Leukemia and Oxidative Therapies Including Intravenous Ascorbic Acid / HDIVC

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A seeming conundrum regarding the ability of some leukemic cells (i.e. CLL) to sequester ascorbate (ASC) has led to confusion regarding the safety and utility of high dose ascorbate delivered via IV (HDIVC). This has led to some apparent confusion between this concern and the apparent positive benefits of HDIVC seen in clinical practice.

As mentioned it is known that CLL cells can sequester ASC and that this may allow them some additional benefit in an oxidant milieu [1]. Added to this information is the data showing that CLL is a polymorphic disorder that likely has a variety of windows of sensitivity to oxidant therapies as well as immunologic resistance to oxidation [2,3].

Case reports from physicians employing HDIVC (such as the author and others) have mostly been either neutral (no response) or positive (stabilization or regression) with respect to CLL. This response variety is common to most cancer types which seem responsive to HDIVC. The likely reason that the dichotomy between earlier basic science concerns regarding ASC and CLL families and the apparent clinical response lies in the sensitivity of these cells to oxidants. As mentioned [1] CLL cells sequester ASC as an apparent antioxidant, but this is not enough redox buffer in the face of oxidative therapies. Two papers [4,5] show that CLL cells are sensitive to H2O2 damage and selective killing. Another paper showed that the use of dual oxidant therapy "(ROS) generating arsenic trioxide (ATO) and ascorbic acid" enhanced Hu1D10-mediated cell death in these cells [6].

UPDATED RESEARCH:

More recent data on the topic have emerged since my first version of this paper and are summarized below. Essentially they give more support for safety of use of vitamin C therapies in leukemia.

A 2018 paper [7] delves deeply into the immunology and tumor biology of vitamin C in inflammatory and cancer progression. It contains some salient points for all cancers and inflammatory conditions (including cancer stem cell activity) showing ascorbate to be critical for modulation of the inflammasome and cancer genome.

Although there is a great deal of data here I will quote the specific portion addressing ascorbate and leukemia and outlining the NEED FOR ascorbate in treating and preventing leukemia. [7]

> "Epigenetic processes regulated by the demethylases are associated with leukaemogenesis and ascorbate availability has been closely linked to this phenomenon. As mentioned above, haematopoietic stem and progenitor cells (HSPCs) accumulate high intracellular concentrations of ascorbate, and this is essential for HSPC differentiation via support of TET2 activity [53]. TET2 inhibition in HSPCs by ascorbate depletion retards differentiation and increases HPSC frequency. TET2 mutations are also known to co-operate with FLT3ITD mutations to cause acute myeloid leukaemia [53]. Ascorbate depletion coupled with FLT3ITD mutations was adequate for leukaemogenesis [53]. It appears then, that ascorbate accumulation within HSCs promotes TET function in vivo, limiting HSPC frequency and suppressing leukaemogenesis. These findings were corroborated in part by another group that described the use of ascorbate as a combination therapy for treating leukaemia [142].

> Patients with leukaemia often have low plasma ascorbate levels [44,47–50] and the capacity for ascorbate to influence the epigenetic drivers of some leukaemias has led to conjecture that increased ascorbate supply may provide clinical benefit to some individuals with leukaemia. Two recent publications have provided support for this hypothesis [143,144]." NOTE – ALL REFERENCES LISTED IN THIS QUOTE ARE CONTAINED IN THE SOURCE PAPER [7]

So again, to underscore the information in the first part of this paper modern tumor biology eliminates the older notions we all had about concern regarding ascorbate and leukemia.

PSEUDO-PROGRESSION:

One reaction mentioned by many clinicians employing HDIVC among other therapies with leukemia and lymphomas is presentation of tumor pseudo-progression. In these cases the patient symptoms and signs may aggravate for one to five weeks in an apparent exacerbation of disease. In most of these cases the patient (if appropriately followed and managed) would have an immune exacerbation which would resolve with no apparent advancement in baseline cancer.

Although pseudo-progression is a known phenomenon in oncology its report in leukemia and lymphoma is largely anecdotal. In the cases of physicians employing HDIVC in these cancers it, though anecdotal, should be reported and patients monitored for this eventuality. It is not a cause to discontinue therapy with HDIVC but rather a potential clinical change to be watchful of.

References:

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