Author's response to reviews

Title: Successful resolution of symmetrical peripheral gangrene after severe acute pancreatitis: a case report

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Object: MS: 1192638481595160- Symmetrical Peripheral Gangrene after fulminant acute pancreatitis

Dr. Chen-Yi Liao et al
Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comments

Answer and response to the reviewers

Review from Deepak Gunjan
**Suggestion 1.**

1. Was any evidence of chronic pancreatitis in this patient? As, this patient had two previous attacks of pancreatitis.

*Answer:* The patient denied steatorrhea, maldigestion or recent body weight loss which excluded possible chronic pancreatitis.

**Suggestion 2.**

2. How the severity of acute pancreatitis calculated (revised Atlanta classification should be used for assigning severity)

*Answer:* According to the revised Atlanta classification, the patient was classified as suffering from severe acute pancreatitis due to persistent organ failure (profound shock lasting for more than 48 h and acute kidney injury with oliguria status post emergent hemodialysis).
Suggestion 3.

How long aspirin and pentoxiphylline was prescribed and in what doses, any recommendations?

The patient was administered two doses of oral aspirin 75 mg/day and two doses of oral pentoxifylline 400 mg/day which lasted for 20 days.

Suggestion 4.

4. Authors don’t mentioned about the vasopressors used for patients in clinical details (as mentioned in abstracts)? Was peripheral gangrene is due to vasopressors toxicity?

Answer: Though high dose vasopressor treatment related to SPG is well described in the literature [8], norepinephrine administered to our patients was at a suboptimal dose and was only used for a brief period (2 days) which did no correlate with the timeline of SPG, which developed 2 days after discontinuation of the vasopressor. Thus, we believe acute pancreatitis in our case was highly associated with the occurrence of SPG.
Suggestion 5.

Was he investigated for coffee-ground vomitus?

Answer: Upper gastrointestinal (GI) panendoscopy was conducted because of vomitus of coffee ground material and revealed Mallory-Weiss tear and acute gastric ulcer with a history of recent hemorrhage.

Suggestion 6.

6. Any information regarding follow-up visits?

Answer: The patient has responded well to the previous treatment and regained normal daily activity during his outpatient follow-up.

Suggestion 7.

1. How the diagnosis of disseminated intravascular coagulation was made?

(This patient had normal platelets, normal PT and aPTT and elevated fibrinogen levels. D-dimers can be elevated in sepsis and any hospitalized patients.)

Answer: The patient had elevated D-dimers which compatible with sepsis but not fulfill the criteria of DIC. I had made modification in the manuscript.

His coagulation profile was consistent with septic shock with elevated D-dimer levels.
and initial central venous pressure recorded as 4 mmHg. A diagnostic screen for sepsis showed unremarkable blood culture results.

**Suggestion 8** Was heparin was considered to treat this patient? If not, why?.

Because of upper gastrointestinal tract bleeding noted on admission, heparin was not considered.

Review from Jayanta Samanta

**Reviewer's report:**

**Suggestion 1.**

Patients vitals like presenting blood pressure, CVP

Use of vasopressors, dose, type, duration

Diagnostic screen for sepsis

Type of fluid and amount of fluid administered, monitoring of the parameters

**Answer:**
His initial vital signs revealed a blood pressure of 74/27 mmHg, a heart rate of 152 beats per minutes, and a body temperature of 38.7°C. His clinical picture was compatible with severe sepsis. CVP level was 4mmHg.

Diagnostic screen for sepsis showed unremarkable blood culture results.

He was treated promptly and aggressively with intravenous fluids with normal saline.

His intravenous fluids were given via bolus of 20 mL/kg, followed by a maintenance rate of 3 mL/kg per h, and he was also prescribed analgesic for pain relief.

**Suggestion2.**

The abstract and the main text have many discrepancies as mentioned in the review comments

Answer: I had made some revision in the main text to be compatible with the abstract.

**Suggestion3.**

Major changes needed

In the abstract section, it has been mentioned in the “case presentation” section that “The cyanosis and gangrene did not resolve in spite of tapering the vasopressor” but now here in the original case description is there any
mention of the use of vasopressor, the type or the dose of the same or when was it tapered.

Answer: I had modified the text with the detail of vasopressor use.

Because of profound shock with poor response to fluid resuscitation, a vasopressor was administered with intravenous norepinephrine at an infusion rate of 4 mcg/min for 2 days through the central venous line and discontinued after his blood pressure was restored.

And in the discussion part

In the present case, we collected laboratory data which did not resemble DIC. Though high dose vasopressor treatment related to SPG is well described in the literature [8], norepinephrine administered to our patients was at a suboptimal dose and was only used for a brief period (2 days) which did no correlate with the timeline of SPG, which developed 2 days after discontinuation of the vasopressor. Thus, we believe acute pancreatitis in our case was highly associated with the occurrence of SPG.

Suggestion4 Authors have described “aggressive conservative management”, but the
nature of which is not clear: regarding the fluid volume status at presentation (central venous pressure etc.) and the amount of fluid resuscitation given. It is clear from the lactic acidosis (lactate level 5.75 mmol/L and high anion gap acidosis) that patient had hypoperfusion and yet there is no mention of the presenting blood pressure or CVP.

Answer:

His initial vital signs revealed a blood pressure of 74/27 mmHg, a heart rate of 152 beats per minutes, and a body temperature of 38.7°C. His clinical picture was compatible with severe sepsis. CVP level was 4mmHg.

Suggestion 5

c. As per table 1, under DIC profile, the authors have interpreted it as “Coagulation profile were consistent with IC. (Table1)” (page 5, line 17).

However, as per the ISTH diagnostic scoring system for DIC (ref: Levi, M; Toh, C-H et al. (2009). "Guidelines for the diagnosis and management of disseminated intravascular coagulation". British Journal of Haematology 145 (5): 24–33)) and the values on table 1, the score is
maximum 3, i.e. <5 and hence not compatible for overt DIC.

Answer: Instead of DIC, the clinical picture and coagulation profile are much compatible with acute pancreatitis and septic shock.

I had modified the content in the manuscript.

**Suggestion6**

d. In the abstract section, authors have mentioned “… … alcohol-related severe acute pancreatitis, who presented with severe sepsis and intractable vomiting”. However, in the actual case description or in table 1, no definite evidence of sepsis has been provided sans the WBC count of 14,000/µL which can very well be explained by it being part of SIRS, commonly seen in patients of acute pancreatitis in the 1st week of illness.

Answer: His initial vital signs revealed a blood pressure of 74/27 mmHg, a heart rate of 152 beats per minutes, and a body temperature of 38.7°C. His clinical picture was compatible with severe sepsis. Though with WBC of 14,000/µL.
Thus, in the absence of a definite evidence of DIC or sepsis and the possible use of vasopressor, the development of SPG can be well explained by vasopressor use, which is very well described in literature, rather than as a sequelae of acute pancreatitis, which the authors have proposed to be the first case report.

Answer:

His initial vital signs revealed a blood pressure of 74/27 mmHg, a heart rate of 152 beats per minute, and a body temperature of 38.7°C. His clinical picture was compatible with severe sepsis.

In the present case, we collected laboratory data which did not resemble DIC. Though high dose vasopressor treatment related to SPG is well described in the literature [8], norepinephrine administered to our patients was at a suboptimal dose and was only used for a brief period (2 days) which did not correlate with the timeline of SPG, which developed 2 days after discontinuation of the vasopressor. Thus, we believe
acute pancreatitis in our case was highly associated with the occurrence of SPG.

**Suggestion 8**

f. Finally, there is total discrepancy in the “Conclusion” mentioned in the abstract from the “conclusion” derived at the end of discussion, which needs to be addressed.

**Answer: I had addressed the conclusion in the abstract and added it in the final conclusion.**

**Suggestion 9**

There are multiple spelling mistakes and grammatical errors in sentence framing that needs to be modified.

**Answer: I had seek for English specialist for help with corrected grammatical errors and spelling mistakes.**