Author's response to reviews

Title: Pancreatitis and myocarditis followed by pulmonary hemorrhage, a rare presentation of leptospirosis- A case report and literature survey

Authors:

Nuwan Ranawaka (nuwan rk@gmail.com)
Vijayabala Jeevagan (jeevaganv@yahoo.com)
Panduka Karunanayake (pandukaru@mail.com)
Saroj Jayasinghe (sarojoffice@yahoo.com)

Version: 3 Date: 27 December 2012

Author's response to reviews: see over
27th Dec 2012

Dr. Philippa Harris, PhD
Executive Editor
BMC-series Journals
BioMed Central

Dear Dr. Philippa Harris

Sending the revised manuscript of “Pancreatitis and myocarditis followed by pulmonary hemorrhage, a rare presentation of leptospirosis- A case report and literature survey”:

MS: 1428781764786316

Thank you very much for reviewing the article and for the suggestions to improve the manuscript. We thoroughly addressed all the concerns raised by the referees and revised the manuscript accordingly.

Responses to the specific comments of referees are attached herewith.

We would be grateful to you, if you could review the revised manuscript and consider the responses to the comments.

Thank you for your kind assistance.

Kind Regards,

Nuwan Ranawaka
University Medical Unit,
National Hospital of Sri Lanka.
Response to the comments of referee 01

Minor essential revisions-

01) “The finding of tachypnea would mean...”-
   The statement is changed as “Tachypnoea was the only abnormality detected on the respiratory examination while the precordial examination was normal.”

02) “The statement about no bleeding manifestation...”-
   The statement is changed as “The hemoglobin level dropped from 13 g/dl to 8 g/dl with the pulmonary hemorrhage and the platelet count dropped from 125000 to 20000 /mm3.”

03) “Pulmonary hemorrhage in combination with pancreatitis in leptospirosis was reported previously by Daher et al...”
   The core theme of our report is about the presentation of leptospirosis as acute pancreatitis then developing other complications. This would raise several diagnostic and management problems.
   In a clinical setup, when a patient presents with acute pancreatitis alone as in this case, the etiological diagnosis of leptospirosis might not be considered in the initial work-up because of the rarity. Later the patient may develop multi-organ failure due to leptospirosis, yet those might be attributed to the multi-organ involvement of acute pancreatitis. Ultimately the etiological diagnosis may get delayed compromising the optimum management. This important aspect is highlighted in our report.

   But in the report of Daher et al. the diagnosis of pancreatitis was mainly made with the histology at the autopsy. Only 3 out of 13 patients have undergone serum amylase level and only 2 patients have had levels more than three times upper normal value. Importantly it is not known at which point of clinical course (whether on presentation or later) they developed the features (clinical or biochemical) of pancreatitis. Thus the above mentioned issues which arise in the clinical management were not addressed in that report.

   The statement is changed as “Pulmonary hemorrhage in combination with pancreatitis in leptospirosis was reported only once previously by Daher Ede F. et al(2003) yet it was not known at which point of clinical course the pancreatitis was developed.”
01) Renal functions of the patient...

The patient was clinically well hydrated on admission. Blood pressure was 110/70 mmHg at presentation. On admission serum creatinine and electrolytes were normal. His blood pressure dropped to 80/60 mmHg at 8 hrs. after the admission. But it was normalized within 1 hour with dopamine infusion. Thereafter he did not develop hypotension throughout the hospital stay. Dopamine infusion was tailed off within 8 hrs.

Central venous pressure (CVP) monitoring was started once he was intubated and before he was recognized to have oliguria and to have deteriorated renal functions. The initial CVP was 10 cm H2O and thereafter it did not drop below that value at any point. The patient was not oliguric during the first 2 days despite the initial episode of transient hypotension. During the 3rd day he gradually developed oliguria with rising serum creatinine level. The latter part of the 3rd day he underwent the hemodialysis. Hemodialysis was offered twice to the patient until the stabilization of renal function and then urine output and the serum creatinine was gradually normalized.

Following statements are added. “The patient was not oliguric during the first 2 days despite the initial episode of transient hypotension which developed 8 hrs after the admission. After recovering from the initial hypotensive episode within 1 hr, he was normotensive, normovolemic with normal CVP throughout the hospital stay. During the 3rd day he gradually developed oliguria with rising serum creatinine level. The latter part of the 3rd day he underwent hemodialysis. Hemodialysis was offered twice to the patient until the stabilization of renal function and then urine output and the serum creatinine was gradually normalized.”

Was the rapid deterioration of his renal function caused by unrecognized 3rd space losses secondary to his pancreatitis?

The patient developed renal failure while he was normotensive and was having normal CVP level suggesting a normal intra-vascular volume. Additionally urinalysis revealed proteinuria of 300 mg/dl and hematuria of 100 per high power field which suggested a renal pathology. Therefore renal failure was less likely to be due to 3rd space loss.

A statement is added. “Proteinuria and hematuria suggested an intra-renal pathology as the aetiology of renal failure. Further, normal CVP level at the time of renal failure ruled out the possibility of hypovolemia or 3rd space loss in pancreatitis being the aetiology.”
Leptospirosis is known to cause multi-organ failure.

Pancreatitis is very rarely associated with leptospirosis and only 21 English articles in the PUBMED database have reported such an association to-date. Further, pancreatitis as a presenting problem was recognized only in 7 reports. (1)

Thus in a clinical setup, when a patient presents with acute pancreatitis alone as in this case, the etiological diagnosis of leptospirosis might not be considered in the initial work-up because of the rarity. Later the patient may develop multi-organ failure due to leptospirosis, yet those might be attributed to the multi-organ involvement of acute pancreatitis. Ultimately the etiological diagnosis may get delayed compromising the patient’s optimum management. Therefore the clinicians, especially in endemics, should well be aware of such presentation. This case highlights the above diagnostic challenge which we faced.

Additionally this case is unique as it is the first ever report of leptospirosis presenting with acute pancreatitis and myocarditis then developing diffuse pulmonary hemorrhages. There was only one report in the literature recorded the combination of pancreatitis and pulmonary hemorrhages added with arrhythmias on ECG. (2) But in that report the diagnosis of pancreatitis was mainly made with the histology at the autopsy. Only 3 out of 13 patients have undergone serum amylase level. Importantly it is not known at which point of clinical course they developed the features of pancreatitis.

Thus this is the first report of leptospirosis presenting with acute pancreatitis and myocarditis then complicated with pulmonary hemorrhages to the best of our knowledge.

This report not only highlights the diagnostic problem but also raises a management issue.

There is conflicting evidence for the routine usage of antibiotics in acute pancreatitis. Guidelines do not recommend routine prophylactic antibiotics currently until further evidence is available. (3, 4) But if the etiology is leptospirosis, there is clearly a place for antibiotics. When acute pancreatitis becomes the presenting problem of leptospirosis, the problem arises since the clues for leptospirosis may be lacking on clinical grounds. Leptospira serology is not performed in each and every patient who presents with pancreatitis especially in resource poor settings where the disease is endemic. Further the routine blood cultures and the culture of pancreatic aspirate would be negative in that instance influencing the decision for antibiotics negatively.

Therefore this case highlights several diagnostic and management problems related to this rare presentation of leptospirosis.
Following statements are added.

“In a clinical setup, when a patient presents with acute pancreatitis alone as in this case, leptospirosis might not be considered as an aetiology in the initial work-up because of the rarity. Later the patient may develop multi-organ failure due to leptospirosis, yet those might be attributed to the multi-organ involvement of acute pancreatitis. Ultimately recognition of leptospirosis might get delayed compromising the optimum management.”

Conclusion is changed.

“Leptospirosis should be considered in patients presenting with pancreatitis which can be complicated with myocarditis and diffuse pulmonary hemorrhages. It should not be mistaken as idiopathic pancreatitis though the clinical presentation and complications would be the same.”

Reference

1. References of the manuscript No. 3, 8-13


Response to the comments of referee 03

We agree with Dr. Vedat Turhan regarding the pancreatic involvement in leptospirosis.

Following statements are added to the discussion.

“Though the recognized incidence of pancreatitis in leptospirosis is infrequent, in reality pancreatic involvement may be more common. Under-recognition could be due to several reasons. Pancreatic involvement could be subclinical or clinically hidden when there are dramatic and rapidly dynamic alterations of clinical and biochemical parameters take place in multi-organ dysfunction in leptospirosis. Thus a clinician may find it difficult to identify each and every complication such as pancreatitis, acalculous cholecystitis, cerebral venous thrombosis and myositis.

Additionally in a clinical setup, when a patient presents with acute pancreatitis alone as in this case, leptospirosis might not be considered as an aetiology in the initial work-up because of the rarity. Later the patient may develop multi-organ failure due to leptospirosis, yet those might be attributed to the multi-organ involvement of acute pancreatitis. Ultimately recognition of leptospirosis may get delayed compromising the optimum management.”

Reference
