Review of: "Targeting the Warburg Effect with Glucosodiene: A Case Report of a 43-year-old Female after Mastectomy of the right breast and axillary clearance with Successful First Case Treatment for Metastatic Triple Negative Breast Cancer (TNBC) of Bone"

Juan Valencia[1]

1 Universidade Federal do Rio de Janeiro

Potential competing interests: No potential competing interests to declare.

General comments:

About the abstract:

It is not completely clear and not well written. It does not mention why the Warburg effect was considered as the basis for this study, if there were other publications mentioning that TNBC is highly glycolytic. It seems that was assumed that that tumor is actually glycolytic. That should be mentioned.

In the part of the diagnostic, it mentions twice the word patient, each trait starts with capital letter, and there is a "." in the middle of the sentence ("The case report presents a 42-year-old female patient with TNBC Patient with MRM, Modified radical mastectomy, With axillary clearance., exhibiting a right breast lump with lymph node metastasis"). Then it mentions that is negative for receptors, and that is redundant as this is a TNBC. It is not clear what the author means when says "no signs of cellular activity".

About the main text:

Here is mentioned that TNBC displays the Warburg effect, but there are not references.

In the first paragraph of the background, I would rather mention first the approach to dissolve cancer cells from within, and then mention that glucosodiene has that property.

Whenever the author refers to glucose metabolism, mentions "known as the Warburg effect". That has been already mentioned, thus I would use either glucose metabolism, or Warburg effect.

The pictures of Figure 2 could be better, at least to have the whole view and not cut as the bottom picture is. This is not reasonable for a scientific publication. There is no explanation about upper and bottom pictures separately in the text of the figure.

The "combined digital tomosynthesis, mammography, and breast sonography revealed a spiculated mass in the right

breast with suspicious segmental calcifications" results are not shown, thus add "data not shown".

Arrows in the pictures indicating the findings of Figure 3 would make easier the understanding of the images.

The main text and the text of the Figures (1-5) are exactly the same. This must be changed. Figure 6 has almost the same text than the main one.

In the first paragraph of page 10 a space is required between "pelvic bone" and "but" ("bonebut").

I would place section 2.3 ("Vital indicators prior to treatment") before than section 2.2 ("Therapeutic interventions"), and then keep with the section 2.4.

In the first paragraph of page 12, the enzyme ASGOT (Aspartate Aminotransferase) does not exist. GOT is Glutamate – Oxaloacetate amino transferase. Same with ASGPT (Alanine Aminotransferase). GPT is Glutamate – Pyruvate amino transferase.

In the second paragraph, ALDH is not Lactate Dehydrogenase. LDH is Lactate Dehydrogenase, and there are two isoforms: LDHA and LDHB. Check it.

In the first paragraph of section 2.4, a space is required between treatment on and July (onJuly). Also, in this paragraph, the gene SGOT (Aspartate Aminotransferase) is used, being different from the ASGOT that was mentioned above. None of them exists. At least here, ASGPT is also used, keeping the same name that before, but this gene does not exist. I would say that when the author mentions ALP (Alkaline Phosphates), means alkaline phosphatase. Is this correct? If so, check the name of the gene, ALP does not exist. Same for AGGT (G-Gutamyl Transpeptidase).

In the third paragraph of section 2.4, LDH is different than the previous mentioned. This would be the right version.

In the **Discussion**, this sentence has to be reviewed: "In-vitro study's discussed the role of high glucose environment at different concentrations of zinc and in the presence or absence of insulin or interleukin (something here) ,the study showed that in the presence of insulin resistance". Also, at the end of that sentence, there is a dot needed: "presence of insulin resistance (here the dot) Notably,…"

Also, there is a dot that is not needed in the sentence "Additionally, the relative expression for ZnT1 and ZIP10 reached values well above 20-fold. [5] so the glucose…"

In addition, in the sentence "Then she is followed by our team, The initial five days… ", is the comma the right punctuation sign here? And if so, the capital letter after it is wrong.

In the sentence "Furthermore, even in the presence of oxygen, glucose was digested to create lactate,…", the word digested is not biochemically correct. Perhaps the expression "converted into lactate" is better. Also following this sentence, the expression "giving rise to the phrase aerobic glycolysis" does not sound good. Perhaps "the term aerobic glycolysis was created".

The expression "As the metabolic pathway", which one? There are 123 metabolic pathways related to energetic

metabolism (see DOI: 10.1038/s41598-017-19010-5). This is used twice in the same sentence.

“Disrupting the tumor's glucose metabolism could potentially reactivate the p53 enzyme,…”. This, in tumors with P53 wild type!

As a general comment on the writing, this manuscript needs more work. It has several mistakes of punctuation, and even more with the names of the enzymes. Some of these mistakes could be catch by the auto corrector of Word.

As a general comment about the scientific findings, I would say that the conventional chemotherapy attempted before the glucosediene disrupted several pathways in the tumor cells. Then, the glucosediene increased the cellular stress of these cells, and that affected the cancer cells and the metastatic foci. However, I would keep the glucosediene treatment to keep the selection process of the cancer cells, avoiding (or trying to avoid) the relapse.