Dear Editor and Reviewers:

I really appreciate for your critical comments and insightful suggestions on our manuscript entitled as "Clinical Laboratory Investigation of a Patient with Extreme High D-dimer (55364)". We have carefully and extensively revised our manuscript. All the changes were shown in blue. Please kindly check the revision and we hope it satisfies your standard and could be accepted for publication in ***World Journal of Clinical Cases***.

Best regards
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Reply to Reviewer 1.

Question (Q)1: Authors should clearly understand how many D-dimer tests could be underestimated due to heterophilic antibodies against Epstein-Barr virus?

Answer (A): Thanks for this comment. However, it's a pity that we can't get the precise data through literature study. Now, in the revised manuscript, we describe:

"However, we can't confirm how many D-dimer tests could be underestimated due to heterophilic antibodies against Epstein-Barr virus, which need to be further investigated."

Q2: What is a role of this finding in era of COVID-19

A2: Thanks for this critical comment. It is true as Reviewer suggested that false positive do exist in serological tests for SARS-CoV-2. Now, in the revised manuscript, we describe:

"Caused by SARS-CoV-2, COVID-19 has become a global pandemic. At the time of writing this case, the understanding of the immunologic characteristics of SARS-COV-2 is still relatively scarce. A variety of serological assays were established for detecting SARS-COV-2, such as chemiluminescence assay (CLIA) and colloidal gold immunochromatographic assay (GICA), both are immunoassay. Moreover, some COVID-19 patients demonstrated abnormal antiphospholipid antibodies and coagulopathy consistently. Therefore, heterophilic antibody should be cautious as one of the factors that contribute to interference even to false-positive results."

Q3: Should the lab quality protocols be changed in new reality and how it would be?

A3: Thanks for this comment. Now, in the revised manuscript, we describe:

"In summary, heterophilic antibodies should be considered when an elevated D-dimer value does not conform with the clinical evidence. It's believed that it could be a better method if there is standardization of D-dimer Reagents. But for now, using different instruments and heterophilic antibody blockers could rule out most of the interference."