. Given the clinical concern later mentioned in the case report for NSTEMI, the acuity and time course of the chest pain should be described.
3. Likewise, the time course of the upper extremity claudication symptoms should be described, as should the presence/absence of lower extremity claudication symptoms (especially given later confirmed lower extremity PAD with poorly compressible arteries).
4. The patient is described as having NYHA Class III heart failure symptoms, but the text does not mention if assessment of his cardiac function was later performed. If investigated, the authors should describe if the patient had heart failure and how this was diagnosed, especially since the discussion of this paper extensively mentions CHF.
5. The authors should mention whether the patient had cerebrovascular symptoms given the possibility of vascular steal syndromes in the setting of later discovered subclavian artery stenosis.
6. The “general” and “systemic cardiovascular examination” sections should be combined into a single physical examination section, especially since the current “general examination” section details pulse examination.
7. The authors describe “cold pulseless upper extremities with blackish discolouration of distal upper limbs” and note absence of “axillary, brachial and radial pulses.” These initial physical exam findings are concerning for acute limb ischemia. The authors should describe how acute limb ischemia was ruled out (e.g. were pulses subsequently detected via Doppler assessment?).
8. The authors should use the term appropriate medical terminology “cyanosis” as opposed to “blackish discolouration” when describing their physical exam findings.
9. The word “electrocardiograph” should instead read “electrocardiogram.”
10. The description of the ECG should be more detailed, at minimum including description of which leads showed ST segment depressions and T wave inversions. If space permits, the ECG should be added as a figure.
11. The authors mention the ECG results are concerning for NSTEMI. As NSTEMI diagnosis necessitates the presence of dynamic cardiac biomarkers, this should be rephrased to “suggesting acute myocardial ischemia.”
12. The paragraph which begins with “On routine blood investigations…” requires significant revision. In the prior paragraph, the authors mention their suspicion for NSTEMI based on ECG results. Therefore, this paragraph should focus on the initial laboratory investigations pertinent to the concern for NSTEMI that would have informed immediate management decisions, namely cardiac biomarkers. The authors mention the CK-MB and troponin I, but do not mention whether these biomarkers were trended over time and whether dynamic changes were observed. This is crucial to know to confirm the diagnosis of NSTEMI. The

patient's creatinine and estimated GFR should be mentioned in this paragraph, given the later diagnosed bilateral renal artery stenosis.

13. CK-MB and troponin I reference ranges should be mentioned.
14. The timeline of the other studies mentioned (homocysteine, CRP, cholesterol, vasculitis labs, ABI, CT aortogram) in relation to the coronary angiogram is unclear. If the authors were concerned for NSTEMI, the timeline of angiography after admission should be made clear. If other studies were pursued later in the care of this patient, they should be mentioned later in the text. If the concern was for NSTEMI, the priority of these studies seems lower than coronary angiogram so it is confusing to present them earlier in the text.
15. If the patient was diagnosed with NSTEMI, the management prior to angiography should be described. Did the patient receive loading doses of aspirin, clopidogrel, or start on a heparin infusion? These details should be mentioned.
16. The ABI should be described for both extremities.
17. The authors are correct in stating that ABI > 1.4 is suggestive of peripheral artery disease, but this finding is usually seen in poorly compressible arteries due to chronic kidney disease or diabetes mellitus, as opposed to atherosclerotic lower extremity PAD. Whether the patient had these comorbidities should be mentioned.
18. The repetition of the figure descriptions for Figure 1,2, and 3, (e.g. description of arrows) in the text is redundant and can be removed.
19. The results of the femoral artery angiography are not mentioned in the text and should be added.
20. The degree of multifocal atherosclerosis seen in this patient at his age is impressive, and it would be helpful to mention whether he had any family history of early coronary artery disease or whether any laboratory testing for inherited atherosclerosis risk factors (e.g. Lipoprotein(a)).
21. The sentence "Multiple severe atherosclerotic stenotic lesions in synchrony at multiple sites is what makes it a unique presentation" should be removed from the case presentation as this section should focus on presentation of objective data regarding this case as opposed to author interpretation, which should be reserved for the discussion.
22. The abbreviations "CAD-TVD" and "CVTS" are not defined elsewhere in the text and should be either defined or removed (preferably, as there are not universally recognized abbreviations).
23. Generic medication names should be used (aspirin and clopidogrel) instead of trade names for ease of readability.
24. The specific type of metoprolol used should be specified (e.g. Metoprolol tartrate).
25. Based on the history provided, the patient had evidence of (at least) severely symptomatic chronic bilateral upper extremity limb ischemia. Was endovascular intervention for the subclavian artery stenoses considered? If not, was surgical revascularization later considered or pursued?
26. Likewise, the rationale behind pursuing medical management only (as opposed to stenting) for the renal artery stenosis should be mentioned.
27. The outcome of the case, including the outcome of CABG and need for any subsequent procedures, should be added.
28. The blood pressure and cholesterol target goals for this patient should be mentioned since the patient was started on statin and antihypertensive therapy.

Discussion:

1. The term "heart attacks" in the first paragraph should be replaced with more appropriate

medical terminology: “myocardial infarction.”
2. The first paragraph focuses on the relationship between RAS and heart failure, but this patient was never diagnosed with heart failure. This should be either removed, or the patient’s diagnosis of heart failure should be clarified in the case presentation section.
3. This discussion does not fit the content of the case presentation. For example, consider the sentence: “In our study, we discovered that patients with peripheral vascular atherosclerosis (PVA) affecting two to three regions of atherosclerosis, along with coronary stenosis exceeding 50 per cent and high to very high scores of cardiovascular risk, had a significant rate of coronary artery disease (CAD) as found by CCTA.” This sentence appears unrelated to the case report as CCTA is not mentioned in the case presentation. A large portion of the discussion also focuses on CCTA and FFR, which is not relevant to the case and was not used in the diagnosis of this patient, who proceeded directly to coronary angiogram.
4. In the last paragraph of the discussion, the sentence “We discovered that patients exhibiting plaque vulnerability had significantly elevated levels of LDL-C, total cholesterol, uric acid, and triglycerides in their serum” is also unrelated to the case presentation.

Is the background of the case’s history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
No

Is the case presented with sufficient detail to be useful for other practitioners?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: inflammatory cardiomyopathy, cardiac sarcoidosis, peripheral artery disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 01 Jan 2024

Saket Toshniwal

Respected sir,

Thank you for reviewing my article and adding your valuable inputs.
The article has been revised according to the instructions and they are as follows

Revisions:

Introduction

1. The interchangeable terms 'peripheral artery disease' and 'peripheral vascular disease' have been rectified and only one term has been used i.e; 'peripheral artery disease'
2. 'Subclavian artery stenosis' has been added to the introduction section.

Case presentation

1. Past history of the patient has been revised and more detailed past history has been added to the text with comment on degree of control of hypertension .
2. Acuity of chest pain has been added along with description of chest pain and time course
3. Time course of the upper extremity claudication symptoms has been added with comment on lower limb claudication symptoms.
4. Heart failure was diagnosed on 2d echocardiogram and this has been added to the text.
5. The patient had no neurological deficits or any cerebrovascular symptoms which has been added to the text.
6. General and systemic examination sections have been combined.
7. Acute limb ischemia was diagnosed via doppler assessment after clinically suspecting it. This has been added to the text.
8. 'Blackish discolouration' has been replaced with 'cyanosed' while describing physical examination.
9. 'Electrocardiograph' has been replaced with 'electrocardiogram'
10. ECG has been described in details as instructed
11. NSTEMI rephrased as "acute myocardial ischemia' as instructed
12. The paragraph starting with "On routine blood investigations..." has been revised and structured as instructed. Cardiac biomarkers has been mentioned before routine investigations which lead to the diagnosis of NSTEMI. Also, serum creatinine and estimated GFR have been mentioned in subsequent paragraphs.
13. Reference range for CKMB and TROP-I have been mentioned
14. The timeline of the study in the article has been revised as instructed and cardiac biomarkers and cardiac evaluation following coronary angiography have been mentioned at first.
15. Management prior to angiography has been added.
16. ABI for both extremities have been mentioned.
17. ABI has been revised and mentioned in the text.
18. The repetition of figure description in the text has been removed.
19. Results of femoral artery angiography has been added.
20. Inherited atherosclerotic factors (Lipoprotein a) has been ruled out, with non significant family history's been added to the text.
21. The sentence " multiple severe atherosclerotic stenotic lesions in synchrony at multiple sites is what makes it a unique presentation" has been removed from case presentation section.

22. Abbrevations such as CAD-TVD and CVTS has been removed.
23. Generic medication names has been used.
24. Specific type of metoprolol detail has been added
25. "Endovascular intervention was considered and advised to the patient but were not willing for the same" added to the text.
26. Renal artery endovascular stunting was advised but the patient was not willing for the same.
27. Outcome of the case couldn't be tracked as the patient failed to maintain follow up. This has been added to the text.
28. Target blood pressure and cholesterol levels have been mentioned.

Discussion:

1. "Heart attacks" have been replaced with "myocardial infarction"
2. The patient was diagnosed to have heart failure with reduced ejection fraction which has been added in the case presentation section.
3. The sentence "In our study, we discovered that patients with peripheral vascular atherosclerosis (PVA) affecting two to three regions of atherosclerosis, along with coronary stenosis exceeding 50 per cent and high to very high scores of cardiovascular risk, had a significant rate of coronary artery disease (CAD) as found by CCTA" has been removed. CCTA and FFR though not used in the diagnosis of our case has been given importance in the discussion section in view of advancement in diagnosis with newer modalities and to shed light upon the literature related to it for the practitioners.
4. The sentence in the last paragraph has been revised.

Kindly review the revisions made.
Thank you

Yours sincerely,
Dr. Saket Toshniwal

Competing Interests: No competing interests were disclosed.

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I must congratulate the authors on a well written case report with relevant information about the existing literature and good discussion points.

The topic under consideration is very important and highlights the need of screening patients with PAD for CAD/coronary stenosis as well, the ABI has been a good tool for the same.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Non communicable diseases , Diabetes mellitus , CAD , NAFLD , medical education , Echocardiography

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.