Peer Review File

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Reviewer A

In this study the authors describe the case report of an African American male with rhabdomyolysis. The levels of creatine kinase are remarkable. This is an important case study towards the better understanding of rhabdomyolysis etiology.

I do however have some comments and suggestions. First could the authors verify if any of the nearly unbelievable CK values were duplicated? i.e. not a measurement error? This reviewer would also appreciate further explanation of the insistence on 'without acute kidney injury' claim. It appears there are symptoms of both kidney dysfunction, as well as function. More information on urine output and myoglobinuria during the hospital stay would be helpful. While urine output is provided for day 2, what about the other 5 days? Trends noticed? Kidney function appears to rely on BUN/creatinine ratio only after IV treatment, yet the patient reported myoglobinuria prior to admittance. Also, the continued rise in CK, AST, and ALT from day 1 to 3 without further injury by itself suggests kidney dysfunction (see refs below). Indeed, BUN increases 50%, so while not reaching the binary definition of 'failure' levels, this suggests some level of injury appears to be occurring to allow values to continue to this unprecedented record. Relying on blood marker standards for kidney injury may not apply to individual cases such as this. Indeed, this case study may contribute to a better understanding of kidney function than relying on a measure that is not specific to rhabdo.

https://pubmed.ncbi.nlm.nih.gov/32205993/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3971360/

Below are some specific points.

• There are a number of miss-capitalizations throughout, such as Creatine, Intravenous, Thyroid, Normal, Bicarbonate, (ex L70) etc…

• There are a number of missing spaces between words (ex L57), and between numbers and units (as in L72), and typos (ex L132 – 'information').

• Can more information be provided on the previous occurrence of rhabdomyolysis? How long before? CK levels? Trigger?

Reply

Daily CK levels were done as mentioned but no rechecks everyday. The highest CK level did correlate with the day pt had worsening symptoms with worsening electrolyte derangements. We have relied on standard definitions of acute kidney injury which per kdigo guideline is as follows

The KDIGO guidelines define AKI as follows :

●Increase in serum creatinine by ≥0.3 mg/dL (≥26.5 micromol/L) within 48 hours, or

● Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days, or

Urine volume <0.5 mL/kg/hour for six hours

missed capitalizations will be addressed (line 67 page 5 bicarbonate, line 69- thyroid

- missed space between words Line 57 (bolus and) and Line 72 (4.5 mg/dl), Line 132 (information) have been corrected

Unfortunately no prior information was available regarding his prior episode of rhabdomyolysis which was 2 years ago and in different state and city. Per pt report he was told that it was due to "dehydration"

CHANGES IN TEXT:

Capitalizations, spacing , spelling errors have been corrected

Added information about the fact that no prior hospitalization records available from previous episode.

Reviewer B

These authors have reported a case in which a young man developed extremely high CK levels following a minor trauma when he fell on his buttocks. The patient required hospitalization for 6 days and received a large volume of intravenous fluid. The peak creatinine kinase level was 4,570,630. The peak creatinine level was 0.9. The peak potassium level was 6.2. An extensive laboratory investigation did not reveal any medical disorder which might predispose him to a severe episode of rhabdomyolysis.

2. The authors indicate that the patient was referred to a specialist and had a muscle biopsy. They should include the results of that biopsy in the case summary.

3. Did the authors measure CK isoenzyme levels in this patient? They did measure aldolase level and it was normal. This seems peculiar and they should add some comment in the discussion as to how this patient had such severe muscle injury but normal aldolase levels.

4. Is it possible that laboratory testing was faulty in this case because of an unknown interfering chemical? Is it possible that the use of marijuana or vaping contributed to this unusual clinical presentation?

Reply: 1) yes thank you for the comment

2) Unfortunately while referral was placed, follow up didn't happen so biopsy never materialized (page 6 , Line 90)

3) CK MB was measured and it was 17.8. Aldolase is glycolytic pathway enzyme that is found in all tissues but predominantly in skeletal muscle, liver, and brain. While increased aldolase levels are not as specific or sensitive for muscle disease as CK levels, aldolase concentrations are occasionally elevated in patients with myositis who have normal CK levels . Also vice versa there are case reports of rhabdomyolysis with significant elevated ck with normal aldolase (https://www.the-rheumatologist.org/article/case-report-whats-causing-this-severe-case-of-rhabdomyolysis/3/?singlepage=1)

4) Interesting point about marijuana. There have been some reports with synthetic cannabinoid use. I will add this point to manuscript

CHANGES IN TEXT:

- added CK MB isozyme level

- added a point about synthetic cannabinoid page 11, line 130. Added reference 12

Reviewer C

I'm not sure how this is recurrent rhabdo? Did he have a history prior? Also sickle cell trait - was that done in this case? people with SCT and rhabdo can have counts in the 2 million CK.

Reply: As mentioned in case description Page 4, Line 45- Pt had history of rhabdomyolysis 2 years prior - hence thats why its recurrent rhabdomyolysis.

Page 4 Line 71- as reports hemoglobinopathy eval was normal(that is no HbS was identified).

CHANGES IN TEXT:

NO CHANGE HAS BEEN MADE AS THESE HAVE BEEN ALREADY MENTIONED IN ORIGINAL MANUSCRIPT