Author’s response to reviews

Title: Lower respiratory tract infection and rapid expansion of an abdominal aortic aneurysm: A case report

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Author’s response to reviews: see over
Dear Editor-in-Chief

We thank the Editors and Reviewers for their hard-work, thorough analysis and comments on this manuscript.

Outlined below is each comment and how we have adjusted the manuscript.

Reviewer 1

Comment 1

‘If one assumes that the patient was symptomatic upon presentation, then this would explain the reason for the rapid expansion and rupture of the aneurysm. This possibility was not addressed in the case report’.

Response to reviewer and action taken:

We have acknowledged that this could represent a symptomatic aneurysm in the text. However, the overall clinical impression was that the patient’s symptoms and signs were due to a lower respiratory tract infection (hypoxia, sepsis and CT confirmed lobar pneumonia). In addition the CT aortogram showed neither a leak nor a rapid increase in size of the aneurysm. Again this has been clarified in the text.

‘However, the tenderness in the epigastrium was a concern and could represent either a symptomatic aneurysm or referred pain from the lobar pneumonia. Thus, the patient was closely observed and the pneumonia treated aggressively with intravenous antibiotics, supplemental oxygen and physiotherapy.’
Comment 2

‘Could the rapid expansion of the aneurysm sac have been a consequence of a mycotic aneurysm? The authors need to explore the possibility of a mycotic aneurysm in the discussion of the case report.’

Response to reviewer and action taken:

This has been addressed and discussed as follows:

‘There is a documented association between ongoing pulmonary sepsis, aortic aneurysms and dissection [5,14]. This has been more commonly reported in thoracic than abdominal aortic aneurysms. However, haematogenous seeding may also effect the abdominal aorta, if there is no contiguous focus of infection [6]. The expansion and change in fat around the AAA found on the repeat CT aortogram suggested inflammation or an impending leak. In the case presented here, it is not clear whether this represented a mycotic AAA. However, the fusiform nature of the pre-existing AAA and lack of air in sac do not support a mycotic AAA. Regardless, there is controversy regarding the use of endovascular approaches in such aneurysms, however there are several reports which actually show better outcomes when compared to conventional surgery in these high risk cases [15].’
Comment 3

‘The patient follow time was also not addressed in the discussion. If we assume that
the patient had a mycotic aneurysm, patient follow up is of up most importance since
the use of EVAR to treat mycotic aneurysms is still controversial.’

Response to reviewer and action taken:

Patient follow-up time has now been addressed. In addition, as suggested by reviewer
1 that our case may represent a mycotic aneurysm, the use of EVAR in treating
mycotic aneurysms has been discussed and supporting references inserted:

‘The patient was followed up clinically at 4, 5 and 7 months postoperatively. CT
scans at 1 and 6 months postoperatively showed good stent position and patency.’

‘In the case presented here, it is not clear whether this represented a mycotic AAA.
However, the fusiform nature of the pre-existing AAA and lack of air in sac do not
support a mycotic AAA. Regardless, there is controversy regarding the use of
endovascular approaches in such aneurysms, however there are several reports
which actually show better outcomes when compared to conventional surgery in these
high risk cases [15].’

Comment 4

‘The discussion needs to be more complete and needs to consider alternative
presentations and treatment methods for this patient’.

Response to reviewer and action taken:
Our tertiary institution offers both open and endovascular repair of aneurysmal diseases. An urgent but thorough discussion was held between the anaesthetists, endovascular radiologists, vascular surgeons and the patient. An endovascular approach appeared more appropriate as a measure to reduce the increased pulmonary risks associated with an open repair in this case and achieve haemodynamic stability. The risk of bacterial spread and graft infection was attenuated by the administration of targeted intravenous antibiotics for a protracted time period. At clinical and radiological follow-up no evidence of graft infection has been detected.

We have re-written the discussion to include all the comments made by reviewer 1 including exploring the possibility of haematogenous seeding and mycotic aneurysm and have explained our choice of EVAR in this case.

'The expansion rate of AAAs varies according to numerous factors. Guidelines suggest 6-12 monthly assessment with an abdominal ultrasound [7]. In small AAAs with a size of 3.0-3.9 cm growth, the growth rate has been reported as an average 0.11 cm annually [2]. AAAs with a diameter of between 4.0-4.9 cm have been found to have a much larger rate of growth with an average rate of 0.79 cm per year in those with continuous expansion compared to 0.27 cm per year with discontinuous (staccato) expansion [3]. Thus the typical expansion rate is about 0.25 cm per annum; however, if the aneurysm diameter increases by 0.4-0.8 cm per year more frequent surveillance is required [7]. The probability of rupture of a 5 and 7 cm AAA is less than 16% and 25% per year respectively [8]. AAA expansion varies individually and inflammation can influence this process and dramatically accelerate AAA expansion as a result of specific cellular immune responses [9,10].
In the case presented here, the AAA had increased in size by ~0.3 cm per annum until admission. In the presence of concomitant sepsis it suddenly expanded. In the wall of an AAA there is up-regulation of pro-inflammatory IL-1β, IL-6 and TNF-α, which have been shown to positively correlate with aneurysm growth [11,12]. Such cytokines, chemokines and growth factors are known to be further potentiated during septic events such as LRTI [13]. One possibility is that concomitant sepsis could increase these specific inflammatory mediators within the AAA wall further weakening the aortic wall, increasing the risk of expansion and rupture.

There is a documented association between ongoing pulmonary sepsis, aortic aneurysms and dissection [5,11]. This has been more commonly reported in thoracic than abdominal aortic aneurysms. However, haematogenous seeding may also effect the abdominal aorta, if there is no contiguous focus of infection [6]. The expansion and change in fat around the AAA found on the repeat CT aortogram suggested inflammation or an impending leak. In the case presented here, it is not clear whether this represented a mycotic AAA. However, the fusiform nature of the pre-existing AAA and lack of air in sac do not support a mycotic AAA. Regardless, there is controversy regarding the use of endovascular approaches in such aneurysms, however there are several reports which actually show better outcomes when compared to conventional surgery in these high risk cases [15].

Comment 5

‘Could this patient have undergone an open operation? What did the aneurysm neck look like on initial CT presentation?’
Response to reviewer and action taken:
The case report section has been re-written to further emphasize the decision-making process in this case and the aneurysm neck size has been stated. In addition, the coronal image of the 7.0 cm aneurysm now demonstrates the measurements at the aneurysm neck.

‘Despite aggressive treatment of the patient’s pneumonia, he remained hypoxic. The options were either an emergency open bifurcated aortic graft or an endovascular aorto-uni-iliac repair with a femoral-to-femoral cross-over procedure. Following a full discussion with the patient, anaesthetists and the endovascular radiologists the latter was performed. The patient had an uncomplicated post-operative recovery.’

‘The neck of the aneurysm did not show any significant angulation and its juxta-renal diameter was 22.1 mm increasing to 25.4 mm in its infra-renal segment. In addition, there was stenosis of the left common iliac artery.’

Reviewer 2

Comment 1

‘This case report is well written and should be of interest to vascular surgeons and chest physicians’.

Comment 2
‘If the authors claim an association between pulmonary sepsis and rapid expansion of the aortic aneurysm, this should be indicated in the abstract, as should their summary statement to monitor such patients.’

**Response to reviewer and action taken:**

This has now been modified.

‘The case highlights the potential association between pulmonary sepsis and rapid AAA expansion. In such cases, a policy of frequent monitoring should be adopted to identify those patients requiring definitive management.’

**Comment 3**

‘What evidence to the authors have to indicate that the rapid expansion was related to the pulmonary sepsis rather than simply evolving rupture?’

**Response to reviewer and action taken:**

This has been further highlighted and discussed in the Discussion section.

‘In the case presented here, the AAA had increased in size by ~0.3 cm per annum until admission. In the presence of concomitant sepsis it suddenly expanded. In the wall of an AAA there is up-regulation of pro-inflammatory IL-1β, IL-6 and TNF-α, which have been shown to positively correlate with aneurysm growth [12,13]. Such cytokines, chemokines and growth factors are known to be further potentiated during septic events such as LRTI [14]. One possibility is that concomitant sepsis could
increase these specific inflammatory mediators within the AAA wall further weakening the aortic wall, increasing the risk of expansion and rupture.’

Comment 4
‘Why was an aorto uni-iliac rather than a bifurcated endovascular repair done?’

Response to reviewer and action taken:
Aorto uni-iliac was performed as there was stenosis of the distal common iliac on one side and this is highlighted in the text.

‘In addition, there was a significant stenosis of the left common iliac artery.’

Comment 5
‘Figures 1 & 3 should include the measurement marker to confirm an increase from 6.1cm to 7.1cm.’

Response to reviewer and action taken:
We have included these measurements and markers inserted into the figures.

Reviewer 3
Comment 1
‘There is little in the report other than temporal association to suggest cause, and other
studies have documented "staccato" aneurysm growth in 65% of aneurysms followed
over time even without obvious known stresses’.
‘Molecular biological explanations, though interesting, are not particularly compelling.’

**Response to reviewer and action taken:**

Staccato growth patterns are now discussed, as is the sudden growth pattern in this case in the discussion. This is to highlight that the sudden expansion seen in this case was indeed associated with other factors such as the concomitant sepsis. In addition molecular explanations have again been discussed.

‘In small AAAs with a size of 3.0-3.9 cm growth, the growth rate has been reported as an average 0.11 cm annually [2]. AAAs with a diameter of between 4.0-4.9 cm have been found to have a much larger rate of growth with an average rate of 0.79 cm per year in those with continuous expansion compared to 0.27 cm per year with discontinuous (staccato) expansion [3]. Thus the typical expansion rate is about 0.25 cm per annum; however, if the aneurysm diameter increases by 0.4-0.8 cm per year more frequent surveillance is required [7]. The probability of rupture of a 5 and 7 cm AAA is less than 16% and 25% per year respectively [8]. AAA expansion varies individually and inflammation can influence this process and dramatically accelerate AAA expansion as a result of specific cellular immune responses [9,10].’

‘In the case presented here, the AAA had increased in size by ~0.3 cm per annum until admission. In the presence of concomitant sepsis it suddenly expanded. In the wall of an AAA there is up-regulation of pro-inflammatory IL-1β, IL-6 and TNF-α, which have been shown to positively correlate with aneurysm growth [12,13]. Such cytokines, chemokines and growth factors are known to be further potentiated during
septic events such as LRTI [14]. One possibility is that concomitant sepsis could increase these specific inflammatory mediators within the AAA wall further weakening the aortic wall, increasing the risk of expansion and rupture.’

**Editorial requests**

‘Please restructure your abstract into the following three sections: Introduction, case presentation and conclusion’.

**Response to request and action taken:**

We have now restructured our abstract.

We hope that the above replies to the reviewer comments satisfy the requirements, if not please let us know. In anticipation of your response.

Yours sincerely,

Dr Steven Naylor  
Dr Zakareya Gamie  
Mr Ravinder Singh Vohra  
Dr Sapna Puppala  
Mr Patrick J. Kent  
Professor D. Julian A. Scott