Author's response to reviews

Title: Spontaneous Splenic Rupture: Deciphering the Infectious Causes

Authors:

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Version: 5
Date: 3 September 2014

Author's response to reviews: see over
Reviewer's report

Title: Spontaneous Splenic Rupture: Deciphering the Infectious Causes

Version: 1 Date: 28 June 2014

Reviewer: Thomas Martin

Which of the following best describes what type of case report this is?: Other

If other, please specify: Diagnostic difficulty in a case of ASR

Has the case been reported coherently?: No

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: No

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:
Reviewer comments:

Background

1. Presentation usually with LEFT, not right, upper quadrant tenderness. Thank you for reviewing our manuscript and taking the time to give such extensive feedback. We have corrected our mistake of RUQ to LUQ as was also seen in this case

2. No reference for common aetiologies
We have now updated this oversight
3. No reference for management options  
We have now corrected this oversight

4. Is vaccination required in cases of conservative management? Not clear in text.  
We have now clarified this point

5. Are the orloff-peskin criteria used in reality? If they are, does the case presented fulfill the definitions for ASR?  
Indeed, the Orloff and Peskin criteria isn’t one which all physicians use on a routine basis but as it is stated, it is a set of criteria that can be employed. In this case, we would argue that 3 of the 4 criteria are met as the 4th require a pathological sample, which this patient did not require.

6. Background too long as introduction – brief background of relevance of ASR then present case then discuss is preferred.  
The background has been made more concise

Case

1. ‘The patient is employed a communications director’ – Correct English usage  
We have now corrected this oversight

2. Do patients ‘endorse’ high-risk sexual behaviours?  
This is a common word used in this context in North America. We have revised the sentence to make it clearer for the reviewer.

3. Examination findings – what region was the abdomen tender? Rebound tenderness? Peritonism? What does ‘significant abdominal tenderness’ mean?  
As the patient did not require urgent surgery, she did not have a surgical abdomen – typically this would include lack of peritonism or rebound tenderness. We have made this sentence clearer.

4. Readers will not be familiar with grade of splenic rupture – what does grade III mean?  
Grade 3 injury is described in the text. We have now also included the detailed description of the grade 3 injury as described in the CT report in the figure legend.

5. Please include comment on size of spleen.  
We have now included this information

6. ‘full infectious diseases work up’? What does this mean?  
This was explained with the subsequent sentences describing the infectious disease work up and their results.

7. ‘followed closely by general surgery’? Is this required?
Yes as patients with splenic rupture can exhibit signs of hemodynamic compromise at any point due to acute blood loss. In such an event, general surgery will need to perform a splenectomy to stop blood loss.

8. Explain EBV serologies in text
The significance of EBV serologies is discussed in the discussion

9. Caution with acronyms that readers may not be familiar with
We have updated the acronym list.

10. Can you provide original CT scans?
Typically, only representative images from CT scans are included in case reports due to size limitations.

Discussion

1. 1st paragraph – is the commentary on how well the case was managed informative to the reader?
As with most case reports, the purpose is to demonstrate how one unique case was managed and what could be learned from the success and mistakes. As such, how the case was managed in context of ultimate patient outcomes is in our minds informative and fundamental to all case reports.

2. 2nd paragraph - Does cat-scratch disease explain the patient’s symptoms? URTI, chills, coryza, sore, sore throat, cough and SOB? I think this may confuse readers.

If CSD is the cause, then the patient could have had a separate URTI infection entirely unrelated to the cat bite.

3. 2nd paragraph – antibiotics are unproven in reducing duration of symptoms in B. henselae infection. They might reduce size of lymphadenopathy. Please consult infection treatment guidelines and reference.

There are no treatment guidelines or standard references that is agreed upon by any international infectious disease societies. In fact, treatment of immunocompetent adults remains a controversial topic. However, most experts in the field do feel that in the setting of disseminated disease (i.e.: liver, spleen, eye or CNS involvement) as this patient potentially had, antibiotics is indicated given the risk of life-threatening complications.

4. Are there recent diagnostic guidelines? 1:128 is likely to be equivocal. Also as unchanged over 3 months does this show no recent infection?

As mentioned in the text, the diagnostic guidelines were met and the citation is given. In particular, the diagnostic criteria set out by the CDC is met (titres greater than 1:64).
5. Does this show assay interference? Reference. Could this be residual antibody from resolved infection years previously? The Bartonella IFA assay is somewhat known for the possibility of false positives as commented upon elsewhere in the paper and as pointed out by the other reviewers of this paper. It is possible that this represents a previous infection but again, little can be concluded from the titres given that there is no standard kinetic of IgG or IgM serology that this can be compared against. In fact, in one study of 30 different individuals with CSD, 45 very distinctly different IgG and IgM serological kinetics were documented. Not everyone had positive IgM serology (Bergmans AM et al. J Clin Microbiol. 1997).

6. Was IgM antibody performed against B. henselae? No. Available standard Bartonella testing from the Public Health of Ontario does not include IgM.

7. EBV history not mentioned in case report? 2 previous episodes of infectious mononucleosis? How were these diagnosed? Recurrent/reactivated EBV is rare – what evidence do we have in this lady? As these episodes occurred more than 30 years ago, this history was gathered from the patient. She does not remember further details of how this was diagnosed.

8. Can you explain the serologies for EBV. Which of the antibodies tested would be expected to become positive first? What about EBV IgM? EBV IgM was not performed and not done routinely by the public health of Ontario.

9. Penultimate paragraph – there are NO clinical features to suggest CSD. Absence of lymphadenopathy, absence of papule/pustule at inoculation site, endocarditis, retinitis, CNS findings. Agreed. This is clearly stated in the penultimate paragraph. “Although the history of a cat bite and clinical improvement after initiation of targeted therapy against Bartonella henselae is consistent with the diagnosis of ASR secondary to Cat Scratch Fever, the Bartonella serologies were inconclusive.”

10. The clinical presentation is more consistent with EBV – prominent pharyngitis 3 weeks prior to ASR, of which EBV is a common cause. This is atypical of EBV because, as this reviewer has stated above, recurrent or reactivation of EBV is quite rare.

11. Failing EBV and CSD are there other potential explanations? Mycoplasma, q-fever, acute HIV (was PCR performed?), was CMV IgM performed? Blood cultures were negative, HIV ELISA test was negative and both CMV IgM and IgG were negative.

12. Are infectious aetiologies rare with ASR? I think they account for over 25% of ASR. Indeed, they do account for 23% of causes of ASR. We have taken out the word “rare” from the last paragraph.
Overall:

1. The paper is too long. The text needs to be more concise.
2. There are numerous unreferenced statements that are often factually incorrect.
3. The structure of the paper makes it difficult to follow.
4. The overall intention of the paper is unclear – is it a description of a rare cause of ASR (ie B. Henselae) or is it a description of a difficult diagnostic case? If the latter there needs to be a much clearer description of the approach to a patient with the symptoms and signs that this patient had combined with ASR.
5. The case description is lacking in details regarding the spleen – pathological specimens and radiological findings.

The overall comments have been addressed individually above.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Reviewer's report

Title: Spontaneous Splenic Rupture: Deciphering the Infectious Causes

Version: 1 Date: 8 July 2014

Reviewer: James Winearls

Which of the following following best describes what type of case report this is?: Unexpected or unusual presentations of a disease

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes
Is there any missing information that you think must be added before publication?: No

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

A well written paper with a good, concise, relevant review of the possible aetiology of atraumatic splenic rupture.

My only comments regard tidying up the abstract a bit.

Thank you for your kind words. The abstract has been made more concise.

"etiology can oft times be difficult" - slightly odd sentence construction.

"sudden atraumatic splenic rupture in the absence of trauma" - double negative as atraumatic splenic rupture clearly happens in the absence of trauma.

These sentences have been revised as per reviewer suggestions.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Declaration of competing interests: I declare that I have no competing interests

Reviewer's report

Title: Spontaneous Splenic Rupture: Deciphering the Infectious Causes
The authors describe an otherwise healthy woman who presented with spontaneous splenic rupture. An extensive workup was significant for homogeneous hepatosplenomegaly with mild liver function impairment. Seroconversion to EBV was noted, in addition to a low-positive IgG to Bartonella sp.

The paper is well written and is of some interest to the general medical community.

My comments follow:
1. Splenic rupture typically presents non-specifically with left (rather than right) upper quadrant abdominal tenderness

Thank you for your kind comments. You are correct about the LUQ tenderness as was seen in the case. The mistake in the background section has now been corrected.
2. Cat Scratch Disease is characterized by granulomatous inflammation in the spleen, with characteristic CT findings of disseminated hypodense areas within the splenic parenchyma. However, these were not the CT findings in this case, and the authors may wish to address this issue in the discussion.

With this suggestion in mind, we have addressed this issue in the discussion.

3. The authors may want to add a Methods section specifying the details of the serology assays. This pertains to both the Bartonella serology which is notoriously problematic, as well as to the EBV early antigen (Diffuse or Restricted?) antibody that was positive. This is a great suggestion and here, we are clearly see evidence of how Bartonella serology can hinder proper diagnosis. The Bartonella henselae serological test used in this paper is the standard indirect fluorescent antibody (IFA) test offered by the Ontario Public Health department. The limitation of this test is that there is considerable cross reactivity from other Bartonella species. As for the EBV testing, the Public Health Ontario Laboratories uses the qualitative detection of EBV VCA IgG, EBV VCA IgM, EBV EA IgG and EBV EBNA IgG antibodies with a qualitative chemiluminescent immune assay test. We have included this information in a supplementary Methods section.

4. For seroconversion in general, and for a potentially small change (anti Bartonella antibodies in this case) in particular, a simultaneous assay of the two sera in parallel is required.

This is a valid point. However, we did not have the option of doing this as the patient was positive at presentation

5. Transthoracic ECHO (why capital?) was negative for "signs of bacterial endocarditis", or for "a vegetation".

This has now been clarified in the text

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Declaration of competing interests: I declare that I have no competing interests
Title: Spontaneous Splenic Rupture: Deciphering the Infectious Causes

Version: 1 Date: 9 August 2014

Reviewer: Mark K Huntington

Which of the following best describes what type of case report this is?:
Other

If other, please specify: Review of unusual condition (not new), prompted by clinical encounter

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

Useful review of an uncommon condition; especially valuable is the authors' discussion of clinical management in the presence of diagnostic uncertainty (a common situation in primary care) in the penultimate paragraph.

Suggestions for improvement:
BACKGROUND paragraph 2: can be made more concise - redundant with Table 1 data, no need to repeat in text unless there is a reason for special emphasis.

Thank you for your kind comments. Paragraph 2 of the background section has been edited as suggested.
BACKGROUND paragraph 3: please include citations for recommendation on sports avoidance in splenic rupture and vaccination in context of splenic rupture (without splenectomy).

We have revised this paragraph to expand on the evidence and recommendations behind long term management of ASR patients.

CASE paragraph 2: consider changing "does not endorse" to "denies"... many do not endorse such activities, yet engage in them, and some endorse them without engaging in them.

This is a valid point. The text has been revised to clarify this point.

CASE final paragraph: malaria is mentioned in table 1 but not in infections ruled out in the workup. As one of the authors is from Africa, it is not clear where the patient originated...comment on malaria may be quite relevant.

This was a Caucasian patient with no previous history of travel to Africa. As such, malaria was not prominent in our differential. Her racial background and travels has now been clarified in the case.

DISCUSSION paragraph 1: Table 1 doesn't really address "speedily manage and stabilize"; consider changing to read "As seen in Table 1, the causes for ASR are varied. A multi-disciplinary approach..."

We have now revised the sentence in light of this suggestion.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Declaration of competing interests: I declare I have no competing interests