Reviewer's report

Title: Localizing chronic Q fever: a challenging query

Version: 1 Date: 12 May 2013

Reviewer: Michael Marks

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This is an interesting article reporting data on a relatively large and well described cohort of patients with chronic Q-Fever. The authors’ data on the use of PET scanning in localisation of lesions is helpful in characterizing this challenging to diagnose infection and adds to the limited data available. The main weakness is the studies retrospective nature and the significant variation in the diagnostic workup that patients underwent which is likely to have influenced the study findings. Despite this the central premise of the authors argument, higher than anticipated rates of vascular/graft infection can be found using PET/CT, is of value to the medical community.

Major Compulsory Revisions

1) Methods: Study design and patients
Patients were recruited based on PCR >1 month / serology >3 months after the acute episode – but large numbers of patients did not have symptomatic acute Q-Fever. How was the timing of onset of acute Q fever determined in patients without a symptomatic episode? This point also related to Table 1 in the calculation of time from episode of acute Q-Fever.

2) Methods: Imaging studies
It would be helpful to have more information on how the PET/CT scans were reviewed and classified as “helpful”. Was a single radiologist responsible for this at each centre? Were the original reports used for this study or were images specifically re-reviewed as part of this work? If the latter was the reviewer blinded to the other clinical data? What cut-off of metabolic activity was taken to be indicative of a site of infection?

3) Result: Proven Chronic Q-Fever Paragraphs 2+3
What percentage of PET+VE lesions were confirmed via PCR/Tissue. Of sites where tissue/fluid was PCR postive (paragraph 2 of this section) what percentage of these lesions were also PET positive.

4) Results: Proven Chronic Q-Fever Paragraph 4
How was death from chronic Q-fever defined and what was the presumed mechanism of death? It would be of interest (although not essential for the manuscript) to know if post-mortems were performed in these cases and if material was PCR positive/showed histological evidence of ongoing Q-Fever.
5) Results/Discussion:
The authors rightly comment that many patients did not undergo a full diagnostic workup. Did you find evidence that once a localization was established further tests were not have been carried out?

6) Results and Discussion (para 4 in particular)
The relatively low sensitivity of PET (33-75%) for IE has been noted in other settings (refs below). A reliance on PET+VE as proof of localisation may have reduced yield especially given the relatively low rates of TEE in the study group and lack of tissue samples. Do the authors consider that many patients may have had two sites of infection – valve + graft/aneurysm – which may have been missed due to reliance of PET and lack of TEE?


Minor Essential Revisions

7) Methods: Study design and patients
Are the authors aware of what percentage of all patients seen with culture-negative endocarditis in their 2 units in the study period underwent testing for Coxiellä?

8) Results: Proven Chronic Q-Fever Paragraph 1
No definition is given for valvular dysfunction. What percentage of valvular dysfunction occurred in people with existing valvulopathy

9) Results: Proven Chronic Q-Fever
Of patients with no definite localisation and possible IE what percentage had minor criteria on ECHO? What percentage of possible IE patients underwent TEE? Given the reduced yield with TTE vs TEE this may significantly affect patients final classification – this would also have implications in the probable and possible Q-fever groups.

10) Discussion Paragraph 1+4:
Use of PET scanning is increasing. Have the authors considered that the higher rate of diagnosis of vascular infections may simply reflect you doing more PET than previous studies.

Discretionary Revisions
None
Minor issues not for publication

11) Results: Proven Chronic Q Fever: paragraph 4 – “3 of whom have been treated for more/greater than 18 months”

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests